

Feverish illness in children: assessment and initial management in children younger than 5 years

Appendices A – L

National Collaborating Centre for Women's and Children's Health

Commissioned by the National Institute for Health and Care Excellence

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This guideline has been fully funded by NICE. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

Implementation of this guidance is the responsibility of local commissioners and/or providers

NCC-WCH Editor: Karen Packham

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Appendix A Scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1.1 *Guideline title*

Feverish illness in children: assessment and initial management in children younger than 5 years

1.2 *Short title*

Feverish illness in children

2 **The remit**

This is a partial update of 'Feverish illness in children', NICE clinical guideline 47 (2007), available from www.nice.org.uk/guidance/CG47. See section 4.3.1 for details of which sections will be updated. We will also carry out an editorial review of all recommendations to ensure that they comply with NICE's duties under equalities legislation.

This update is being undertaken as part of the guideline review cycle.

3 **Clinical need for the guideline**

3.1 *Epidemiology*

- a) Feverish illness in young children is most frequently caused by self-limiting viral infections. However, some viral infections do lead to more serious illnesses that need support and treatment in hospital. In addition, fever may be a presenting feature of bacterial illnesses such as meningitis, septicaemia, urinary tract infections and pneumonia. Feverish

illness may be associated with a variety of more severe symptoms and signs, such as cough, breathlessness, vomiting, diarrhoea, rash and/or convulsions. Many symptoms and signs are non-specific and may offer no specific clue to the cause of the fever.

- b) Feverish illness in young children is a great concern for parents and carers. It has been reported that 60% of children younger than 12 months in England and Wales have a GP consultation for infection, as do 36% of children aged between 1 and 4 years, and 20% of those aged between 5 and 15 years. It is one of the most common medical complaints presenting to accident and emergency departments.
- c) The introduction of vaccination programmes for *Haemophilus influenzae* type B, meningococcal C and pneumococcal conjugate are likely to have significantly reduced the level of admissions to hospital resulting from associated diseases. For example, early analysis of the pneumococcal vaccination programme in England showed that the incidence of pneumococcal related disease has fallen 38% in children younger than 2 years since vaccination was introduced. However, evidence suggests an increase in the prevalence of disease caused by sub-types of bacteria not covered by vaccination programmes.
- d) Potentially serious cases of feverish illness are likely to be rare, so it is important that information is in place to help healthcare professionals distinguish these from mild cases.

3.2 Current practice

- a) Feverish illness in young children is a diagnostic challenge for healthcare professionals because it is often difficult to identify the cause, and to distinguish between mild or moderate illness and more severe illness. To further complicate assessment and diagnosis, the clinical picture often changes rapidly in young children.
- b) The aim of this guideline update is to revise recommendations on the topics listed in section 4.3.1 in the light of new evidence.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 *Population*

4.1.1 **Groups that will be covered**

- a) Children from birth up to their 5th birthday presenting with a fever that has not been previously diagnosed.
- b) No patient subgroups have been identified as needing specific consideration.

4.1.2 **Groups that will not be covered**

- a) Children already admitted to hospital.
- b) Children with a pre-existing comorbidity for which fever is already covered by an established management plan by their specialist team; for example, cystic fibrosis, immunosuppression, sickle cell disease and cerebral shunts.
- c) Children with recurring fever.
- d) Children diagnosed with tropical diseases.

4.2 *Healthcare setting*

- a) All settings in which care is funded by the NHS.

4.3 *Clinical management*

4.3.1 Key clinical issues that will be covered

a) The predictive value of the following symptoms and signs, alone or in combination, as initial indications of serious illness:

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and other sounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb
- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

If evidence is found on additional signs and symptoms they will added to the above list.

b) The predictive value of heart rate, including:

- how heart rate changes with temperature
- whether heart rate outside the normal range is a sign of serious illness.

- c) The predictive value of pro-calcitonin and/or C-reactive protein markers.
- d) Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease.
- e) The predictive value of the clinical response to paracetamol or NSAIDs.
- f) Effect on fever and associated symptoms of treatment with:
 - paracetamol alone or NSAIDs alone, compared with placebo and with one another
 - alternating paracetamol and NSAIDs strategies, compared with placebo, either drug alone, and taking both at the same time
 - paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone.
- g) Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

4.3.2 Clinical issues that will not be covered

The following areas will not be updated, except for specific parts that relate to the topics in section 4.3.1 and alterations to wording to comply with equalities issues or maintain consistency with areas that have been updated.

- a) Types of thermometers and the site of temperature measurement.
- b) Format of the 'traffic light' system for diagnosis.
- c) Diagnosis of specific illness (outside initial risk assessment as part of the 'traffic light' system).
- d) Management of specific illnesses.
- e) Imported infections.

- f) Tests, management and the use of antibiotics by a non-paediatric practitioner.
- g) Management by remote assessment.
- h) Management by a paediatric specialist.
- i) Advice for home care.

4.4 *Main outcomes*

- a) Mortality.
- b) Morbidity, including symptomatic relief of fever and associated symptoms such as discomfort.
- c) Appropriate disposition (for example, home management or referral to hospital).
- d) Accuracy of diagnosis of serious illness.
- e) Appropriate use of antibiotics.
- f) Parents and carer satisfaction.

4.5 *Economic aspects*

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. In this guideline, the cost-effectiveness of alternative NSAID and paracetamol regimens will be examined, considering both the effect on immediate outcomes (reduction in fever) and longer term outcomes (morbidity and mortality), if data are available. A review of the economic evidence will be conducted and new economic analyses will be carried out. If data are not available, a 'what if' model may be developed to support GDG recommendations on the cost-effectiveness of different scenarios.

The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.6 *Status*

4.6.1 *Scope*

This is the final scope.

4.6.2 *Timing*

The development of the guideline recommendations will begin in December 2011.

5 *Related NICE guidance*

5.1 *Published guidance*

5.1.1 *NICE guidance to be updated*

This guideline will update and replace the following NICE guidance:

- Feverish illness in children. NICE clinical guideline 47 (2007). Available from www.nice.org.uk/guidance/CG47

5.1.2 *Other related NICE guidance*

- Bacterial meningitis and meningococcal septicaemia. NICE clinical guideline 102 (2010). Available from www.nice.org.uk/guidance/CG102
- Diarrhoea and vomiting in children under 5. NICE clinical guideline 84 (2009). Available from www.nice.org.uk/guidance/CG84
- Amantadine, oseltamivir and zanamivir for the treatment of influenza. NICE technology appraisal guidance 168 (2009). Available from www.nice.org.uk/guidance/TA168
- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76
- Oseltamivir, amantadine and zanamivir for the prophylaxis of influenza. NICE technology appraisal guidance 158 (2008). Available from www.nice.org.uk/guidance/TA158
- Urinary tract infection in children. NICE clinical guideline 54 (2007). Available from www.nice.org.uk/guidance/CG54

5.1.3 *Guidance under development*

NICE is currently developing the following related guidance (details available from the NICE website):

- Antibiotics for neonatal infection. NICE clinical guideline. Publication expected September 2012.

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).

Appendix B Stakeholders

2013 Stakeholder organisations

3M Health Care UK
Action for Sick Children
Airedale NHS Trust
Alder Hey Children's NHS Foundation Trust
Anglesey Local Health Board
Arrowe Park Hospital
Aspirin Foundation
Association of Anaesthetists of Great Britain and Ireland
Association of Child Psychotherapists, The
Association of Paediatric Emergency Medicine
Barking, Havering and Redbridge Hospitals NHS Trust
Barnet Primary Care Trust
Barnsley Hospital NHS Foundation Trust
Barnsley Primary Care Trust
Barts and the London NHS Trust
Birmingham Children's Hospital NHS Foundation Trust
Bolton Hospitals NHS Trust
Boots
Bradford District Care Trust
Bristol-Myers Squibb Pharmaceuticals Ltd
British Association for Counselling and Psychotherapy
British Infection Association
British Medical Association
British Medical Journal
British National Formulary
British Paediatric Allergy, Immunology & Infection Group
British Psychological Society
British Society for Antimicrobial Chemotherapy
British Society for Immunology
British Society of Paediatric Gastroenterology Hepatology and Nutrition
Broomfield Hospital
Calderdale and Huddersfield NHS Trust
Calderdale Primary Care Trust

Cambridge University Hospitals NHS Foundation Trust
Camden Link
Care Quality Commission (CQC)
Central & North West London NHS Foundation Trust
Children living with Inherited Metabolic Diseases
Church Grange Surgery
College of Emergency Medicine
Commission for Social Care Inspection
Confidential Enquiry into Maternal and Child Health
Co-operative Pharmacy Association
County Durham Primary Care Trust
Crookes Healthcare Limited
Croydon Primary Care Trust
David Lewis Centre, The
Department for Communities and Local Government
Department of Health
Department of Health, Social Services and Public Safety - Northern Ireland
Division of Public Health & Primary Health Care
Dorset Primary Care Trust
Eaton Foundation
Encephalitis Society
Epilepsy Action
Faculty of Public Health
George Eliot Hospital NHS Trust
Great Western Hospitals NHS Foundation Trust
Greater Manchester Ambulance Service NHS Trust
Hampshire Partnership NHS Trust
Health Protection Agency
Health Quality Improvement Partnership
Healthcare Improvement Scotland
Healthcare Infection Society
Heart of England NHS Foundation Trust
Herpes Viruses Association
Hertfordshire Partnership NHS Trust
Hindu Council UK
Huddersfield Central Primary Care Trust
Humber NHS Foundation Trust
Independent Healthcare Advisory Services
Infection Control Nurses Association

Infection Prevention Society
Institute of Biomedical Science
Lancashire Care NHS Foundation Trust
Leeds Teaching Hospitals NHS Trust
Leukemia Research Fund
Lewisham University Hospital
Liverpool Primary Care Trust
London Ambulance Service NHS Trust
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
McNeil Products
Medicines and Healthcare products Regulatory Agency
Medicines for Children Research Network
Medway NHS Foundation Trust
Meningitis Research Foundation
Meningitis Trust
Meningitis UK
Mid Staffordshire NHS Foundation Trust
Ministry of Defence
National Clinical Guideline Centre
National Collaborating Centre for Cancer
National Collaborating Centre for Mental Health
National Collaborating Centre for Women's and Children's Health
National Institute for Health Research Health Technology Assessment Programme
National Patient Safety Agency
National Pharmacy Association
National Public Health Service for Wales
National Reyes Syndrome Foundation of the UK
National Treatment Agency for Substance Misuse
National Youth Advocacy Service
Neonatal & Paediatric Pharmacists Group
NHS Cambridgeshire
NHS Clinical Knowledge Summaries
NHS Confederation
NHS Connecting for Health
NHS Derbyshire county
NHS Direct
NHS Milton Keynes
NHS Newcastle

NHS Pathways
NHS Plus
NHS Sefton
NHS Sheffield
NHS Sickle Cell & Thalassaemia Screening Programme
NHS South Birmingham
NHS Warwickshire Primary Care Trust
North East London Foundation Trust
North Somerset Primary Care Trust
North Tees and Hartlepool NHS Foundation Trust
North Yorkshire & York Primary Care Trust
Northwick Park and St Mark's Hospitals
Nottingham City Hospital
Paracetamol Information Centre
PERIGON Healthcare Ltd
Pfizer
Public Health Wales NHS Trust
Queen Mary's Hospital NHS Trust
Reckitt-Benckiser
Rotherham Primary Care Trust
Royal Berkshire NHS Foundation Trust
Royal Brompton Hospital & Harefield NHS Trust
Royal College of Anaesthetists
Royal College of General Practitioners
Royal College of General Practitioners in Wales
Royal College of Midwives
Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Paediatrics and Child Health, Gastroenterology, Hepatology and Nutrition
Royal College of Pathologists
Royal College of Physicians
Royal College of Psychiatrists
Royal College of Radiologists
Royal College of Surgeons of England
Royal Pharmaceutical Society
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex NHS Trust

Scottish Intercollegiate Guidelines Network
SEE BETSI CADWALADR - North Wales NHS Trust
Sheffield Children's Hospital
Sheffield Primary Care Trust
Sheffield Teaching Hospitals NHS Foundation Trust
Social Care Institute for Excellence
Society for Academic Primary Care
Society for General Microbiology
Solent Healthcare
South Asian Health Foundation
South East Coast Ambulance Service
South London Cardiac and Stroke Network
South Staffordshire and Shropshire Healthcare NHS Foundation Trust
South Western Ambulance Service NHS Foundation Trust
Staffordshire Ambulance Service NHS Trust
Stockport Primary Care Trust
Sunfield
Sussex Ambulance Services NHS Trust
Tameside Hospital NHS Foundation Trust
The Association of the British Pharmaceutical Industry
The British In Vitro Diagnostics Association
The Princess Alexandra Hospital NHS Trust
The Rotherham NHS Foundation Trust
Thermo Fisher Scientific
UK Clinical Pharmacy Association
UK Specialised Services Public Health Network
University College London Hospital NHS Foundation Trust
University of Bristol
University of Southampton
Welsh Government
Welsh Scientific Advisory Committee
Western Cheshire Primary Care Trust
Wirral Community NHS Trust
Wirral University Teaching Hospital NHS Foundation Trust
Wishaw General Hospital
Wyre Forest Primary Care Trust
York Hospitals NHS Foundation Trust
Yorkshire Ambulance Service NHS Trust

2007 Stakeholder organisations

Action for Sick Children
Acute Care Collaborating Centre
Addenbrookes NHS Trust
Airedale General Hospital – Acute Trust
Anglesey Local Health Board
Aspirin Foundation
Association of Child Psychotherapists
Association of Medical Microbiologists
Association of Paediatric Emergency Medicine
Association of the British Pharmaceuticals Industry (ABPI)
Barking Havering & Redbridge Acute Trust
Barnet PCT
Barnsley PCT
Barts and the London NHS Trust – London
Bedfordshire & Hertfordshire NHS Strategic Health Authority
Birmingham Children's Hospital
Bolton Hospitals NHS Trust
Boots Healthcare International
Bristol-Myers Squibb Pharmaceuticals Ltd
British National Formulary (BNF)
British Psychological Society
British Society for Antimicrobial Chemotherapy
Calderdale and Huddersfield Acute Trust
CASPE
CEMACH
Chronic Conditions Collaborating Centre
Church Grange Surgery
CIS'ters
CLIMB – Children Living with Inherited Metabolic Disorders
Clinovia Ltd
College of Emergency Medicine
Coloplast Limited
Commission for Social Care Inspection
Connecting for Health
Conwy & Denbighshire Acute Trust
Co-operative Pharmacy Association
Craven Harrogate and Rural District PCT
Crookes Healthcare Limited

Croydon PCT
David Lewis Centre
Department of Health
Department of Primary Care
East Cambridgeshire and Fenland PCT
Eaton Foundation
Encephalitis Society
Faculty of Public Health
Good Hope Hospitals NHS Trust
Great Ormond Street Hospital for Children NHS Trust
Greater Manchester Ambulance Service NHS Trust
Hampshire Partnership NHS Trust
Health Protection Agency
Healthcare Commission
Heart of England NHS Foundation Trust
Herpes Viruses Association
Hertfordshire Partnership NHS Trust
Hospital Infection Society
Infection Control Nurses Association of the British Isles
Institute of Biomedical Science
King's College Acute Trust
Leeds Teaching Hospitals NHS Trust
Leukaemia Research Fund
Liverpool PCT
Luton and Dunstable Hospital NHS Trust
Maidstone and Tunbridge Wells NHS Trust
Medicines and Healthcare products Regulatory Agency (MHRA)
Medway NHS Trust
Meningitis Research Foundation
Meningitis Trust
Mental Health Collaborating Centre
Mid Essex Hospitals NHS Trust
Mid Staffordshire General Hospitals NHS Trust
Milton Keynes PCT
National Childbirth Trust
National Collaborating Centre for Cancer
National Collaborating Centre for Nursing and Supportive Care (NCC-NSC)
National Collaborating Centre for Primary Care
National Collaborating Centre for Women's and Children's Health (NCC-WCH)

National Coordinating Centre for Health Technology Assessment (NCCHTA)
National Patient Safety Agency
National Public Health Service – Wales
National Reyes Syndrome Foundation of the UK
National Youth Advocacy Service
Neonatal & Paediatric Pharmacists Group (NPPG)
Newcastle PCT
NHS Direct
NHS Pathways
NHS Quality Improvement Scotland
NICE – Guidelines Health Economists for information
NICE – Implementation Consultant – Region East
NICE – Implementation Consultant – Region London/SE
NICE – Implementation Consultant – Region NW & NE
NICE – Implementation Consultant – Region SW
NICE – Implementation Consultant – Region West Midlands
NICE – R&D for information
North Eastern Derbyshire PCT
North Lincolnshire PCT
North Tees and Hartlepool Acute Trust
North West London Hospitals NHS Trust
Northwick Park and St Mark's Hospitals NHS Trust
Paracetamol Information Centre
Patient and Public Involvement Programme (PPIP) for NICE
PERIGON (formerly the NHS Modernisation Agency)
Princess Alexandra Hospital NHS Trust
Prodigy
Queen Mary's Hospital NHS Trust (Sidcup)
Reckitt Benckiser Healthcare (UK) Ltd
Regional Public Health Group – London
Rotherham PCT
Royal Bolton Hospitals NHS Trust
Royal College of General Practitioners
Royal College of General Practitioners Wales
Royal College of Nursing
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Physicians of London
Royal College of Surgeons of England

Royal Liverpool Children's Hospital
Royal Pharmaceutical Society of Great Britain
Royal Society of Medicine
Royal United Hospital Bath NHS Trust
Royal West Sussex Trust
Sandwell & West Birmingham NHS Trust
Scottish Intercollegiate Guidelines Network (SIGN)
Sedgefield PCT
Sheffield Children's Hospital Trust
Sheffield PCT
Society for Academic Primary Care
South Birmingham PCT
South East Sheffield PCT
South Huddersfield and Central Huddersfield PCTs
South Yorkshire Ambulance Service NHS Trust
Specialist Advisory Committee on Antimicrobial Resistance (SACAR)
Staffordshire Ambulance HQ
Staffordshire Moorlans PCT
Stockport PCT
Sussex Ambulance Services NHS Trust
Tameside and Glossop Acute Trust
Tameside and Glossop PCT
UK Specialised Services Public Health Network
UKCPA – Infection Management Group
University College London Hospitals (UCLH) Acute Trust
University Hospital Lewisham NHS Trust
University of Bristol
University of Southampton
Welsh Assembly Government
Welsh Scientific Advisory Committee (WSAC)
Wirral Hospital Acute Trust
Wyre Forest Primary Care Trust

Appendix C Declarations of interest

All GDG members' interests were recorded on declaration forms provided by NICE. The form covered consultancies, fee-paid work, shareholdings, fellowships and support from the healthcare industry. GDG members' interests are listed in this section. No material conflicts of interest were identified.

This appendix includes all interests declared on or before 15 March 2013.

Table C.1 GDG members' declarations of interest

GDG member	Interest
Leah Bowen	Non-personal pecuniary PhD studentship funded by National Institute of Health Care Research School of Primary Care at University of Bristol.
Richard Bowker	No interests declared
John Crimmins	No interests declared
Penny McDougall	No interests declared
Edward Purcell	Personal pecuniary interests Attended educational meeting sponsored by Berlin Chemi/Abbot in November 2012. Taught at a workshop about systematic reviewing in May 2011. The workshop was funded by Abbott. Presented at a symposium in September 2012. The symposium was funded by Berlin Chemi. Currently writing a paper for Wyeth about infant feeding.
Debra Quantrill	No interests declared
Martin Richardson	No interests declared
Andrew Riordan	Non-personal pecuniary Undertaking a retrospective study on the use of Zanamivir in children aged under 2. This work is funded by Glaxo Smith Kline. Personal non-pecuniary Research on diagnostic usefulness of procalcitonin is undertaken at the institute where he is working, the Alder Hey Children's NHS Foundation Trust. Has published studies on bio-markers in meningococcal diseases (Pediatric Critical Care Medicine) and on how to use C-reactive protein (Arch Dis Child Educ Pract Ed 2010).

Damian Roland

Personal pecuniary interests

Director and co-founder of The Paediatric Emergency Medicine Leicester Academic Group (PEMLA) a non-profit making social enterprise .

Funded by NIHR to undertake a Doctoral Research Fellowship.

Personal non-pecuniary interest

Recipient of HIEC grant looking at POPS (The Paediatric Observation Priority Score) a scoring system based on the NICE table.

Guideline member of BTS oxygen guideline update.

Council member and trustee of RCPCH

Advisor on Map of Medicine as paediatric emergency medicine specialist.

Speaker at the Children and Young People Urgent Care – launch of high volume pathway event. Talk entitled “Implementing NICE guidelines”, Chiltern Clinical Commissioning Group, September 2012.

Table C.2 NCC staff members’ declarations of interest

NCC-WCH staff	Interest
Zosia Beckles	No interests declared
Jiri Chard	No interests declared
Hannah-Rose Douglas	No interests declared
Ella Fields	No interests declared
M Stephen Murphy	No interests declared
Nitara Prasannan	No interests declared
Cristina Visintin	No interests declared
Zipporah Iheozor-Ejiofor	No interests declared

Appendix D Review protocols

Chapter 5

Review question

What is the value (as shown by likelihood ratios, sensitivity, specificity, positive predictive value and negative predictive value) of the following symptoms and signs, alone or in combination, as initial indications of serious illness?:

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and othersounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb
- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

Details	
Review question	<p>The predictive value of the following symptoms and signs, alone or in combination, as initial indications of serious illness:</p> <ul style="list-style-type: none">• abnormal skin or mucosal colour (for example, pallor or, cyanosis)• appearing ill to a healthcare professional or parent• altered responsiveness or cry• altered breathing (for example, nasal flaring, grunting, chest indrawing,)• respiratory rate

Details	
	<ul style="list-style-type: none"> • pulmonary (lung) crackles and other sounds • oxygen desaturation • dehydration • capillary refill time • cold hands and feet • poor feeding • persistent fever (5 days or more) • height of fever • limb or joint swelling • unwillingness to weight bear or to use a limb • bulging fontanelle • rash (blanching or non-blanching) • focal neurological signs • focal seizures • new lumps • neck stiffness • vomiting • status epilepticus (prolonged or continuous fits). <p>If evidence is found on additional signs and symptoms they will be added to the above list.</p>
Objectives	<ul style="list-style-type: none"> • To assess and up-date the evidence base on which the current traffic light system for non-specific symptoms of serious illness is based. • Symptoms for specific serious conditions will not be examined as these are covered elsewhere in the guideline.
Language	English
Study design	<p>Diagnostic accuracy/prognostic studies:</p> <ul style="list-style-type: none"> • randomised controlled trials (RCTs) • cohort studies/case-series • case-control studies
Status	Published papers
Population	Children aged 5 or under presenting with fever
Intervention	<ul style="list-style-type: none"> • abnormal skin or mucosal colour (for example pallor or, cyanosis), • appearing ill to a healthcare professional or parent • altered responsiveness or cry • altered breathing (for example, nasal flaring, grunting, chest indrawing.) • respiratory rate • pulmonary (lung) crackles and other sounds • oxygen desaturation • dehydration • capillary refill time • cold hands and feet • poor feeding • persistent fever (5 days or more) • height of fever • limb or joint swelling • unwillingness to weight bear or to use a limb • bulging fontanelle • rash (blanching or non-blanching) • focal neurological signs • focal seizures • new lumps • neck stiffness

Details	
	<ul style="list-style-type: none"> • vomiting • status epilepticus (prolonged or continuous fits). <p>Other factors identified in literature (unknown number).</p>
Comparator or reference standard	
Outcomes	Detecting serious illness (Sensitivity, specificity, PPV, NPV, ROC, calibration).
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Issues relating to race (different signs and symptoms) and religion (physical assessment) may impact on the interpretation of evidence

Chapter 5

Heart rate

Review question

The predictive value of heart rate, including:

- how heart rate changes with temperature?
- whether heart rate outside the normal range detects serious illness?
- whether heart rate and temperature outside normal range detects serious illness?

Details	
Review question	The predictive value of heart rate, including: <ul style="list-style-type: none"> • how heart rate changes with temperature • whether heart rate outside the normal range detects serious illness.
Objectives	New evidence has become available since the 2007 guideline. To ascertain how heart rate changes with temperature, and if this differs between benign and serious bacterial causes. This will improve precision and accuracy of diagnosis.
Language	English
Study design	Diagnostic accuracy/prognostic studies evaluating clinical outcomes: cohort studies
Status	Published papers
Population	Children aged 5 or under
Intervention	<ul style="list-style-type: none"> • Heart rate with fever with serious cause • Heart rate with serious cause
Comparator or reference standard	Heart rate with fever with benign cause Normal heart rate
Outcomes	Detecting serious illness (Sensitivity, specificity, PPV, NPV, ROC, calibration).
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (January 2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Issues of race (differences in physiology) and religion (use of tests) may impact on the interpretation of evidence

Chapter 8

Children 3 months and older

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

	Details
Review question	<p>As outlined in the scope:</p> <p>“The predictive value of pro-calcitonin and/or C reactive protein markers.”</p> <p>The review question examines:</p> <p>“What is the predictive value of the following markers for identifying serious illness in children with fever who are aged 5 years or less :</p> <ul style="list-style-type: none"> • Procalcitonin • C-reactive protein • Procalcitonin and C-reactive protein”
Objectives	<p>New evidence has become available since the 2007 guideline.</p> <p>The main aim is to ascertain if PCT should now be recommended.</p>
Language	English
Study design	<p>Diagnostic accuracy/prognostic studies evaluating clinical outcomes:</p> <ul style="list-style-type: none"> • randomised controlled trials (RCTs) • prospective cohort studies
Status	Published papers
Population	Children aged 5 or under presenting with fever
Intervention	<ul style="list-style-type: none"> • Pro-calcitonin levels • C reactive protein levels • PCT & CRP
Reference standard	<p>One or any combination of the following:</p> <ul style="list-style-type: none"> • Blood culture • Urine culture • Cerebrospinal fluid culture • Synovial fluid culture • Chest X-ray • Scintigraphy • Full blood count • Signs and symptoms
Outcomes	Detecting serious illness (Sensitivity, specificity, PPV, NPV, AUC, calibration).
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (January 2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence

Details	
Equality	Issues of race (differences in physiology) and religion (use of tests) may impact on the interpretation of evidence

Chapter 8

Response to antipyretic medication

Review question

What is the predictive value of the clinical response to paracetamol or NSAIDs?

	Details
Review question	The predictive value of the clinical response to paracetamol or NSAIDs.
Objectives	To assess if clinical response of a child to paracetamol or NSAIDs can be used to predict the course of the illness
Language	English
Study design	Effectiveness and efficacy: <ul style="list-style-type: none"> • randomised controlled trials (RCTs) • cohort studies
Status	Published full papers
Population	Children aged 5 or under presenting with fever
Intervention	<ul style="list-style-type: none"> • Paracetamol alone • Ibuprofen alone • Alternating paracetamol and Ibuprofen • Combining paracetamol and Ibuprofen
Comparator or reference standard	Final diagnosis: serious infectious disease – from gold standard test or follow-up
Outcomes	Detecting serious illness (Sensitivity, specificity, PPV, NPV, ROC, calibration).
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (January 2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Issues relating to religion (use of pharmaceuticals) may impact on the interpretation of evidence

Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

	Details
Review question	Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the illness.
Objectives	New evidence has become available since the last guideline was published. To assess if use of paracetamol or NSAIDs prevents diagnosis of potentially serious illness. This can be via masking an illness or slowing immune response.
Language	English
Study design	Effectiveness and efficacy: <ul style="list-style-type: none"> • randomised controlled trials (RCTs) • cohort studies (n > 1000 and long-term follow-up)
Status	Published full papers
Population	Children aged 5 or under presenting with fever
Intervention	<ul style="list-style-type: none"> • Paracetamol alone • Ibuprofen alone • Alternating paracetamol and Ibuprofen • Combined paracetamol and Ibuprofen
Comparator or reference standard	No treatment
Outcomes	<ul style="list-style-type: none"> • Mortality • Morbidity of underlying condition
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (January 2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Issues relating to religion (use of pharmaceuticals) may impact on the interpretation of evidence

9.3 Physical and drug interventions

Review question

Effect on fever and associated symptoms of treatment with:

- Paracetamol alone or NSAIDs alone, compared with placebo and with one another
- Alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time
- Paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone.

Details	
Review question as stated in scope	<p>Effect on fever and associated symptoms of treatment with:</p> <ul style="list-style-type: none"> • paracetamol alone or NSAIDs alone, compared with placebo and with one another • alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time • paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone <p>This question can be unpackaged to these comparisons:</p> <ul style="list-style-type: none"> • Paracetamol vs. placebo • Ibuprofen vs. placebo • Paracetamol and ibuprofen combined vs. placebo • Paracetamol and ibuprofen alternating vs. placebo • Paracetamol vs. ibuprofen • Paracetamol vs. paracetamol and ibuprofen combined • Paracetamol vs. paracetamol and ibuprofen alternating • Ibuprofen vs. paracetamol and ibuprofen combined • Ibuprofen vs. paracetamol and ibuprofen alternating • Paracetamol and ibuprofen combined vs. paracetamol and ibuprofen alternating
Objectives	To ascertain if paracetamol or ibuprofen is more effective at treating specific symptoms of fever in children age 5 years or less
Language	English
Study design	randomised controlled trials (RCTs)
Status	Published full papers only
Population	Children aged 5 or under with fever
Intervention	<ul style="list-style-type: none"> • Paracetamol • Ibuprofen • Alternating paracetamol or ibuprofen • Combined paracetamol or ibuprofen
Comparator or reference standard	<ul style="list-style-type: none"> • Ibuprofen (see note – no other NSAIDs being used) • Paracetamol • Alternating paracetamol or ibuprofen • Combined paracetamol or ibuprofen • Placebo
Outcomes	<ul style="list-style-type: none"> • Change in physical signs and symptoms <ul style="list-style-type: none"> ◦ Fever (temperature – mean change, AUC, proportion without fever by 3 hours and 8 hours) ◦ Discomfort (PRIMARY OUTCOME) • Quality of life • Adverse events of the intervention

Details	
Other criteria for inclusion/exclusion of studies	Exclude non-human studies
Search strategies	See separate document
Review strategies	<ul style="list-style-type: none"> • Evidence will be assessed for quality according to the process described in the NICE guidelines manual (January 2009) • A list of excluded studies will be provided following weeding • Evidence tables and an evidence profile will be used to summarise the evidence
Equality	Issues relating to religion (use of pharmaceuticals) may impact on the interpretation of evidence

Appendix E Search strategies

2013 Search strategies

Chapter 5

Review question

What is the value (as shown by likelihood ratios, sensitivity, specificity, positive predictive value and negative predictive value) of the following symptoms and signs, alone or in combination, as initial indications of serious illness?

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and othersounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb
- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q2_traffic_light_dx_combined_medline_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/

29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp "SIGNS AND SYMPTOMS"/
54	(sign? adj2 symptom\$).tw.
55	or/53-54
56	(sign? or symptom\$ or complain\$).ti,ab.
57	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).ti,ab.
58	(presenting adj3 (feature? or finding? or factor?)).ti,ab.
59	presentation?.ti,ab.

60	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).ti,ab.
61	or/55-60
62	((ill or sick) adj3 (look\$ or appear\$)).ti,ab.
63	unwell.ti,ab.
64	CYANOSIS/
65	cyano\$.ti,ab.
66	exp SKIN/
67	(skin\$ or pallor).ti,ab.
68	exp PURPURA/
69	(purpura\$ or petechia\$ or rash or mottled).ti,ab.
70	exp BEHAVIOR/ or IRRITABLE MOOD/
71	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).ti,ab.
72	VOMITING/
73	(vomit\$ or emes\$).ti,ab.
74	RESPIRATION DISORDERS/
75	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).ti,ab.
76	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).ti,ab.
77	NOSE/
78	((nose or nasal or nostril? or alar) adj3 flar\$).ti,ab.
79	RESPIRATORY RATE/ or TACHYPNEA/
80	((respirat\$ or breath\$) adj3 rate?).ti,ab.
81	tachypn\$.ti,ab.
82	RESPIRATORY SOUNDS/
83	((respirat\$ or breath\$) adj3 sound?).ti,ab.
84	(crackl\$ or grunt\$).ti,ab.
85	CRANIAL FONTANELLES/
86	(fontanel\$ adj3 (bulg\$ or tens\$)).ti,ab.
87	FEEDING BEHAVIOR/ or SUCKING BEHAVIOR/
88	BOTTLE FEEDING/ or BREAST FEEDING/
89	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).ti,ab.
90	DEHYDRATION/

91	dehydrat\$.ti,ab.
92	OLIGURIA/
93	oliguri\$.ti,ab.
94	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).ti,ab.
95	OXYGEN/bl [blood]
96	exp OXIMETRY/
97	(oxygen adj2 (desaturat\$ or saturat\$)).ti,ab.
98	CAPILLARIES/
99	REGIONAL BLOOD FLOW/
100	MICROCIRCULATION/
101	(capill?ary refill time? or CRT).ti,ab.
102	CHILLS/ or SHIVERING/
103	((cold or chill\$) adj3 (hand? or feet or foot)).ti,ab.
104	(shiver\$ or rigor? or chill?).ti,ab.
105	EDEMA/
106	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).ti,ab.
107	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).ti,ab.
108	(limb? adj3 tender\$).ti,ab.
109	exp NEUROLOGICAL MANIFESTATIONS/
110	(focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).ti,ab.
111	SEIZURES/
112	((focal or partial or local\$) adj3 seiz\$).ti,ab.
113	NECK PAIN/
114	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).ti,ab.
115	STATUS EPILEPTICUS/
116	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).ti,ab.
117	(fit? or seiz\$ or convuls\$).ti,ab.
118	or/62-117
119	and/5,8,52,61,118
120	exp COHORT STUDIES/
121	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or

	analys\$)).tw.
122	retrospective\$.ti.
123	or/120-122
124	and/5,52,55,123
125	limit 124 to yr="2006 -Current"
126	or/119,125
127	limit 126 to english language
128	LETTER/
129	EDITORIAL/
130	NEWS/
131	exp HISTORICAL ARTICLE/
132	ANECDOTES AS TOPIC/
133	COMMENT/
134	(letter or comment* or abstracts).ti.
135	or/128-134
136	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
137	135 not 136
138	ANIMALS/ not HUMANS/
139	exp ANIMALS, LABORATORY/
140	exp ANIMAL EXPERIMENTATION/
141	exp MODELS, ANIMAL/
142	exp RODENTIA/
143	(rat or rats or mouse or mice).ti.
144	or/137-143
145	127 not 144

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_Q2_traffic_light_dx_combined_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.

Feverish illness in children (appendices)

3	or/1-2
4	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
5	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
6	mening\$.ti,ab.
7	(sepsis or septic?emi\$).ti,ab.
8	bacter?emi\$.ti,ab.
9	or/7-8
10	pneumon\$.ti,ab.
11	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
12	(arthritis\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
13	py?arth\$.ti,ab.
14	or/12-13
15	osteomyelit\$.ti,ab.
16	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
17	((upper or lower) adj5 urin\$).ti,ab.
18	UTI.ti,ab.
19	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
20	(pyelonephr\$ or pyonephr\$).ti,ab.
21	or/16-20
22	(mucocutaneous adj3 lymph\$).ti,ab.
23	MCLS.ti,ab.
24	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
25	or/22-24
26	pyrogen\$.ti,ab.
27	or/5-6,9-11,14-15,21,25-26
28	(sign? adj2 symptom\$).tw.
29	(sign? or symptom\$ or complain\$).ti,ab.
30	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).ti,ab.
31	(presenting adj3 (feature? or finding? or factor?)).ti,ab.
32	presentation?.ti,ab.

33	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).ti,ab.
34	or/28-33
35	((ill or sick) adj3 (look\$ or appear\$)).ti,ab.
36	unwell.ti,ab.
37	cyano\$.ti,ab.
38	(skin\$ or pallor).ti,ab.
39	(purpura\$ or petechia\$ or rash or mottled).ti,ab.
40	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).ti,ab.
41	(vomit\$ or emes\$).ti,ab.
42	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).ti,ab.
43	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).ti,ab.
44	((nose or nasal or nostril? or alar) adj3 flar\$).ti,ab.
45	((respirat\$ or breath\$) adj3 rate?).ti,ab.
46	tachypn\$.ti,ab.
47	((respirat\$ or breath\$) adj3 sound?).ti,ab.
48	(crackl\$ or grunt\$).ti,ab.
49	(fontanel\$ adj3 (bulg\$ or tens\$)).ti,ab.
50	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).ti,ab.
51	dehydrat\$.ti,ab.
52	oliguri\$.ti,ab.
53	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).ti,ab.
54	(oxygen adj2 (desaturat\$ or saturat\$)).ti,ab.
55	(capill?ary refill time? or CRT).ti,ab.
56	((cold or chill\$) adj3 (hand? or feet or foot)).ti,ab.
57	(shiver\$ or rigor? or chill?).ti,ab.
58	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).ti,ab.
59	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).ti,ab.
60	(limb? adj3 tender\$).ti,ab.
61	(focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).ti,ab.
62	((focal or partial or local\$) adj3 seiz\$).ti,ab.
63	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).ti,ab.

64	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).ti,ab.
65	(fit? or seiz\$ or convuls\$).ti,ab.
66	or/35-65
67	and/3-4,27,34,66
68	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
69	retrospective\$.ti.
70	or/68-69
71	and/3,27-28,70
72	limit 71 to yr="2006 -Current"
73	or/67,72

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q2_traffic_light_dx_combined_cctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febril\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15

17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.

48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp "SIGNS AND SYMPTOMS"/
54	(sign? adj2 symptom\$).tw.
55	or/53-54
56	(sign? or symptom\$ or complain\$).ti,ab.
57	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).ti,ab.
58	(presenting adj3 (feature? or finding? or factor?)).ti,ab.
59	presentation?.ti,ab.
60	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).ti,ab.
61	or/55-60
62	((ill or sick) adj3 (look\$ or appear\$)).ti,ab.
63	unwell.ti,ab.
64	CYANOSIS/
65	cyano\$.ti,ab.
66	exp SKIN/
67	(skin\$ or pallor).ti,ab.
68	exp PURPURA/
69	(purpura\$ or petechia\$ or rash or mottled).ti,ab.
70	exp BEHAVIOR/ or IRRITABLE MOOD/
71	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).ti,ab.
72	VOMITING/
73	(vomit\$ or emes\$).ti,ab.
74	RESPIRATION DISORDERS/
75	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).ti,ab.
76	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).ti,ab.
77	NOSE/
78	((nose or nasal or nostril? or alar) adj3 flar\$).ti,ab.

79	RESPIRATORY RATE/ or TACHYPNEA/
80	((respirat\$ or breath\$) adj3 rate?).ti,ab.
81	tachypn\$.ti,ab.
82	RESPIRATORY SOUNDS/
83	((respirat\$ or breath\$) adj3 sound?).ti,ab.
84	(crackl\$ or grunt\$).ti,ab.
85	CRANIAL FONTANELLES/
86	(fontanel\$ adj3 (bulg\$ or tens\$)).ti,ab.
87	FEEDING BEHAVIOR/ or SUCKING BEHAVIOR/
88	BOTTLE FEEDING/ or BREAST FEEDING/
89	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).ti,ab.
90	DEHYDRATION/
91	dehydrat\$.ti,ab.
92	OLIGURIA/
93	oliguri\$.ti,ab.
94	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).ti,ab.
95	OXYGEN/bl [blood]
96	exp OXIMETRY/
97	(oxygen adj2 (desaturat\$ or saturat\$)).ti,ab.
98	CAPILLARIES/
99	REGIONAL BLOOD FLOW/
100	MICROCIRCULATION/
101	(capill?ary refill time? or CRT).ti,ab.
102	CHILLS/ or SHIVERING/
103	((cold or chill\$) adj3 (hand? or feet or foot)).ti,ab.
104	(shiver\$ or rigor? or chill?).ti,ab.
105	EDEMA/
106	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).ti,ab.
107	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).ti,ab.
108	(limb? adj3 tender\$).ti,ab.
109	exp NEUROLOGICAL MANIFESTATIONS/

110	((focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).ti,ab.
111	SEIZURES/
112	((focal or partial or local\$) adj3 seiz\$).ti,ab.
113	NECK PAIN/
114	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).ti,ab.
115	STATUS EPILEPTICUS/
116	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).ti,ab.
117	(fit? or seiz\$ or convuls\$).ti,ab.
118	or/62-117
119	and/5,8,52,61,118
120	exp COHORT STUDIES/
121	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
122	retrospective\$.ti.
123	or/120-122
124	and/5,52,55,123
125	limit 124 to yr="2006 -Current"
126	or/119,125

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_Q2_traffic_light_dx_combined_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	FEVER.kw.
7	(fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw,tx.
8	or/6-7
9	BACTERIAL INFECTIONS.kw.

10	(CRITICAL ILLNESS or ACUTE DISEASE).kw.
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw,tx.
12	or/9-11
13	MENINGITIS, BACTERIAL.kw.
14	MENINGOENCEPHALITIS.kw.
15	mening\$.tw,tx.
16	or/13-15
17	SEPSIS.kw.
18	BACTEREMIA.kw.
19	(sepsis or septic?emi\$).tw,tx.
20	bacter?emi\$.tw,tx.
21	or/17-20
22	PNEUMONIA.kw.
23	pneumon\$.tw,tx.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX.kw.
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw,tx.
27	or/25-26
28	ARTHRITIS, INFECTIOUS.kw.
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw,tx.
30	py?arth\$.tw,tx.
31	or/28-30
32	OSTEOMYELITIS.kw.
33	osteomyelit\$.tw,tx.
34	or/32-33
35	URINARY TRACT INFECTIONS.kw.
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw,tx.
37	((upper or lower) adj5 urin\$).tw,tx.
38	UTI.tw,tx.
39	CYSTITIS.kw.

40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw,tx.
41	PYELONEPHRITIS.kw.
42	(pyelonephr\$ or pyonephr\$).tw,tx.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME.kw.
45	(mucocutaneous adj3 lymph\$).tw,tx.
46	MCLS.tw,tx.
47	(kawasaki\$ adj (disease? or syndrome?)).tw,tx.
48	or/44-47
49	PYROGENS.kw.
50	pyrogen\$.tw,tx.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	"SIGNS AND SYMPTOMS".kw.
54	(sign? adj2 symptom\$).tw.
55	or/53-54
56	(sign? or symptom\$ or complain\$).tw,tx.
57	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).tw,tx.
58	(presenting adj3 (feature? or finding? or factor?)).tw,tx.
59	presentation?.tw,tx.
60	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).tw,tx.
61	or/55-60
62	((ill or sick) adj3 (look\$ or appear\$)).tw,tx.
63	unwell.tw,tx.
64	CYANOSIS.kw.
65	cyano\$.tw,tx.
66	SKIN.kw.
67	(skin\$ or pallor).tw,tx.
68	PURPURA.kw.
69	(purpura\$ or petechia\$ or rash or mottled).tw,tx.
70	(BEHAVIOR or IRRITABLE MOOD).kw.

71	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).tw,tx.
72	VOMITING.kw.
73	(vomit\$ or emes\$).tw,tx.
74	RESPIRATION DISORDERS.kw.
75	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).tw,tx.
76	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).tw,tx.
77	NOSE.kw.
78	((nose or nasal or nostril? or alar) adj3 flar\$).tw,tx.
79	(RESPIRATORY RATE or TACHYPNEA).kw.
80	((respirat\$ or breath\$) adj3 rate?).tw,tx.
81	tachypn\$.tw,tx.
82	RESPIRATORY SOUNDS.kw.
83	((respirat\$ or breath\$) adj3 sound?).tw,tx.
84	(crackl\$ or grunt\$).tw,tx.
85	CRANIAL FONTANELLES.kw.
86	(fontanel\$ adj3 (bulg\$ or tens\$)).tw,tx.
87	(FEEDING BEHAVIOR or SUCKING BEHAVIOR).kw.
88	(BOTTLE FEEDING or BREAST FEEDING).kw.
89	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).tw,tx.
90	DEHYDRATION.kw.
91	dehydrat\$.tw,tx.
92	OLIGURIA.kw.
93	oliguri\$.tw,tx.
94	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).tw,tx.
95	OXYGEN.kw.
96	OXIMETRY.kw.
97	(oxygen adj2 (desaturat\$ or saturat\$)).tw,tx.
98	CAPILLARIES.kw.
99	REGIONAL BLOOD FLOW.kw.
100	MICROCIRCULATION.kw.
101	(capill?ary refill time? or CRT).tw,tx.

102	(CHILLS or SHIVERING).kw.
103	((cold or chill\$) adj3 (hand? or feet or foot)).tw,tx.
104	(shiver\$ or rigor? or chill?).tw,tx.
105	EDEMA.kw.
106	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).tw,tx.
107	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).tw,tx.
108	(limb? adj3 tender\$).tw,tx.
109	NEUROLOGICAL MANIFESTATIONS.kw.
110	(focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).tw,tx.
111	SEIZURES.kw.
112	((focal or partial or local\$) adj3 seiz\$).tw,tx.
113	NECK PAIN.kw.
114	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).tw,tx.
115	STATUS EPILEPTICUS.kw.
116	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).tw,tx.
117	(fit? or seiz\$ or convuls\$).tw,tx.
118	or/62-117
119	and/5,8,52,61,118
120	COHORT STUDIES.kw.
121	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
122	retrospective\$.ti.
123	or/120-122
124	and/5,52,55,123
125	or/119,124

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012

FICu_Q2_traffic_light_dx_combined_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/

4	(child\$ or toddler\$).tw.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febril\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	menin\$.tw.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).tw.
20	bacter?emi\$.tw.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.tw.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
30	py?arth\$.tw.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.tw.
34	or/32-33

35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw.
37	((upper or lower) adj5 urin\$).tw.
38	UTI.tw.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).tw.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).tw.
46	MCLS.tw.
47	(kawasaki\$ adj (disease? or syndrome?)).tw.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.tw.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp "SIGNS AND SYMPTOMS"/
54	(sign? adj2 symptom\$).tw.
55	or/53-54
56	(sign? or symptom\$ or complain\$).tw.
57	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).tw.
58	(presenting adj3 (feature? or finding? or factor?)).tw.
59	presentation?.tw.
60	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).tw.
61	or/55-60
62	((ill or sick) adj3 (look\$ or appear\$)).tw.
63	unwell.tw.
64	CYANOSIS/
65	cyano\$.tw.

66	exp SKIN/
67	(skin\$ or pallor).tw.
68	exp PURPURA/
69	(purpura\$ or petechia\$ or rash or mottled).tw.
70	exp BEHAVIOR/ or IRRITABLE MOOD/
71	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).tw.
72	VOMITING/
73	(vomit\$ or emes\$).tw.
74	RESPIRATION DISORDERS/
75	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).tw.
76	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).tw.
77	NOSE/
78	((nose or nasal or nostril? or alar) adj3 flar\$).tw.
79	RESPIRATORY RATE/ or TACHYPNEA/
80	((respirat\$ or breath\$) adj3 rate?).tw.
81	tachypn\$.tw.
82	RESPIRATORY SOUNDS/
83	((respirat\$ or breath\$) adj3 sound?).tw.
84	(crackl\$ or grunt\$).tw.
85	CRANIAL FONTANELLES/
86	(fontanel\$ adj3 (bulg\$ or tens\$)).tw.
87	FEEDING BEHAVIOR/ or SUCKING BEHAVIOR/
88	BOTTLE FEEDING/ or BREAST FEEDING/
89	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).tw.
90	DEHYDRATION/
91	dehydrat\$.tw.
92	OLIGURIA/
93	oliguri\$.tw.
94	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).tw.
95	OXYGEN/
96	exp OXIMETRY/

97	(oxygen adj2 (desaturat\$ or saturat\$)).tw.
98	CAPILLARIES/
99	REGIONAL BLOOD FLOW/
100	MICROCIRCULATION/
101	(capill?ary refill time? or CRT).tw.
102	CHILLS/ or SHIVERING/
103	((cold or chill\$) adj3 (hand? or feet or foot)).tw.
104	(shiver\$ or rigor? or chill?).tw.
105	EDEMA/
106	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).tw.
107	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).tw.
108	(limb? adj3 tender\$).tw.
109	exp NEUROLOGIC MANIFESTATIONS/
110	(focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).tw.
111	SEIZURES/
112	((focal or partial or local\$) adj3 seiz\$).tw.
113	NECK PAIN/
114	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).tw.
115	STATUS EPILEPTICUS/
116	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).tw.
117	(fit? or seiz\$ or convuls\$).tw.
118	or/62-117
119	and/5,8,52,61,118
120	exp COHORT STUDIES/
121	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
122	retrospective\$.ti.
123	or/120-122
124	and/5,52,55,123
125	or/119,124

Database(s): Embase 1980 to 2012 Week 39

FICu_Q2_traffic_light_dx_combined_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	FEVER/
5	HYPERTHERMIA/ or HYPERPYREXIA/
6	PYREXIA IDIOPATHICA/
7	(fever\$ or febr\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/4-7
9	exp BACTERIAL INFECTION/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	BACTERIAL MENINGITIS/
14	MENINGOENCEPHALITIS/
15	menin\$.ti,ab.
16	or/13-15
17	SEPTICEMIA/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	HERPES SIMPLEX ENCEPHALITIS/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp INFECTIOUS ARTHRITIS/

29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	exp OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTION/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGEN/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp SYMPTOMATOLOGY/
54	(sign? adj2 symptom\$).tw.
55	or/53-54
56	(sign? or symptom\$ or complain\$).ti,ab.
57	(clinical adj3 (manifestation? or feature? or finding? or aspect? or marker?)).ti,ab.
58	(presenting adj3 (feature? or finding? or factor?)).ti,ab.
59	presentation?.ti,ab.

60	(physical adj3 (manifestaion? or characteristic? or feature? or finding?)).ti,ab.
61	or/55-60
62	((ill or sick) adj3 (look\$ or appear\$)).ti,ab.
63	unwell.ti,ab.
64	CYANOSIS/
65	cyano\$.ti,ab.
66	exp SKIN/
67	(skin\$ or pallor).ti,ab.
68	exp RASH/
69	(purpura\$ or petechia\$ or rash or mottled).ti,ab.
70	BEHAVIOR CHANGE/ or IRRITABILITY/
71	(behav\$ or respon\$ or non?respon\$ or cry\$ or cries or irritab\$).ti,ab.
72	VOMITING/
73	(vomit\$ or emes\$).ti,ab.
74	BREATHING DISORDER/ or TACHYPNEA/
75	((respirat\$ or breath\$) adj3 (distress\$ or disorder? or alter\$)).ti,ab.
76	((chest or sternal or sternum or intercostal) adj3 (in drawing or in?drawing or recess\$ or retract\$)).ti,ab.
77	NOSE/
78	((nose or nasal or nostril? or alar) adj3 flar\$).ti,ab.
79	RESPIRATORY RATE/
80	((respirat\$ or breath\$) adj3 rate?).ti,ab.
81	tachypn\$.ti,ab.
82	ABNORMAL RESPIRATORY SOUND/
83	((respirat\$ or breath\$) adj3 sound?).ti,ab.
84	(crackl\$ or grunt\$).ti,ab.
85	exp FONTANEL/
86	(fontanel\$ adj3 (bulg\$ or tens\$)).ti,ab.
87	FEEDING BEHAVIOR/ or SUCKING/
88	exp INFANT FEEDING/
89	((refus\$ or poor) adj3 (feed\$ or fed or suck\$)).ti,ab.
90	DEHYDRATION/

91	dehydrat\$.ti,ab.
92	OLIGURIA/
93	oliguri\$.ti,ab.
94	((reduc\$ or low\$) adj2 urin\$ adj2 (volume? or output? or level?)).ti,ab.
95	OXYGEN SATURATION/
96	exp OXIMETRY/
97	(oxygen adj2 (desaturat\$ or saturat\$)).ti,ab.
98	CAPILLARY/
99	CAPILLARY FLOW/
100	(capill?ary refill time? or CRT).ti,ab.
101	CHILL/ or SHIVERING/ or RIGOR/
102	((cold or chill\$) adj3 (hand? or feet or foot)).ti,ab.
103	(shiver\$ or rigor? or chill?).ti,ab.
104	exp EDEMA/
105	(edem\$ or oedem\$ or sw#ll\$ or lump? or bump?).ti,ab.
106	((unwill\$ or unable or inability) adj3 (weight bear\$ or weight?bear\$ or bear weight or "use limb?")).ti,ab.
107	(limb? adj3 tender\$).ti,ab.
108	(focal adj2 (neurologic\$ or CNS) adj2 (sign? or deficit? or manifestation? or symptom? or dysfunction?)).ti,ab.
109	SEIZURE/
110	((focal or partial or local\$) adj3 seiz\$).ti,ab.
111	MUSCLE STIFFNESS/ or NECK PAIN/
112	((neck or cervical) adj3 (ache or pain\$ or stiff\$)).ti,ab.
113	EPILEPTIC STATE/
114	(stat\$ adj3 (epileptic\$ or absence or grand mal or petit mal)).ti,ab.
115	(fit? or seiz\$ or convuls\$).ti,ab.
116	or/62-115
117	and/3,8,52,61,116
118	COHORT ANALYSIS/
119	LONGITUDINAL STUDY/
120	FOLLOW UP/
121	PROSPECTIVE STUDY/

122	RETROSPECTIVE STUDY/
123	((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
124	retrospective\$.ti.
125	or/118-124
126	and/3,52,55,125
127	limit 126 to yr="2006 -Current"
128	or/117,127
129	limit 128 to english language
130	conference abstract.pt.
131	letter.pt. or LETTER/
132	note.pt.
133	editorial.pt.
134	(letter or comment* or abstracts).ti.
135	or/130-134
136	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
137	135 not 136
138	ANIMAL/ not HUMAN/
139	NONHUMAN/
140	exp ANIMAL EXPERIMENT/
141	exp EXPERIMENTAL ANIMAL/
142	ANIMAL MODEL/
143	exp RODENT/
144	(rat or rats or mouse or mice).ti.
145	or/137-144
146	129 not 145

Collated search strategies: Q2 scoring systems

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q2_scoring_systems_medline_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.

3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.

34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	SEVERITY OF ILLNESS INDEX/
55	(scor\$ adj system\$).ti,ab.
56	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).ti,ab.
57	((logistic or risk or predict\$) adj3 model\$).ti,ab.
58	(Yale or Rochester).ti,ab.
59	or/54-58
60	and/53,59
61	limit 60 to english language
62	LETTER/
63	EDITORIAL/
64	NEWS/

65	exp HISTORICAL ARTICLE/
66	ANECDOTES AS TOPIC/
67	COMMENT/
68	CASE REPORT/
69	(letter or comment* or abstracts).ti.
70	or/62-69
71	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
72	70 not 71
73	ANIMALS/ not HUMANS/
74	exp ANIMALS, LABORATORY/
75	exp ANIMAL EXPERIMENTATION/
76	exp MODELS, ANIMAL/
77	exp RODENTIA/
78	(rat or rats or mouse or mice).ti.
79	or/72-78
80	61 not 79

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_Q2_scoring_systems_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.
3	or/1-2
4	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
5	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
6	mening\$.ti,ab.
7	(sepsis or septic?emi\$).ti,ab.
8	bacter?emi\$.ti,ab.
9	or/7-8
10	pneumon\$.ti,ab.
11	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.

12	(arthritis\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
13	py?arth\$.ti,ab.
14	or/12-13
15	osteomyelit\$.ti,ab.
16	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
17	((upper or lower) adj5 urin\$).ti,ab.
18	UTI.ti,ab.
19	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
20	(pyelonephr\$ or pyonephr\$).ti,ab.
21	or/16-20
22	(mucocutaneous adj3 lymph\$).ti,ab.
23	MCLS.ti,ab.
24	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
25	or/22-24
26	pyrogen\$.ti,ab.
27	or/5-6,9-11,14-15,21,25-26
28	and/3-4,27
29	(scor\$ adj system\$).ti,ab.
30	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).ti,ab.
31	((logistic or risk or predict\$) adj3 model\$).ti,ab.
32	(Yale or Rochester).ti,ab.
33	or/29-32
34	and/28,33

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q2_scoring_systems_cctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.

5	or/1-4
6	exp FEVER/
7	(fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/

36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	SEVERITY OF ILLNESS INDEX/
55	(scor\$ adj system\$).ti,ab.
56	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).ti,ab.
57	((logistic or risk or predict\$) adj3 model\$).ti,ab.
58	(Yale or Rochester).ti,ab.
59	or/54-58
60	and/53,59

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_Q2_scoring_systems_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	FEVER.kw.
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw,tx.
8	or/6-7
9	BACTERIAL INFECTIONS.kw.
10	(CRITICAL ILLNESS or ACUTE DISEASE).kw.
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw,tx.
12	or/9-11
13	MENINGITIS, BACTERIAL.kw.
14	MENINGOENCEPHALITIS.kw.
15	mening\$.tw,tx.
16	or/13-15
17	SEPSIS.kw.
18	BACTEREMIA.kw.
19	(sepsis or septic?emi\$).tw,tx.
20	bacter?emi\$.tw,tx.
21	or/17-20
22	PNEUMONIA.kw.
23	pneumon\$.tw,tx.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX.kw.
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw,tx.
27	or/25-26

28	ARTHRITIS, INFECTIOUS.kw.
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw,tx.
30	py?arth\$.tw,tx.
31	or/28-30
32	OSTEOMYELITIS.kw.
33	osteomyelit\$.tw,tx.
34	or/32-33
35	URINARY TRACT INFECTIONS.kw.
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw,tx.
37	((upper or lower) adj5 urin\$).tw,tx.
38	UTI.tw,tx.
39	CYSTITIS.kw.
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw,tx.
41	PYELONEPHRITIS.kw.
42	(pyelonephr\$ or pyonephr\$).tw,tx.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME.kw.
45	(mucocutaneous adj3 lymph\$).tw,tx.
46	MCLS.tw,tx.
47	(kawasaki\$ adj (disease? or syndrome?)).tw,tx.
48	or/44-47
49	PYROGENS.kw.
50	pyrogen\$.tw,tx.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	SEVERITY OF ILLNESS INDEX.kw.
55	(scor\$ adj system\$).ti,ab.
56	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).ti,ab.
57	((logistic or risk or predict\$) adj3 model\$).ti,ab.
58	(Yale or Rochester).ti,ab.

59	or/54-58
60	and/53,59

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012
FICu_Q2_scoring_systems_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.tw.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).tw.
20	bacter?emi\$.tw.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.tw.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw.

27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
30	py?arth\$.tw.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.tw.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw.
37	((upper or lower) adj5 urin\$).tw.
38	UTI.tw.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).tw.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).tw.
46	MCLS.tw.
47	(kawasaki\$ adj (disease? or syndrome?)).tw.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.tw.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	SEVERITY OF ILLNESS INDEX/
55	(scor\$ adj system\$).tw.
56	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).tw.
57	((logistic or risk or predict\$) adj3 model\$).tw.

58	(Yale or Rochester).tw.
59	or/54-58
60	and/53,59

Database(s): Embase 1980 to 2012 Week 39

FICu_Q2_scoring_systems_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	FEVER/
5	HYPERTHERMIA/ or HYPERPYREXIA/
6	PYREXIA IDIOPATHICA/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/4-7
9	exp BACTERIAL INFECTION/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	BACTERIAL MENINGITIS/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPTICEMIA/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23

25	HERPES SIMPLEX ENCEPHALITIS/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp INFECTIOUS ARTHRITIS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	exp OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTION/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGEN/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/3,8,52
54	SCORING SYSTEM/
55	(scor\$ adj system\$).ti,ab.

56	((illness or severity or risk) adj3 (classif\$ or criteri\$ or assess\$ or index\$ or indice? or scale? or scor\$)).ti,ab.
57	((logistic or risk or predict\$) adj3 model\$).ti,ab.
58	(Yale or Rochester).ti,ab.
59	or/54-58
60	and/53,59
61	limit 60 to english language
62	conference abstract.pt.
63	letter.pt. or LETTER/
64	note.pt.
65	editorial.pt.
66	CASE REPORT/ or CASE STUDY/
67	(letter or comment* or abstracts).ti.
68	or/62-67
69	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
70	68 not 69
71	ANIMAL/ not HUMAN/
72	NONHUMAN/
73	exp ANIMAL EXPERIMENT/
74	exp EXPERIMENTAL ANIMAL/
75	ANIMAL MODEL/
76	exp RODENT/
77	(rat or rats or mouse or mice).ti.
78	or/70-77
79	61 not 78

Chapter 5

Heart rate

Review question

The predictive value of heart rate, including:

- how heart rate changes with temperature?
- whether heart rate outside the normal range detects serious illness?
- whether heart rate and temperature outside normal range detects serious illness?

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q6_heart_rate_medline_rerun1_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	HEART RATE/
7	PULSE/
8	exp TACHYCARDIA/ or BRADYCARDIA/
9	(heart adj (rate? or beat?)).ti,ab.
10	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or bradyarrhythmi\$).ti,ab.
11	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).ti,ab.
12	or/6-11
13	exp FEVER/
14	exp BODY TEMPERATURE/
15	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
16	or/13-15
17	and/5,12,16
18	REFERENCE STANDARDS/ or REFERENCE VALUES/
19	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).ti,ab.
20	or/18-19
21	and/17,20
22	exp BACTERIAL INFECTIONS/

23	CRITICAL ILLNESS/ or ACUTE DISEASE/
24	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
25	or/22-24
26	exp MENINGITIS, BACTERIAL/
27	MENINGOENCEPHALITIS/
28	mening\$.ti,ab.
29	or/26-28
30	SEPSIS/
31	exp BACTEREMIA/
32	(sepsis or septic?emi\$).ti,ab.
33	bacter?emi\$.ti,ab.
34	or/30-33
35	exp PNEUMONIA/
36	pneumon\$.ti,ab.
37	or/35-36
38	ENCEPHALITIS, HERPES SIMPLEX/
39	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
40	or/38-39
41	exp ARTHRITIS, INFECTIOUS/
42	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
43	py?arth\$.ti,ab.
44	or/41-43
45	OSTEOMYELITIS/
46	osteomyelit\$.ti,ab.
47	or/45-46
48	exp URINARY TRACT INFECTIONS/
49	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
50	((upper or lower) adj5 urin\$).ti,ab.
51	UTI.ti,ab.
52	exp CYSTITIS/

53	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
54	exp PYELONEPHRITIS/
55	(pyelonephr\$ or pyonephr\$).ti,ab.
56	or/48-55
57	MUCOCUTANEOUS LYMPH NODE SYNDROME/
58	(mucocutaneous adj3 lymph\$).ti,ab.
59	MCLS.ti,ab.
60	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
61	or/57-60
62	exp PYROGENS/
63	pyrogen\$.ti,ab.
64	or/62-63
65	or/25,29,34,37,40,44,47,56,61,64
66	"PREDICTIVE VALUE OF TESTS"/
67	DIAGNOSIS, DIFFERENTIAL/
68	PROGNOSIS/
69	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).ti,ab.
70	or/66-69
71	and/17,65,70
72	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or febril\$ or pyrex\$)).ti,ab.
73	and/5,72
74	or/21,71,73
75	limit 74 to english language
76	LETTER/
77	EDITORIAL/
78	NEWS/
79	exp HISTORICAL ARTICLE/
80	ANECDOTES AS TOPIC/
81	COMMENT/
82	CASE REPORT/

83	(letter or comment* or abstracts).ti.
84	or/76-83
85	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
86	84 not 85
87	ANIMALS/ not HUMANS/
88	exp ANIMALS, LABORATORY/
89	exp ANIMAL EXPERIMENTATION/
90	exp MODELS, ANIMAL/
91	exp RODENTIA/
92	(rat or rats or mouse or mice).ti.
93	or/86-92
94	75 not 93

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_Q6_heart_rate_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.
3	or/1-2
4	(heart adj (rate? or beat?)).ti,ab.
5	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or bradyarrhythmi\$).ti,ab.
6	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).ti,ab.
7	or/4-6
8	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
9	and/3,7-8
10	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).ti,ab.
11	and/9-10
12	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
13	mening\$.ti,ab.
14	(sepsis or septic?emi\$).ti,ab.

15	bacter?emi\$.ti,ab.
16	or/14-15
17	pneumon\$.ti,ab.
18	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
19	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
20	py?arth\$.ti,ab.
21	or/19-20
22	osteomyelit\$.ti,ab.
23	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
24	((upper or lower) adj5 urin\$).ti,ab.
25	UTI.ti,ab.
26	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
27	(pyelonephr\$ or pyonephr\$).ti,ab.
28	or/23-27
29	(mucocutaneous adj3 lymph\$).ti,ab.
30	MCLS.ti,ab.
31	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
32	or/29-31
33	pyrogen\$.ti,ab.
34	or/12-13,16-18,21-22,28,32-33
35	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).ti,ab.
36	and/9,34-35
37	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or febril\$ or pyrex\$)).ti,ab.
38	and/3,37
39	or/11,36,38

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q6_heart_rate_ctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	HEART RATE/
7	PULSE/
8	exp TACHYCARDIA/ or BRADYCARDIA/
9	(heart adj (rate? or beat?)).ti,ab.
10	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or bradyarrhythmi\$).ti,ab.
11	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).ti,ab.
12	or/6-11
13	exp FEVER/
14	exp BODY TEMPERATURE/
15	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
16	or/13-15
17	and/5,12,16
18	REFERENCE STANDARDS/ or REFERENCE VALUES/
19	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).ti,ab.
20	or/18-19
21	and/17,20
22	exp BACTERIAL INFECTIONS/
23	CRITICAL ILLNESS/ or ACUTE DISEASE/
24	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
25	or/22-24
26	exp MENINGITIS, BACTERIAL/
27	MENINGOENCEPHALITIS/

28	mening\$.ti,ab.
29	or/26-28
30	SEPSIS/
31	exp BACTEREMIA/
32	(sepsis or septic?emi\$).ti,ab.
33	bacter?emi\$.ti,ab.
34	or/30-33
35	exp PNEUMONIA/
36	pneumon\$.ti,ab.
37	or/35-36
38	ENCEPHALITIS, HERPES SIMPLEX/
39	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
40	or/38-39
41	exp ARTHRITIS, INFECTIOUS/
42	(arthritis\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
43	py?arth\$.ti,ab.
44	or/41-43
45	OSTEOMYELITIS/
46	osteomyelit\$.ti,ab.
47	or/45-46
48	exp URINARY TRACT INFECTIONS/
49	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
50	((upper or lower) adj5 urin\$).ti,ab.
51	UTI.ti,ab.
52	exp CYSTITIS/
53	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
54	exp PYELONEPHRITIS/
55	(pyelonephr\$ or pyonephr\$).ti,ab.
56	or/48-55
57	MUCOCUTANEOUS LYMPH NODE SYNDROME/
58	(mucocutaneous adj3 lymph\$).ti,ab.

59	MCLS.ti,ab.
60	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
61	or/57-60
62	exp PYROGENS/
63	pyrogen\$.ti,ab.
64	or/62-63
65	or/25,29,34,37,40,44,47,56,61,64
66	"PREDICTIVE VALUE OF TESTS"/
67	DIAGNOSIS, DIFFERENTIAL/
68	PROGNOSIS/
69	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).ti,ab.
70	or/66-69
71	and/17,65,70
72	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or febril\$ or pyrex\$)).ti,ab.
73	and/5,72
74	or/21,71,73

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_Q6_heart_rate_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	HEART RATE.kw.
7	PULSE.kw.
8	(TACHYCARDIA or BRADYCARDIA).kw.
9	(heart adj (rate? or beat?)).tw,tx.
10	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or

	bradyarrhythmi\$).tw,tx.
11	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).tw,tx.
12	or/6-11
13	FEVER.kw.
14	BODY TEMPERATURE.kw.
15	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw,tx.
16	or/13-15
17	and/5,12,16
18	(REFERENCE STANDARDS or REFERENCE VALUES).kw.
19	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).tw,tx.
20	or/18-19
21	and/17,20
22	BACTERIAL INFECTIONS.kw.
23	(CRITICAL ILLNESS or ACUTE DISEASE).kw.
24	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw,tx.
25	or/22-24
26	MENINGITIS, BACTERIAL.kw.
27	MENINGOENCEPHALITIS.kw.
28	mening\$.tw,tx.
29	or/26-28
30	SEPSIS.kw.
31	BACTEREMIA.kw.
32	(sepsis or septic?emi\$).tw,tx.
33	bacter?emi\$.tw,tx.
34	or/30-33
35	PNEUMONIA.kw.
36	pneumon\$.tw,tx.
37	or/35-36
38	ENCEPHALITIS, HERPES SIMPLEX.kw.
39	(encephalit\$ adj5 (herpe\$ or HSV)).tw,tx.
40	or/38-39

41	ARTHRITIS, INFECTIOUS.kw.
42	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw,tx.
43	py?arth\$.tw,tx.
44	or/41-43
45	OSTEOMYELITIS.kw.
46	osteomyelit\$.tw,tx.
47	or/45-46
48	URINARY TRACT INFECTIONS.kw.
49	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw,tx.
50	((upper or lower) adj5 urin\$).tw,tx.
51	UTI.tw,tx.
52	CYSTITIS.kw.
53	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw,tx.
54	PYELONEPHRITIS.kw.
55	(pyelonephr\$ or pyonephr\$).tw,tx.
56	or/48-55
57	MUCOCUTANEOUS LYMPH NODE SYNDROME.kw.
58	(mucocutaneous adj3 lymph\$).tw,tx.
59	MCLS.tw,tx.
60	(kawasaki\$ adj (disease? or syndrome?)).tw,tx.
61	or/57-60
62	PYROGENS.kw.
63	pyrogen\$.tw,tx.
64	or/62-63
65	or/25,29,34,37,40,44,47,56,61,64
66	"PREDICTIVE VALUE OF TESTS".kw.
67	DIAGNOSIS, DIFFERENTIAL.kw.
68	PROGNOSIS.kw.
69	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).tw,tx.
70	or/66-69
71	and/17,65,70

72	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or feбри\$ or pyrex\$)).tw.tx.
73	and/5,72
74	or/21,71,73

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012

FICu_Q6_heart_rate_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	HEART RATE/
7	PULSE/
8	exp TACHYCARDIA/ or BRADYCARDIA/
9	(heart adj (rate? or beat?)).tw.
10	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or bradyarrhythmi\$).tw.
11	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).tw.
12	or/6-11
13	exp FEVER/
14	exp BODY TEMPERATURE/
15	(fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
16	or/13-15
17	and/5,12,16
18	REFERENCE STANDARDS/ or REFERENCE VALUES/
19	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).tw.
20	or/18-19
21	and/17,20
22	exp BACTERIAL INFECTIONS/
23	CRITICAL ILLNESS/ or ACUTE DISEASE/

24	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
25	or/22-24
26	exp MENINGITIS, BACTERIAL/
27	MENINGOENCEPHALITIS/
28	mening\$.tw.
29	or/26-28
30	SEPSIS/
31	exp BACTEREMIA/
32	(sepsis or septic?emi\$).tw.
33	bacter?emi\$.tw.
34	or/30-33
35	exp PNEUMONIA/
36	pneumon\$.tw.
37	or/35-36
38	ENCEPHALITIS, HERPES SIMPLEX/
39	(encephalit\$ adj5 (herpe\$ or HSV)).tw.
40	or/38-39
41	exp ARTHRITIS, INFECTIOUS/
42	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
43	py?arth\$.tw.
44	or/41-43
45	OSTEOMYELITIS/
46	osteomyelit\$.tw.
47	or/45-46
48	exp URINARY TRACT INFECTIONS/
49	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw.
50	((upper or lower) adj5 urin\$).tw.
51	UTI.tw.
52	exp CYSTITIS/
53	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.

54	exp PYELONEPHRITIS/
55	(pyelonephr\$ or pyonephr\$).tw.
56	or/48-55
57	MUCOCUTANEOUS LYMPH NODE SYNDROME/
58	(mucocutaneous adj3 lymph\$).tw.
59	MCLS.tw.
60	(kawasaki\$ adj (disease? or syndrome?)).tw.
61	or/57-60
62	exp PYROGENS/
63	pyrogen\$.tw.
64	or/62-63
65	or/25,29,34,37,40,44,47,56,61,64
66	"PREDICTIVE VALUE OF TESTS"/
67	DIAGNOSIS, DIFFERENTIAL/
68	PROGNOSIS/
69	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).tw.
70	or/66-69
71	and/17,65,70
72	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or feбри\$ or pyrex\$)).tw.
73	and/5,72
74	or/21,71,73

Database(s): Embase 1980 to 2012 Week 39

FICu_Q6_heart_rate_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	exp "HEART RATE AND RHYTHM"/
5	exp TACHYCARDIA/
6	exp BRADYCARDIA/

7	(heart adj (rate? or beat?)).ti,ab.
8	(heart?rate? or heart?beat? or puls\$ or arrhythmi\$ or tachycardi\$ or tachyarrhythmi\$ or bradycardi\$ or bradyarrhythmi\$).ti,ab.
9	(cardi\$ adj3 (monitor\$ or observ\$ or rate?)).ti,ab.
10	or/4-9
11	FEVER/
12	HYPERTHERMIA/ or HYPERPYREXIA/
13	PYREXIA IDIOPATHICA/
14	exp BODY TEMPERATURE/ or BRAIN TEMPERATURE/ or CORE TEMPERATURE/ or SKIN TEMPERATURE/
15	(fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
16	or/11-15
17	and/3,10,16
18	REFERENCE VALUE/ or STANDARD/
19	((refer\$ or normal) adj3 (range? or interval? or value? or standard?)).ti,ab.
20	or/18-19
21	and/17,20
22	exp BACTERIAL INFECTION/
23	CRITICAL ILLNESS/ or ACUTE DISEASE/
24	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
25	or/22-24
26	BACTERIAL MENINGITIS/
27	MENINGOENCEPHALITIS/
28	mening\$.ti,ab.
29	or/26-28
30	SEPTICEMIA/
31	exp BACTEREMIA/
32	(sepsis or septic?emi\$).ti,ab.
33	bacter?emi\$.ti,ab.
34	or/30-33
35	exp PNEUMONIA/
36	pneumon\$.ti,ab.

37	or/35-36
38	HERPES SIMPLEX ENCEPHALITIS/
39	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
40	or/38-39
41	exp INFECTIOUS ARTHRITIS/
42	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
43	py?arth\$.ti,ab.
44	or/41-43
45	exp OSTEOMYELITIS/
46	osteomyelit\$.ti,ab.
47	or/45-46
48	exp URINARY TRACT INFECTION/
49	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
50	((upper or lower) adj5 urin\$).ti,ab.
51	UTI.ti,ab.
52	exp CYSTITIS/
53	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
54	exp PYELONEPHRITIS/
55	(pyelonephr\$ or pyonephr\$).ti,ab.
56	or/48-55
57	MUCOCUTANEOUS LYMPH NODE SYNDROME/
58	(mucocutaneous adj3 lymph\$).ti,ab.
59	MCLS.ti,ab.
60	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
61	or/57-60
62	exp PYROGEN/
63	pyrogen\$.ti,ab.
64	or/62-63
65	or/25,29,34,37,40,44,47,56,61,64
66	PREDICTIVE VALUE/ or DIAGNOSTIC VALUE/
67	DIFFERENTIAL DIAGNOSIS/

68	PROGNOSIS/
69	((infect\$ or ill\$) adj3 (identif\$ or diagnos\$ or predict\$ or distinguish\$ or prognos\$)).ti,ab.
70	or/66-69
71	and/17,65,70
72	((pulse? or heart\$ or cardiac or tachycardi\$) adj5 (increas\$ or decreas\$ or change\$ or relat\$ or correlat\$ or attribute\$ or vary\$ or varies or varia\$ or centile? or range?) adj5 (temperature? or fever\$ or febris\$ or pyrex\$)).ti,ab.
73	and/3,72
74	or/21,71,73
75	limit 74 to english language
76	conference abstract.pt.
77	letter.pt. or LETTER/
78	note.pt.
79	editorial.pt.
80	CASE REPORT/ or CASE STUDY/
81	(letter or comment* or abstracts).ti.
82	or/76-81
83	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
84	82 not 83
85	ANIMAL/ not HUMAN/
86	NONHUMAN/
87	exp ANIMAL EXPERIMENT/
88	exp EXPERIMENTAL ANIMAL/
89	ANIMAL MODEL/
90	exp RODENT/
91	(rat or rats or mouse or mice).ti.
92	or/84-91
93	75 not 92

Chapter 8

Children 3 months and older

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q1_PCT_CRP_dx_medline_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23

25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	CALCITONIN/
55	PROTEIN PRECURSOR/

56	procalcitonin.nm.
57	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
58	or/54-57
59	C-REACTIVE PROTEIN/
60	c-reactive protein.nm.
61	((c reactive or c?reactive) adj1 protein\$).ti,ab.
62	CRP.ti,ab.
63	or/59-62
64	or/58,63
65	and/53,64
66	limit 65 to english language
67	LETTER/
68	EDITORIAL/
69	NEWS/
70	exp HISTORICAL ARTICLE/
71	ANECDOTES AS TOPIC/
72	COMMENT/
73	CASE REPORT/
74	(letter or comment* or abstracts).ti.
75	or/67-74
76	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
77	75 not 76
78	ANIMALS/ not HUMANS/
79	exp ANIMALS, LABORATORY/
80	exp ANIMAL EXPERIMENTATION/
81	exp MODELS, ANIMAL/
82	exp RODENTIA/
83	(rat or rats or mouse or mice).ti.
84	or/77-83
85	66 not 84

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_Q1_PCT_CRP_dx_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.
3	or/1-2
4	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
5	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
6	mening\$.ti,ab.
7	(sepsis or septic?emi\$).ti,ab.
8	bacter?emi\$.ti,ab.
9	or/7-8
10	pneumon\$.ti,ab.
11	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
12	(arthritis\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
13	py?arth\$.ti,ab.
14	or/12-13
15	osteomyelit\$.ti,ab.
16	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
17	((upper or lower) adj5 urin\$).ti,ab.
18	UTI.ti,ab.
19	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
20	(pyelonephr\$ or pyonephr\$).ti,ab.
21	or/16-20
22	(mucocutaneous adj3 lymph\$).ti,ab.
23	MCLS.ti,ab.
24	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
25	or/22-24
26	pyrogen\$.ti,ab.
27	or/5-6,9-11,14-15,21,25-26

28	and/3-4,27
29	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
30	((c reactive or c?reactive) adj1 protein\$).ti,ab.
31	CRP.ti,ab.
32	or/29-31
33	and/28,32

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q1_PCT_CRP_dx_cctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp BACTERIAL INFECTIONS/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20

22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51

53	and/5,8,52
54	CALCITONIN/
55	PROTEIN PRECURSOR/
56	[procalcitonin.nm.]
57	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
58	or/54-57
59	C-REACTIVE PROTEIN/
60	[c-reactive protein.nm.]
61	((c reactive or c?reactive) adj1 protein\$).ti,ab.
62	CRP.ti,ab.
63	or/59-62
64	or/58,63
65	and/53,64

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_Q1_PCT_CRP_dx_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	FEVER.kw.
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw,tx.
8	or/6-7
9	BACTERIAL INFECTIONS.kw.
10	(CRITICAL ILLNESS or ACUTE DISEASE).kw.
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw,tx.
12	or/9-11
13	MENINGITIS, BACTERIAL.kw.

14	MENINGOENCEPHALITIS.kw.
15	mening\$.tw,tx.
16	or/13-15
17	SEPSIS.kw.
18	BACTEREMIA.kw.
19	(sepsis or septic?emi\$).tw,tx.
20	bacter?emi\$.tw,tx.
21	or/17-20
22	PNEUMONIA.kw.
23	pneumon\$.tw,tx.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX.kw.
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw,tx.
27	or/25-26
28	ARTHRITIS, INFECTIOUS.kw.
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw,tx.
30	py?arth\$.tw,tx.
31	or/28-30
32	OSTEOMYELITIS.kw.
33	osteomyelit\$.tw,tx.
34	or/32-33
35	URINARY TRACT INFECTIONS.kw.
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw,tx.
37	((upper or lower) adj5 urin\$).tw,tx.
38	UTI.tw,tx.
39	CYSTITIS.kw.
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw,tx.
41	PYELONEPHRITIS.kw.
42	(pyelonephr\$ or pyonephr\$).tw,tx.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME.kw.

45	(mucocutaneous adj3 lymph\$).tw,tx.
46	MCLS.tw,tx.
47	(kawasaki\$ adj (disease? or syndrome?)).tw,tx.
48	or/44-47
49	PYROGENS.kw.
50	pyrogen\$.tw,tx.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	CALCITONIN.kw.
55	PROTEIN PRECURSOR.kw.
56	(pro?calcitonin\$ or calcitonin\$ or PCT).tw,tx.
57	or/54-56
58	C-REACTIVE PROTEIN.kw.
59	((c reactive or c?reactive) adj1 protein\$).tw,tx.
60	CRP.tw,tx.
61	or/58-60
62	or/57,61
63	and/53,62

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012
 FiCu_Q1_PCT_CRP_dx_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
8	or/6-7
9	exp BACTERIAL INFECTIONS/

10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
12	or/9-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.tw.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).tw.
20	bacter?emi\$.tw.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.tw.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
30	py?arth\$.tw.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.tw.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw.
37	((upper or lower) adj5 urin\$).tw.
38	UTI.tw.
39	exp CYSTITIS/

40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).tw.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).tw.
46	MCLS.tw.
47	(kawasaki\$ adj (disease? or syndrome?)).tw.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.tw.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/5,8,52
54	CALCITONIN/
55	PROTEIN PRECURSOR/
56	(pro?calcitonin\$ or calcitonin\$ or PCT).tw.
57	or/54-56
58	C-REACTIVE PROTEIN/
59	((c reactive or c?reactive) adj1 protein\$).tw.
60	CRP.tw.
61	or/58-60
62	or/57,61
63	and/53,62

Database(s): Embase 1980 to 2012 Week 39

FICu_Q1_PCT_CRP_dx_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	FEVER/

5	HYPERTHERMIA/ or HYPERPYREXIA/
6	PYREXIA IDIOPATHICA/
7	(fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/4-7
9	exp BACTERIAL INFECTION/
10	CRITICAL ILLNESS/ or ACUTE DISEASE/
11	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
12	or/9-11
13	BACTERIAL MENINGITIS/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPTICEMIA/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	HERPES SIMPLEX ENCEPHALITIS/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp INFECTIOUS ARTHRITIS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	exp OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTION/

36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGEN/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	and/3,8,52
54	PROCALCITONIN/
55	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
56	or/54-55
57	C REACTIVE PROTEIN/
58	((c reactive or c?reactive) adj1 protein\$).ti,ab.
59	CRP.ti,ab.
60	or/57-59
61	or/56,60
62	and/53,61
63	limit 62 to english language
64	conference abstract.pt.
65	letter.pt. or LETTER/
66	note.pt.

67	editorial.pt.
68	CASE REPORT/ or CASE STUDY/
69	(letter or comment* or abstracts).ti.
70	or/64-69
71	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
72	70 not 71
73	ANIMAL/ not HUMAN/
74	NONHUMAN/
75	exp ANIMAL EXPERIMENT/
76	exp EXPERIMENTAL ANIMAL/
77	ANIMAL MODEL/
78	exp RODENT/
79	(rat or rats or mouse or mice).ti.
80	or/72-79
81	63 not 80

Collated search strategies: health economics

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q1_PCT_CRP_dx_economic_medline_rerun2_011012

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/

10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp INFANT/
23	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
24	exp CHILD/
25	(child\$ or toddler\$).ti,ab.
26	or/22-25
27	exp FEVER/
28	(fever\$ or febril\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
29	or/27-28
30	exp BACTERIAL INFECTIONS/
31	CRITICAL ILLNESS/ or ACUTE DISEASE/
32	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
33	or/30-32
34	exp MENINGITIS, BACTERIAL/
35	MENINGOENCEPHALITIS/
36	mening\$.ti,ab.
37	or/34-36
38	SEPSIS/
39	exp BACTEREMIA/
40	(sepsis or septic?emi\$).ti,ab.

41	bacter?emi\$.ti,ab.
42	or/38-41
43	exp PNEUMONIA/
44	pneumon\$.ti,ab.
45	or/43-44
46	ENCEPHALITIS, HERPES SIMPLEX/
47	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
48	or/46-47
49	exp ARTHRITIS, INFECTIOUS/
50	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
51	py?arth\$.ti,ab.
52	or/49-51
53	OSTEOMYELITIS/
54	osteomyelit\$.ti,ab.
55	or/53-54
56	exp URINARY TRACT INFECTIONS/
57	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
58	((upper or lower) adj5 urin\$).ti,ab.
59	UTI.ti,ab.
60	exp CYSTITIS/
61	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
62	exp PYELONEPHRITIS/
63	(pyelonephr\$ or pyonephr\$).ti,ab.
64	or/56-63
65	MUCOCUTANEOUS LYMPH NODE SYNDROME/
66	(mucocutaneous adj3 lymph\$).ti,ab.
67	MCLS.ti,ab.
68	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
69	or/65-68
70	exp PYROGENS/
71	pyrogen\$.ti,ab.

72	or/70-71
73	or/33,37,42,45,48,52,55,64,69,72
74	and/26,29,73
75	CALCITONIN/
76	PROTEIN PRECURSOR/
77	procalcitonin.nm.
78	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
79	or/75-78
80	C-REACTIVE PROTEIN/
81	c-reactive protein.nm.
82	((c reactive or c?reactive) adj1 protein\$).ti,ab.
83	CRP.ti,ab.
84	or/80-83
85	or/79,84
86	and/74,85
87	limit 86 to english language
88	LETTER/
89	EDITORIAL/
90	NEWS/
91	exp HISTORICAL ARTICLE/
92	ANECDOTES AS TOPIC/
93	COMMENT/
94	CASE REPORT/
95	(letter or comment* or abstracts).ti.
96	or/88-95
97	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
98	96 not 97
99	ANIMALS/ not HUMANS/
100	exp ANIMALS, LABORATORY/
101	exp ANIMAL EXPERIMENTATION/
102	exp MODELS, ANIMAL/

103	exp RODENTIA/
104	(rat or rats or mouse or mice).ti.
105	or/98-104
106	87 not 105
107	and/21,106

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q1_PCT_CRP_dx_economic_cctr_rerun2_011012

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp INFANT/

23	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
24	exp CHILD/
25	(child\$ or toddler\$).ti,ab.
26	or/22-25
27	exp FEVER/
28	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
29	or/27-28
30	exp BACTERIAL INFECTIONS/
31	CRITICAL ILLNESS/ or ACUTE DISEASE/
32	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
33	or/30-32
34	exp MENINGITIS, BACTERIAL/
35	MENINGOENCEPHALITIS/
36	mening\$.ti,ab.
37	or/34-36
38	SEPSIS/
39	exp BACTEREMIA/
40	(sepsis or septic?emi\$).ti,ab.
41	bacter?emi\$.ti,ab.
42	or/38-41
43	exp PNEUMONIA/
44	pneumon\$.ti,ab.
45	or/43-44
46	ENCEPHALITIS, HERPES SIMPLEX/
47	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
48	or/46-47
49	exp ARTHRITIS, INFECTIOUS/
50	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
51	py?arth\$.ti,ab.
52	or/49-51
53	OSTEOMYELITIS/

54	osteomyelit\$.ti,ab.
55	or/53-54
56	exp URINARY TRACT INFECTIONS/
57	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
58	((upper or lower) adj5 urin\$).ti,ab.
59	UTI.ti,ab.
60	exp CYSTITIS/
61	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
62	exp PYELONEPHRITIS/
63	(pyelonephr\$ or pyonephr\$).ti,ab.
64	or/56-63
65	MUCOCUTANEOUS LYMPH NODE SYNDROME/
66	(mucocutaneous adj3 lymph\$).ti,ab.
67	MCLS.ti,ab.
68	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
69	or/65-68
70	exp PYROGENS/
71	pyrogen\$.ti,ab.
72	or/70-71
73	or/33,37,42,45,48,52,55,64,69,72
74	and/26,29,73
75	CALCITONIN/
76	PROTEIN PRECURSOR/
77	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
78	or/75-77
79	C-REACTIVE PROTEIN/
80	((c reactive or c?reactive) adj1 protein\$).ti,ab.
81	CRP.ti,ab.
82	or/79-81
83	or/78,82
84	and/74,83

85	and/21,84
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Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012, EBM Reviews - NHS Economic Evaluation Database 3rd Quarter 2012

FICu_Q1_PCT_CRP_dx_economic_nhseedhta_rerun2_011012

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp INFANT/
23	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
24	exp CHILD/
25	(child\$ or toddler\$).tw.
26	or/22-25

27	exp FEVER/
28	((fever\$ or feбри\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
29	or/27-28
30	exp BACTERIAL INFECTIONS/
31	CRITICAL ILLNESS/ or ACUTE DISEASE/
32	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
33	or/30-32
34	exp MENINGITIS, BACTERIAL/
35	MENINGOENCEPHALITIS/
36	mening\$.tw.
37	or/34-36
38	SEPSIS/
39	exp BACTEREMIA/
40	(sepsis or septic?emi\$).tw.
41	bacter?emi\$.tw.
42	or/38-41
43	exp PNEUMONIA/
44	pneumon\$.tw.
45	or/43-44
46	ENCEPHALITIS, HERPES SIMPLEX/
47	(encephalit\$ adj5 (herpe\$ or HSV)).tw.
48	or/46-47
49	exp ARTHRITIS, INFECTIOUS/
50	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
51	py?arth\$.tw.
52	or/49-51
53	OSTEOMYELITIS/
54	osteomyelit\$.tw.
55	or/53-54
56	exp URINARY TRACT INFECTIONS/
57	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$

	or uro?gen\$) adj5 infect\$).tw.
58	((upper or lower) adj5 urin\$).tw.
59	UTI.tw.
60	exp CYSTITIS/
61	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.
62	exp PYELONEPHRITIS/
63	(pyelonephr\$ or pyonephr\$).tw.
64	or/56-63
65	MUCOCUTANEOUS LYMPH NODE SYNDROME/
66	(mucocutaneous adj3 lymph\$).tw.
67	MCLS.tw.
68	(kawasaki\$ adj (disease? or syndrome?)).tw.
69	or/65-68
70	exp PYROGENS/
71	pyrogen\$.tw.
72	or/70-71
73	or/33,37,42,45,48,52,55,64,69,72
74	and/26,29,73
75	CALCITONIN/
76	PROTEIN PRECURSOR/
77	(pro?calcitonin\$ or calcitonin\$ or PCT).tw.
78	or/75-77
79	C-REACTIVE PROTEIN/
80	((c reactive or c?reactive) adj1 protein\$).ti,ab.
81	CRP.ti,ab.
82	or/79-81
83	or/78,82
84	and/74,83

Database(s): Embase 1980 to 2012 Week 39

FICu_Q1_PCT_CRP_dx_economic_embase_rerun2_011012

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	budget*.ti,ab.
8	cost*.ti.
9	(economic* or pharmaco?economic*).ti.
10	(price* or pricing*).ti,ab.
11	(cost* adj2 (effective* or utilit* or benefit* or minimi* or unit* or estimat* or variable*)).ab.
12	(financ* or fee or fees).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp CHILD/
19	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
20	or/18-19
21	FEVER/
22	HYPERTHERMIA/ or HYPERPYREXIA/
23	PYREXIA IDIOPATHICA/
24	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
25	or/21-24
26	exp BACTERIAL INFECTION/
27	CRITICAL CARE/ or ACUTE DISEASE/
28	((bacteri\$ or streptococc\$ or staphylococc\$ or serious\$) adj (infect\$ or ill\$)).ti,ab.
29	or/26-28

30	BACTERIAL MENINGITIS/
31	MENINGOENCEPHALITIS/
32	mening\$.ti,ab.
33	or/30-32
34	SEPTICEMIA/
35	exp BACTEREMIA/
36	(sepsis or septic?emi\$).ti,ab.
37	bacter?emi\$.ti,ab.
38	or/34-37
39	exp PNEUMONIA/
40	pneumon\$.ti,ab.
41	or/39-40
42	HERPES SIMPLEX ENCEPHALITIS/
43	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
44	or/42-43
45	exp INFECTIOUS ARTHRITIS/
46	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
47	py?arth\$.ti,ab.
48	or/45-47
49	exp OSTEOMYELITIS/
50	osteomyelit\$.ti,ab.
51	or/49-50
52	exp URINARY TRACT INFECTION/
53	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
54	((upper or lower) adj5 urin\$).ti,ab.
55	UTI.ti,ab.
56	exp CYSTITIS/
57	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
58	exp PYELONEPHRITIS/
59	(pyelonephr\$ or pyonephr\$).ti,ab.
60	or/52-59

61	MUCOCUTANEOUS LYMPH NODE SYNDROME/
62	(mucocutaneous adj3 lymph\$).ti,ab.
63	MCLS.ti,ab.
64	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
65	or/61-64
66	exp PYROGEN/
67	pyrogen\$.ti,ab.
68	or/66-67
69	or/29,33,38,41,44,48,51,60,65,68
70	and/20,25,69
71	PROCALCITONIN/
72	(pro?calcitonin\$ or calcitonin\$ or PCT).ti,ab.
73	or/71-72
74	C REACTIVE PROTEIN/
75	((c reactive or c?reactive) adj1 protein\$).ti,ab.
76	CRP.ti,ab.
77	or/74-76
78	or/73,77
79	and/70,78
80	limit 79 to english language
81	conference abstract.pt.
82	letter.pt. or LETTER/
83	note.pt.
84	editorial.pt.
85	CASE REPORT/ or CASE STUDY/
86	(letter or comment* or abstracts).ti.
87	or/81-86
88	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
89	87 not 88
90	ANIMAL/ not HUMAN/
91	NONHUMAN/

92	exp ANIMAL EXPERIMENT/
93	exp EXPERIMENTAL ANIMAL/
94	ANIMAL MODEL/
95	exp RODENT/
96	(rat or rats or mouse or mice).ti.
97	or/89-96
98	80 not 97
99	and/17,98

Chapter 8

Response to antipyretic medication

Review question

What is the predictive value of the clinical response to paracetamol or NSAIDs?

Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

9.3 Physical and drug interventions

Review question

Effect on fever and associated symptoms of treatment with:

- Paracetamol alone or NSAIDs alone, compared with placebo and with one another
- Alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time
- Paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone.

Collated search strategies for the above review questions on antipyretic interventions

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q3-5_antipyretics_post-2006_medline_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp ANTIPYRETICS/
10	(anti pyretic? or anti?pyretic?).ti,ab.
11	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
12	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or

	anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
15	ACETAMINOPHEN/
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
17	IBUPROFEN/
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
19	or/9-18
20	and/5,8,19
21	limit 20 to english language
22	LETTER/
23	EDITORIAL/
24	NEWS/
25	exp HISTORICAL ARTICLE/
26	ANECDOTES AS TOPIC/
27	COMMENT/
28	CASE REPORT/
29	(letter or comment* or abstracts).ti.
30	or/22-29
31	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
32	30 not 31
33	ANIMALS/ not HUMANS/
34	exp ANIMALS, LABORATORY/
35	exp ANIMAL EXPERIMENTATION/
36	exp MODELS, ANIMAL/
37	exp RODENTIA/
38	(rat or rats or mouse or mice).ti.
39	or/32-38
40	21 not 39

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_Q3-5_antipyretics_post-2006_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.
3	or/1-2
4	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
5	(anti pyretic? or anti?pyretic?).ti,ab.
6	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
7	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
8	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
9	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or dispol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
10	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
11	or/5-10
12	and/3-4,11

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q3-5_antipyretics_post-2006_ctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/6-7
9	exp ANTIPYRETICS/
10	(anti pyretic? or anti?pyretic?).ti,ab.

11	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
12	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
15	ACETAMINOPHEN/
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
17	IBUPROFEN/
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
19	or/9-18
20	and/5,8,19

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_Q3-5_antipyretics_post-2006_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	FEVER.kw.
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw,tx.
8	or/6-7
9	ANTIPYRETICS.kw.
10	(anti pyretic? or anti?pyretic?).tw,tx.
11	ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL.kw.
12	(NSAID? or NAID? or NSAIA? or NSAIM?).tw,tx.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw,tx.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw,tx.

15	ACETAMINOPHEN.kw.
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).tw,tx.
17	IBUPROFEN.kw.
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).tw,tx.
19	or/9-18
20	and/5,8,19

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012

FICu_Q3-5_antipyretics_post-2006_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
8	or/6-7
9	exp ANALGESICS, NON-NARCOTIC/
10	(anti pyretic? or anti?pyretic?).tw.
11	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
12	(NSAID? or NAID? or NSAIA? or NSAIM?).tw.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
15	ACETAMINOPHEN/
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).tw.
17	IBUPROFEN/
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).tw.
19	or/9-18

20	and/5,8,19
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Database(s): Embase 1980 to 2012 Week 39

FICu_Q3-5_antipyretics_post-2006_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	FEVER/
5	HYPERTHERMIA/ or HYPERPYREXIA/
6	PYREXIA IDIOPATHICA/
7	((fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
8	or/4-7
9	ANTIPYRETIC AGENT/
10	(anti pyretic? or anti?pyretic?).ti,ab.
11	exp NONSTEROID ANTIINFLAMMATORY AGENT/
12	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
15	PARACETAMOL/
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
17	IBUPROFEN/
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
19	or/9-18
20	and/3,8,19
21	limit 20 to english language
22	conference abstract.pt.
23	letter.pt. or LETTER/
24	note.pt.
25	editorial.pt.

26	CASE REPORT/ or CASE STUDY/
27	(letter or comment* or abstracts).ti.
28	or/22-27
29	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
30	28 not 29
31	ANIMAL/ not HUMAN/
32	NONHUMAN/
33	exp ANIMAL EXPERIMENT/
34	exp EXPERIMENTAL ANIMAL/
35	ANIMAL MODEL/
36	exp RODENT/
37	(rat or rats or mouse or mice).ti.
38	or/30-37
39	21 not 38

Collated search strategies on antipyretic intervention: health economics

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_Q3-5_antipyretics_economic_medline_rerun2_011012

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.

13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp INFANT/
23	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
24	exp CHILD/
25	(child\$ or toddler\$).ti,ab.
26	or/22-25
27	exp FEVER/
28	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
29	or/27-28
30	exp ANTIPYRETICS/
31	(anti pyretic? or anti?pyretic?).ti,ab.
32	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
33	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
34	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
35	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
36	ACETAMINOPHEN/
37	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
38	IBUPROFEN/
39	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
40	or/30-39
41	and/26,29,40

42	LETTER/
43	EDITORIAL/
44	NEWS/
45	exp HISTORICAL ARTICLE/
46	ANECDOTES AS TOPIC/
47	COMMENT/
48	CASE REPORT/
49	(letter or comment* or abstracts).ti.
50	or/42-49
51	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52	50 not 51
53	ANIMALS/ not HUMANS/
54	exp ANIMALS, LABORATORY/
55	exp ANIMAL EXPERIMENTATION/
56	exp MODELS, ANIMAL/
57	exp RODENTIA/
58	(rat or rats or mouse or mice).ti.
59	or/52-58
60	41 not 59
61	limit 60 to english language
62	and/21,61

**Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials
September 2012**

FICu_Q3-5_antipyretics_economic_cctr_rerun2_011012

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/

7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp INFANT/
23	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
24	exp CHILD/
25	(child\$ or toddler\$).ti,ab.
26	or/22-25
27	exp FEVER/
28	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
29	or/27-28
30	exp ANTIPYRETICS/
31	(anti pyretic? or anti?pyretic?).ti,ab.
32	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
33	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
34	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
35	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
36	ACETAMINOPHEN/

37	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
38	IBUPROFEN/
39	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
40	or/30-39
41	and/26,29,40
42	and/21,41

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012, EBM Reviews - NHS Economic Evaluation Database 3rd Quarter 2012

FICu_Q3-5_antipyretics_economic_htanhseed_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.
3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	exp FEVER/
7	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).tw.
8	or/6-7
9	exp ANTIPYRETICS/
10	(anti pyretic? or anti?pyretic?).tw.
11	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
12	(NSAID? or NAID? or NSAIA? or NSAIM?).tw.
13	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
14	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
15	ACETAMINOPHEN/
16	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).tw.
17	IBUPROFEN/
18	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).tw.

19	or/9-18
20	and/5,8,19

Database(s): Embase 1980 to 2012 Week 39

FICu_Q3-5_antipyretics_economic_embase_rerun2_011012

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.
17	or/1-16
18	exp CHILD/
19	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
20	or/18-19
21	FEVER/
22	HYPERTHERMIA/ or HYPERPYREXIA/
23	PYREXIA IDIOPATHICA/
24	(fever\$ or febrile\$ or hyper therm\$ or hyper?therm\$ or pyrex\$ or hyper?pyrex\$ or temperature?).ti,ab.
25	or/21-24
26	ANTIPYRETIC AGENT/

27	(anti pyretic? or anti?pyretic?).ti,ab.
28	exp NONSTEROID ANTIINFLAMMATORY AGENT/
29	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
30	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
31	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
32	PARACETAMOL/
33	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
34	IBUPROFEN/
35	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
36	or/26-35
37	and/20,25,36
38	conference abstract.pt.
39	letter.pt. or LETTER/
40	note.pt.
41	editorial.pt.
42	CASE REPORT/ or CASE STUDY/
43	(letter or comment* or abstracts).ti.
44	or/38-43
45	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
46	44 not 45
47	ANIMAL/ not HUMAN/
48	NONHUMAN/
49	exp ANIMAL EXPERIMENT/
50	exp EXPERIMENTAL ANIMAL/
51	ANIMAL MODEL/
52	exp RODENT/
53	(rat or rats or mouse or mice).ti.
54	or/46-53
55	37 not 54

56	and/17,55
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Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

Database(s): Ovid MEDLINE(R) 1946 to September Week 3 2012

FICu_antipyretics_masking_medline_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	*INFECTION/ or *COMMUNICABLE DISEASES/
7	VIRUS DISEASES/
8	exp BACTERIAL INFECTIONS/
9	CRITICAL ILLNESS/ or ACUTE DISEASE/
10	((bacteri\$ or virus or viral or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
11	(infect\$ adj disease?).ti.
12	or/6-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/

23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp ANTIPYRETICS/

54	(anti pyretic? or anti?pyretic?).ti,ab.
55	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
56	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
57	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
58	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
59	ACETAMINOPHEN/
60	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
61	IBUPROFEN/
62	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
63	or/53-62
64	and/5,52,63
65	limit 64 to english language
66	LETTER/
67	EDITORIAL/
68	NEWS/
69	exp HISTORICAL ARTICLE/
70	ANECDOTES AS TOPIC/
71	COMMENT/
72	CASE REPORT/
73	(letter or comment* or abstracts).ti.
74	or/66-73
75	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
76	74 not 75
77	ANIMALS/ not HUMANS/
78	exp ANIMALS, LABORATORY/
79	exp ANIMAL EXPERIMENTATION/
80	exp MODELS, ANIMAL/
81	exp RODENTIA/
82	(rat or rats or mouse or mice).ti.

83	or/76-82
84	65 not 83

**Database(s): Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations
September 28, 2012**

FICu_antipyretics_masking_mip_rerun2_011012

#	Searches
1	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
2	(child\$ or toddler\$).ti,ab.
3	or/1-2
4	((bacteri\$ or virus or viral or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
5	(infect\$ adj disease?).ti.
6	mening\$.ti,ab.
7	(sepsis or septic?emi\$).ti,ab.
8	bacter?emi\$.ti,ab.
9	pneumon\$.ti,ab.
10	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
11	(arthritis\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
12	py?arth\$.ti,ab.
13	osteomyelit\$.ti,ab.
14	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
15	((upper or lower) adj5 urin\$).ti,ab.
16	UTI.ti,ab.
17	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
18	(pyelonephr\$ or pyonephr\$).ti,ab.
19	(mucocutaneous adj3 lymph\$).ti,ab.
20	MCLS.ti,ab.
21	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
22	pyrogen\$.ti,ab.
23	or/4-22
24	(anti pyretic? or anti?pyretic?).ti,ab.

25	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
26	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
27	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
28	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
29	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
30	or/24-29
31	and/3,23,30

Database(s): EBM Reviews - Cochrane Central Register of Controlled Trials September 2012

FICu_antipyretics_masking_cctr_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).ti,ab.
3	exp CHILD/
4	(child\$ or toddler\$).ti,ab.
5	or/1-4
6	*INFECTION/ or *COMMUNICABLE DISEASES/
7	VIRUS DISEASES/
8	exp BACTERIAL INFECTIONS/
9	CRITICAL ILLNESS/ or ACUTE DISEASE/
10	((bacteri\$ or virus or viral or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
11	(infect\$ adj disease?).ti.
12	or/6-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.ti,ab.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/

19	(sepsis or septic?emi\$).ti,ab.
20	bacter?emi\$.ti,ab.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.ti,ab.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
30	py?arth\$.ti,ab.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.ti,ab.
34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
37	((upper or lower) adj5 urin\$).ti,ab.
38	UTI.ti,ab.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).ti,ab.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).ti,ab.
46	MCLS.ti,ab.
47	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
48	or/44-47
49	exp PYROGENS/

50	pyrogen\$.ti,ab.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp ANTIPYRETICS/
54	(anti pyretic? or anti?pyretic?).ti,ab.
55	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
56	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
57	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
58	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
59	ACETAMINOPHEN/
60	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
61	IBUPROFEN/
62	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
63	or/53-62
64	and/5,52,63

Database(s): EBM Reviews - Cochrane Database of Systematic Reviews 2005 to September 2012, EBM Reviews - Database of Abstracts of Reviews of Effects 3rd Quarter 2012

FICu_antipyretics_masking_cdsrdare_rerun2_011012

#	Searches
1	INFANT.kw.
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw,tx.
3	CHILD.kw.
4	(child\$ or toddler\$).tw,tx.
5	or/1-4
6	(INFECTION or COMMUNICABLE DISEASES).kw.
7	VIRUS DISEASES.kw.
8	BACTERIAL INFECTIONS.kw.
9	(CRITICAL ILLNESS or ACUTE DISEASE).kw.
10	((bacteri\$ or virus or viral or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj

	(infect\$ or ill\$ or disease?).tw,tx.
11	(infect\$ adj disease?).ti.
12	or/6-11
13	MENINGITIS, BACTERIAL.kw.
14	MENINGOENCEPHALITIS.kw.
15	mening\$.tw,tx.
16	or/13-15
17	SEPSIS.kw.
18	BACTEREMIA.kw.
19	(sepsis or septic?emi\$).tw,tx.
20	bacter?emi\$.tw,tx.
21	or/17-20
22	PNEUMONIA.kw.
23	pneumon\$.tw,tx.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX.kw.
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw,tx.
27	or/25-26
28	ARTHRITIS, INFECTIOUS.kw.
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw,tx.
30	py?arth\$.tw,tx.
31	or/28-30
32	OSTEOMYELITIS.kw.
33	osteomyelit\$.tw,tx.
34	or/32-33
35	URINARY TRACT INFECTIONS.kw.
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw,tx.
37	((upper or lower) adj5 urin\$).tw,tx.
38	UTI.tw,tx.
39	CYSTITIS.kw.
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw,tx.

41	PYELONEPHRITIS.kw.
42	(pyelonephr\$ or pyonephr\$).tw,tx.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME.kw.
45	(mucocutaneous adj3 lymph\$).tw,tx.
46	MCLS.tw,tx.
47	(kawasaki\$ adj (disease? or syndrome?)).tw,tx.
48	or/44-47
49	PYROGENS.kw.
50	pyrogen\$.tw,tx.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	ANTIPYRETICS.kw.
54	(anti pyretic? or anti?pyretic?).tw,tx.
55	ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL.kw.
56	(NSAID? or NAID? or NSAIA? or NSAIM?).tw,tx.
57	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw,tx.
58	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw,tx.
59	ACETAMINOPHEN.kw.
60	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).tw,tx.
61	IBUPROFEN.kw.
62	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).tw,tx.
63	or/53-62
64	and/5,52,63

Database(s): EBM Reviews - Health Technology Assessment 3rd Quarter 2012
 FICu_antipyretics_masking_hta_rerun2_011012

#	Searches
1	exp INFANT/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies).tw.

3	exp CHILD/
4	(child\$ or toddler\$).tw.
5	or/1-4
6	INFECTION/ or COMMUNICABLE DISEASES/
7	VIRUS DISEASES/
8	exp BACTERIAL INFECTIONS/
9	CRITICAL ILLNESS/ or ACUTE DISEASE/
10	((bacteri\$ or virus or viral or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).tw.
11	(infect\$ adj disease?).ti.
12	or/6-11
13	exp MENINGITIS, BACTERIAL/
14	MENINGOENCEPHALITIS/
15	mening\$.tw.
16	or/13-15
17	SEPSIS/
18	exp BACTEREMIA/
19	(sepsis or septic?emi\$).tw.
20	bacter?emi\$.tw.
21	or/17-20
22	exp PNEUMONIA/
23	pneumon\$.tw.
24	or/22-23
25	ENCEPHALITIS, HERPES SIMPLEX/
26	(encephalit\$ adj5 (herpe\$ or HSV)).tw.
27	or/25-26
28	exp ARTHRITIS, INFECTIOUS/
29	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).tw.
30	py?arth\$.tw.
31	or/28-30
32	OSTEOMYELITIS/
33	osteomyelit\$.tw.

34	or/32-33
35	exp URINARY TRACT INFECTIONS/
36	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).tw.
37	((upper or lower) adj5 urin\$).tw.
38	UTI.tw.
39	exp CYSTITIS/
40	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).tw.
41	exp PYELONEPHRITIS/
42	(pyelonephr\$ or pyonephr\$).tw.
43	or/35-42
44	MUCOCUTANEOUS LYMPH NODE SYNDROME/
45	(mucocutaneous adj3 lymph\$).tw.
46	MCLS.tw.
47	(kawasaki\$ adj (disease? or syndrome?)).tw.
48	or/44-47
49	exp PYROGENS/
50	pyrogen\$.tw.
51	or/49-50
52	or/12,16,21,24,27,31,34,43,48,51
53	exp ANALGESICS, NON-NARCOTIC/
54	(anti pyretic? or anti?pyretic?).tw.
55	exp ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
56	(NSAID? or NAID? or NSAIA? or NSAIM?).tw.
57	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
58	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).tw.
59	ACETAMINOPHEN/
60	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or dispol or medinol or hedex or panadol or parapaed or tylenol).tw.
61	IBUPROFEN/
62	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or

	orbifen or fenbid).tw.
63	or/53-62
64	and/5,52,63

Database(s): Embase 1980 to 2012 Week 39

FICu_antipyretics_masking_embase_rerun2_011012

#	Searches
1	exp CHILD/
2	(infan\$ or neonat\$ or newborn\$ or baby or babies or child\$ or toddler\$).ti,ab.
3	or/1-2
4	*INFECTION/ or *COMMUNICABLE DISEASE/
5	VIRAL INFECTION/
6	exp BACTERIAL INFECTION/
7	CRITICAL ILLNESS/ or ACUTE DISEASE/
8	((bacteri\$ or viral or virus or streptococc\$ or staphylococc\$ or serious\$ or severe\$ or critical\$ or acute\$) adj (infect\$ or ill\$ or disease?)).ti,ab.
9	(infect\$ adj disease?).ti.
10	or/4-9
11	BACTERIAL MENINGITIS/
12	MENINGOENCEPHALITIS/
13	mening\$.ti,ab.
14	or/11-13
15	SEPTICEMIA/
16	exp BACTEREMIA/
17	(sepsis or septic?emi\$).ti,ab.
18	bacter?emi\$.ti,ab.
19	or/15-18
20	exp PNEUMONIA/
21	pneumon\$.ti,ab.
22	or/20-21
23	HERPES SIMPLEX ENCEPHALITIS/
24	(encephalit\$ adj5 (herpe\$ or HSV)).ti,ab.

25	or/23-24
26	exp INFECTIOUS ARTHRITIS/
27	(arthrit\$ adj3 (bacteri\$ or septic\$ or infect\$ or suppurat\$ or purulen\$ or pyogen\$)).ti,ab.
28	py?arth\$.ti,ab.
29	or/26-28
30	exp OSTEOMYELITIS/
31	osteomyelit\$.ti,ab.
32	or/30-31
33	exp URINARY TRACT INFECTION/
34	((urin\$ or bladder\$ or genito?urin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urolog\$ or uro gen\$ or uro?gen\$) adj5 infect\$).ti,ab.
35	((upper or lower) adj5 urin\$).ti,ab.
36	UTI.ti,ab.
37	exp CYSTITIS/
38	(cystit\$ or pyocystit\$ or pyelocystit\$ or cystopyelit\$).ti,ab.
39	exp PYELONEPHRITIS/
40	(pyelonephr\$ or pyonephr\$).ti,ab.
41	or/33-40
42	MUCOCUTANEOUS LYMPH NODE SYNDROME/
43	(mucocutaneous adj3 lymph\$).ti,ab.
44	MCLS.ti,ab.
45	(kawasaki\$ adj (disease? or syndrome?)).ti,ab.
46	or/42-45
47	exp PYROGEN/
48	pyrogen\$.ti,ab.
49	or/47-48
50	or/10,14,19,22,25,29,32,41,46,49
51	ANTIPYRETIC AGENT/
52	(anti pyretic? or anti?pyretic?).ti,ab.
53	exp NONSTEROID ANTIINFLAMMATORY AGENT/
54	(NSAID? or NAID? or NSAIA? or NSAIM?).ti,ab.
55	((non steroid\$ or non?steroid\$) adj3 (anti inflammatory or anti?inflammatory or anti rheumatic or

	anti?rheumatic) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
56	((aspirin like or aspirin?like or anti nocicept\$ or anti?nocicept\$) adj3 (agent? or ana?lgesi\$ or drug? or medicine?)).ti,ab.
57	PARACETAMOL/
58	(paracetamol or acetaminophen or alvedon or anadin or calpol or perfalgan or disprol or medinol or hedex or panadol or parapaed or tylenol).ti,ab.
59	IBUPROFEN/
60	(ibuprofen or brufen or calprofen or cuprofen or arthrofen or ebufac or rimafen or feverfen or nurofen or orbifen or fenbid).ti,ab.
61	or/51-60
62	and/3,50,61
63	limit 62 to english language
64	conference abstract.pt.
65	letter.pt. or LETTER/
66	note.pt.
67	editorial.pt.
68	CASE REPORT/ or CASE STUDY/
69	(letter or comment* or abstracts).ti.
70	or/64-69
71	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
72	70 not 71
73	ANIMAL/ not HUMAN/
74	NONHUMAN/
75	exp ANIMAL EXPERIMENT/
76	exp EXPERIMENTAL ANIMAL/
77	ANIMAL MODEL/
78	exp RODENT/
79	(rat or rats or mouse or mice).ti.
80	or/72-79
81	63 not 80

2007 Search strategies

FEVER_bacterial_causes_medline_261005

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. exp BACTERIAL INFECTIONS/
31. exp BACTERIA/
32. bacteri\$.tw.
33. eubacteri\$.tw.
34. bacillacea\$.tw.
35. or/30-34
36. and/29,35
37. exp GREAT BRITAIN/

38. and/36-37

39. limit 38 to yr="1992 - 2005"

FEVER_bacterial_cause_embase_261005

1. PREMATURITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp FEVER/

19. PYREXIA IDIOPATHICA/

20. fever\$.tw.

21. febril\$.tw.

22. hypertherm\$.tw.

23. pyrexia\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGEN/

27. pyrogen\$.tw.

28. or/18-27

29. and/17,28

30. exp BACTERIUM/

31. BACTERIAL STRAIN/

32. exp BACTERIAL INFECTION/

33. bacteri\$.tw.

34. eubacteri\$.tw.

35. bacillacea\$.tw.

36. or/30-35

37. and/29,36
 38. UNITED KINGDOM/
 39. and/37-38
 40. limit 39 to yr="1992 - 2006"
- FEVER_bacterial_cause_cinahl_261005**
1. INFANT, PREMATURE/
 2. INFANT, POSTMATURE/
 3. LOW BIRTH WEIGHT/
 4. (low adj birth adj weight).tw.
 5. lbw.tw.
 6. VERY LOW BIRTH WEIGHT/
 7. vlbw.tw.
 8. INFANT, NEWBORN/
 9. neonat\$.tw.
 10. newborn\$.tw.
 11. exp INFANT/
 12. infan\$.tw.
 13. PRESCHOOL CHILD/
 14. (baby or babies).tw.
 15. (child\$ adj5 pre?school).tw.
 16. toddler\$.tw.
 17. or/1-16
 18. exp FEVER/
 19. "FEVER OF UNKNOWN ORIGIN"/
 20. fever\$.tw.
 21. febril\$.tw.
 22. hypertherm\$.tw.
 23. pyrexia\$.tw.
 24. MALIGNANT HYPERTHERMIA/
 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
 26. exp PYROGENS/
 27. pyrogen\$.tw.
 28. or/18-27
 29. and/17,28
 30. exp BACTERIAL INFECTIONS/
 31. exp BACTERIA/
 32. bacteri\$.tw.
 33. eubacteri\$.tw.
 34. bacillacea\$.tw.

- 35. or/30-34
- 36. and/29,35
- 37. exp GREAT BRITAIN/
- 38. and/36-37
- 39. limit 38 to yr="1992 - 2005"

FEVER_consultation_referral_medline_280206

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. INFANT, VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. CHILD, PRESCHOOL/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. "FEVER OF UNKNOWN ORIGIN"/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 26. exp PYROGENS/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. BACTERIAL INFECTIONS/
- 31. (bacteri\$ adj infect\$).tw.
- 32. or/30-31
- 33. exp MENINGITIS, BACTERIAL/

-
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
 35. meningococc\$.tw.
 36. or/33-35
 37. SEPTICEMIA/
 38. septicemi\$.tw.
 39. septicaemia\$.tw.
 40. or/37-39
 41. BACTEREMIA/
 42. bacteremi\$.tw.
 43. bacteraemia\$.tw.
 44. or/41-43
 45. exp PNEUMONIA/
 46. pneumoni\$.tw.
 47. or/45-46
 48. HERPES SIMPLEX/
 49. herpes simplex.tw.
 50. or/48-49
 51. exp ARTHRITIS, INFECTIOUS/
 52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
 53. pyarthrosis.tw.
 54. pyoarthritis.tw.
 55. or/51-54
 56. STAPHYLOCOCCAL INFECTIONS/
 57. STREPTOCOCCAL INFECTIONS/
 58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
 59. or/56-58
 60. OSTEOMYELITIS/
 61. osteomyeliti\$.tw.
 62. or/60-61
 63. exp URINARY TRACT INFECTIONS/
 64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
 65. UTI.tw.
 66. ((upper or lower) adj5 urin\$).tw.
 67. exp CYSTITIS/
 68. cystitis\$.tw.
 69. PYELONEPHRITIS/
 70. pyelonephriti\$.tw.

- 71. pyonephrosi\$.tw.
- 72. pyelocystiti\$.tw.
- 73. or/63-72
- 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 75. (mucocutaneous adj2 lymph\$).tw.
- 76. mcls.tw.
- 77. (kawasaki adj (disease or syndrome)).tw.
- 78. or/74-77
- 79. or/32,36,40,44,47,50,55,59,62,73,78
- 80. and/29,79
- 81. "REFERRAL AND CONSULTATION"/
- 82. refer\$.tw.
- 83. consult\$.tw.
- 84. or/81-83
- 85. "ATTITUDE TO HEALTH"/
- 86. DECISION MAKING/
- 87. "HEALTH KNOWLEDGE, ATTITUDES, PRACTICE"/
- 88. or/85-87
- 89. or/84-88
- 90. and/80,89
- 91. animal/ not (human/ or (human/ and animal/))
- 92. 90 not 91

FEVER_consultation_referral_embase_280206

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.

17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTION/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. BACTERIAL MENINGITIS/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. BACTERIAL ARTHRITIS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.

- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTION/
- 57. STREPTOCOCCAL INFECTION/
- 58. straphylococc\$.tw.
- 59. streptococc\$.tw.
- 60. or/56-59
- 61. OSTEOMYELITIS/
- 62. osteomyeliti\$.tw.
- 63. or/61-62
- 64. exp URINARY TRACT INFECTION/
- 65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 66. UTI.tw.
- 67. ((upper or lower) adj5 urin\$).tw.
- 68. exp CYSTITIS/
- 69. cystitis\$.tw.
- 70. or/64-69
- 71. PYELONEPHRITIS/
- 72. pyelonephriti\$.tw.
- 73. pyonephrosi\$.tw.
- 74. pyelocystiti\$.tw.
- 75. or/71-74
- 76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 77. (mucocutaneous adj2 lymph\$).tw.
- 78. mcls.tw.
- 79. (kawasaki adj (disease or syndrome)).tw.
- 80. or/76-79
- 81. or/32,36,40,44,47,50,55,60,63,70,75,80
- 82. and/29,81
- 83. PATIENT REFERRAL/
- 84. refer\$.tw.
- 85. consult\$.tw.
- 86. or/83-85
- 87. ATTITUDE/
- 88. DECISION MAKING/
- 89. or/87-88
- 90. or/86,89
- 91. and/82,90
- 92. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

93. 91 not 92

FEVER_consultation_referral_cinahl_280206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35

37. exp SEPSIS/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTION/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. CYSTITIS/
68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/

75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79
81. "REFERRAL AND CONSULTATION"/
82. refer\$.tw.
83. consult\$.tw.
84. or/81-83
85. "ATTITUDE TO HEALTH"/
86. DECISION MAKING/
87. "HEALTH KNOWLEDGE, ATTITUDES, PRACTICE"/
88. or/85-87
89. or/84,88
90. and/80,89

FEVER_diagnosis_capillary_refill_medline_240406

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/

- 22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 23. meningococc\$.tw.
- 24. or/21-23
- 25. SEPTICEMIA/
- 26. septicemi\$.tw.
- 27. septicaemia\$.tw.
- 28. or/25-27
- 29. BACTEREMIA/
- 30. bacteremi\$.tw.
- 31. bacteraemia\$.tw.
- 32. or/29-31
- 33. exp PNEUMONIA/
- 34. pneumoni\$.tw.
- 35. or/33-34
- 36. HERPES SIMPLEX/
- 37. herpes simplex.tw.
- 38. or/36-37
- 39. exp ARTHRITIS, INFECTIOUS/
- 40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 41. pyarthrosis.tw.
- 42. pyoarthritis.tw.
- 43. or/39-42
- 44. STAPHYLOCOCCAL INFECTIONS/
- 45. STREPTOCOCCAL INFECTIONS/
- 46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 47. or/44-46
- 48. OSTEOMYELITIS/
- 49. osteomyeliti\$.tw.
- 50. or/48-49
- 51. exp URINARY TRACT INFECTIONS/
- 52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 53. UTI.tw.
- 54. ((upper or lower) adj5 urin\$).tw.
- 55. exp CYSTITIS/
- 56. cystitis\$.tw.
- 57. PYELONEPHRITIS/
- 58. pyelonephriti\$.tw.

59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp MICROCIRCULATION/
69. CAPILLARIES/
70. capillar\$.tw.
71. or/68-70
72. exp "SENSITIVITY AND SPECIFICITY"/
73. (sensitivity or specificity).tw.
74. (predictive adj value\$).tw.
75. LIKELIHOOD FUNCTIONS/
76. (likelihood adj (estimate\$ or ratio\$)).tw.
77. exp DIAGNOSTIC ERRORS/
78. (false adj (negative\$ or positive\$)).tw.
79. "REPRODUCIBILITY OF RESULTS"/
80. DIAGNOSIS, DIFFERENTIAL/
81. (differential adj diagnos\$).tw.
82. or/72-81
83. and/17,67,71,82
84. animal/ not (human/ or (human/ and animal/))
85. 83 not 84

FEVER_diagnosis_capillary_refill_embase_240406

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/

12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTION/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. BACTERIAL MENINGITIS/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. BACTERIAL ARTHRITIS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTION/
45. STREPTOCOCCAL INFECTION/
46. straphylococc\$.tw.
47. streptococc\$.tw.
48. or/44-47
49. OSTEOMYELITIS/

50. osteomyeliti\$.tw.
51. or/49-50
52. exp URINARY TRACT INFECTION/
53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
54. UTI.tw.
55. ((upper or lower) adj5 urin\$).tw.
56. exp CYSTITIS/
57. cystitis\$.tw.
58. or/52-57
59. PYELONEPHRITIS/
60. pyelonephriti\$.tw.
61. pyonephrosi\$.tw.
62. pyelocystiti\$.tw.
63. or/59-62
64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
65. (mucocutaneous adj2 lymph\$).tw.
66. mcls.tw.
67. (kawasaki adj (disease or syndrome)).tw.
68. or/64-67
69. or/20,24,28,32,35,38,43,48,51,58,63,68
70. CAPILLARY FLOW/
71. capillar\$.tw.
72. or/70-71
73. exp "SENSITIVITY AND SPECIFICITY"/
74. (sensitivity or specificity).tw.
75. (predictive adj value\$).tw.
76. STATISTICAL MODEL/
77. (likelihood adj (estimate\$ or ratio\$)).tw.
78. DIAGNOSTIC ERROR/
79. (false adj (negative\$ or positive\$)).tw.
80. REPRODUCIBILITY/
81. DIFFERENTIAL DIAGNOSIS/
82. (differential adj diagnos\$).tw.
83. or/73-82
84. and/17,69,72,83
85. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
86. 84 not 85

FEVER_diagnosis_capillary_refill_cinahl_240406

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. exp SEPSIS/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.

38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTION/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. capillar\$.tw.
69. and/17,67-68

FEVER_diagnosis_health_economics_medline_100506

1. INFANT, PREMATURE/
2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.
3. INFANT, POSTMATURE/
4. ((postmature\$ or postterm\$ or post?term\$) adj (baby or babies or child\$ or infan\$)).tw.
5. INFANT, NEWBORN/

6. neonat\$.tw.
7. newborn\$.tw.
8. exp INFANT/
9. infan\$.tw.
10. INFANT, SMALL FOR GESTATIONAL AGE/
11. (small adj2 gestational age).tw.
12. INFANT, LOW BIRTH WEIGHT/
13. INFANT, VERY LOW BIRTH WEIGHT/
14. (low adj birth adj weight).tw.
15. (low adj birth?weight).tw.
16. lbw.tw.
17. vlbw.tw.
18. (baby or babies).tw.
19. CHILD, PRESCHOOL/
20. toddler\$.tw.
21. exp CHILD/
22. child\$.tw.
23. ADOLESCENT/
24. adolescen\$.tw.
25. juvenile\$.tw.
26. youth\$.tw.
27. teen\$.tw.
28. PUBERTY/
29. pubert\$.tw.
30. pubesc\$.tw.
31. MINORS/
32. minors.tw.
33. or/1-32
34. BACTERIAL INFECTIONS/
35. (bacteri\$ adj infect\$).tw.
36. or/34-35
37. exp MENINGITIS, BACTERIAL/
38. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
39. meningococc\$.tw.
40. or/37-39
41. SEPTICEMIA/
42. septicemi\$.tw.
43. septicaemia\$.tw.

44. or/41-43
45. BACTEREMIA/
46. bacteremi\$.tw.
47. bacteraemia\$.tw.
48. or/45-47
49. exp PNEUMONIA/
50. pneumoni\$.tw.
51. or/49-50
52. HERPES SIMPLEX/
53. herpes simplex.tw.
54. or/52-53
55. exp ARTHRITIS, INFECTIOUS/
56. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
57. pyarthrosis.tw.
58. pyoarthritis.tw.
59. or/55-58
60. STAPHYLOCOCCAL INFECTIONS/
61. STREPTOCOCCAL INFECTIONS/
62. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
63. or/60-62
64. OSTEOMYELITIS/
65. osteomyeliti\$.tw.
66. or/64-65
67. exp URINARY TRACT INFECTIONS/
68. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
69. UTI.tw.
70. ((upper or lower) adj5 urin\$).tw.
71. exp CYSTITIS/
72. cystitis\$.tw.
73. PYELONEPHRITIS/
74. pyelonephriti\$.tw.
75. pyonephrosi\$.tw.
76. pyelocystiti\$.tw.
77. or/67-76
78. MUCOCUTANEOUS LYMPH NODE SYNDROME/
79. (mucocutaneous adj2 lymph\$).tw.
80. mcls.tw.
81. (kawasaki adj (disease or syndrome)).tw.

- 82. or/78-81
- 83. or/36,40,44,48,51,54,59,63,66,77,82
- 84. HEMATOLOGIC TESTS/
- 85. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
- 86. or/84-85
- 87. exp BLOOD CELL COUNT/
- 88. ((blood or platelet\$) adj (count\$ or number\$)).tw.
- 89. leu?ocyte\$.tw.
- 90. or/87-89
- 91. BLOOD SEDIMENTATION/
- 92. ((blood or erythrocyte) adj sedimentation).tw.
- 93. or/91-92
- 94. C-REACTIVE PROTEIN/
- 95. c reactive protein\$.tw.
- 96. CRP.tw.
- 97. or/94-96
- 98. CALCITONIN/
- 99. calcitoni\$.tw.
- 100. PROTEIN PRECURSORS/
- 101. procalcitonin.tw.
- 102. or/98-101
- 103. DIAGNOSTIC TECHNIQUES, UROLOGICAL/
- 104. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
- 105. or/103-104
- 106. URINALYSIS/
- 107. ((urine or urinary) adj2 (analys\$ or test\$)).tw.
- 108. or/106-107
- 109. REAGENT KITS, DIAGNOSTIC/
- 110. REAGENT STRIPS/
- 111. "INDICATORS AND REAGENTS"/
- 112. (reagent\$ adj (kit\$ or strip\$)).tw.
- 113. (dipstick\$ or dip?stick\$).tw.
- 114. or/109-113
- 115. exp MICROSCOPY/
- 116. microscopy\$.tw.
- 117. (dipslide\$ or dip?slide\$).tw.
- 118. or/115-117
- 119. SPINAL PUNCTURE/
- 120. ((lumbar or spinal) adj puncture\$).tw.

- 121. CEREBROSPINAL FLUID/
- 122. cerebrospinal fluid.tw.
- 123. or/119-122
- 124. X-RAYS/
- 125. x ray\$.tw.
- 126. or/124-125
- 127. exp MICROCIRCULATION/
- 128. CAPILLARIES/
- 129. capillar\$.tw.
- 130. or/127-129
- 131. exp OXIMETRY/
- 132. pulse oximetry.tw.
- 133. or/131-132
- 134. BLOOD GLUCOSE/
- 135. blood glucose.tw.
- 136. or/134-135
- 137. RADIOGRAPHY, THORACIC/
- 138. ((chest or thoracic) adj2 radiograph\$.tw.
- 139. or/137-138
- 140. X-RAYS/
- 141. x ray\$.tw.
- 142. or/140-141
- 143. or/86,90,93,97,102,105,108,114,118,123,126,130,133,136,139,142
- 144. ECONOMICS/
- 145. "COSTS AND COST ANALYSIS"/
- 146. COST ALLOCATION/
- 147. COST-BENEFIT ANALYSIS/
- 148. COST CONTROL/
- 149. COST SAVINGS/
- 150. COST OF ILLNESS/
- 151. COST SHARING/
- 152. HEALTH CARE COSTS/
- 153. DIRECT SERVICE COSTS/
- 154. DRUG COSTS/
- 155. EMPLOYER HEALTH COSTS/
- 156. HOSPITAL COSTS/
- 157. HEALTH RESOURCES/
- 158. "HEALTH SERVICES NEEDS AND DEMAND"/
- 159. HEALTH PRIORITIES/

- 160. HEALTH EXPENDITURES/
- 161. CAPITAL EXPENDITURES/
- 162. FINANCIAL MANAGEMENT/
- 163. FINANCIAL MANAGEMENT, HOSPITAL/
- 164. QUALITY-ADJUSTED LIFE YEARS/
- 165. "DEDUCTIBLES AND COINSURANCE"/
- 166. MEDICAL SAVINGS ACCOUNTS/
- 167. ECONOMICS, HOSPITAL/
- 168. ECONOMICS, MEDICAL/
- 169. ECONOMICS, NURSING/
- 170. ECONOMICS, PHARMACEUTICAL/
- 171. MODELS, ECONOMIC/
- 172. MODELS, ECONOMETRIC/
- 173. RESOURCE ALLOCATION/
- 174. HEALTH CARE RATIONING/
- 175. "FEES AND CHARGES"/
- 176. BUDGETS/
- 177. VALUE OF LIFE/
- 178. (financ\$ or fiscal\$ or funding).tw.
- 179. (QALY\$ or life?year\$).tw.
- 180. (econom\$ or cost\$).tw.
- 181. pharmacoeconomic\$.tw.
- 182. ec.fs.
- 183. or/144-182
- 184. and/33,83,143,183
- 185. animal/ not (human/ or (human/ and animal/))
- 186. 184 not 185

FEVER_diagnosis_health_economics_embase_100506

- 1. PREMATURETY/
- 2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.
- 3. exp NEWBORN/
- 4. neonat\$.tw.
- 5. newborn\$.tw.
- 6. NEWBORN PERIOD/
- 7. PERINATAL PERIOD/
- 8. perinatal\$.tw.
- 9. postnatal\$.tw.
- 10. exp INFANT/
- 11. INFANCY/

12. BABY/
13. infan\$.tw.
14. (baby or babies).tw.
15. SMALL FOR DATE INFANT/
16. (small adj2 (date or "gestational age")).tw.
17. lbw.tw.
18. vlbw.tw.
19. CHILD/
20. CHILDHOOD/
21. PRESCHOOL CHILD/
22. SCHOOL CHILD/
23. child\$.tw.
24. PREPUBERTY/
25. PUBERTY/
26. prepube\$.tw.
27. pubert\$.tw.
28. pubesc\$.tw.
29. ADOLESCENCE/
30. adolescen\$.tw.
31. JUVENILE/
32. ADOLESCENT/
33. juvenile\$.tw.
34. minors.tw.
35. youth\$.tw.
36. teen\$.tw.
37. or/1-36
38. BACTERIAL INFECTION/
39. (bacteri\$ adj infect\$).tw.
40. or/38-39
41. BACTERIAL MENINGITIS/
42. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
43. meningococc\$.tw.
44. or/41-43
45. SEPTICEMIA/
46. septicemi\$.tw.
47. septicaemia\$.tw.
48. or/45-47
49. BACTEREMIA/

- 50. bacteremi\$.tw.
- 51. bacteraemia\$.tw.
- 52. or/49-51
- 53. exp PNEUMONIA/
- 54. pneumoni\$.tw.
- 55. or/53-54
- 56. HERPES SIMPLEX/
- 57. herpes simplex.tw.
- 58. or/56-57
- 59. BACTERIAL ARTHRITIS/
- 60. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 61. pyarthrosis.tw.
- 62. pyoarthritis.tw.
- 63. or/59-62
- 64. STAPHYLOCOCCAL INFECTION/
- 65. STREPTOCOCCAL INFECTION/
- 66. straphylococc\$.tw.
- 67. streptococc\$.tw.
- 68. or/64-67
- 69. OSTEOMYELITIS/
- 70. osteomyeliti\$.tw.
- 71. or/69-70
- 72. exp URINARY TRACT INFECTION/
- 73. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 74. UTI.tw.
- 75. ((upper or lower) adj5 urin\$).tw.
- 76. exp CYSTITIS/
- 77. cystitis\$.tw.
- 78. or/72-77
- 79. PYELONEPHRITIS/
- 80. pyelonephriti\$.tw.
- 81. pyonephrosi\$.tw.
- 82. pyelocystiti\$.tw.
- 83. or/79-82
- 84. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 85. (mucocutaneous adj2 lymph\$).tw.
- 86. mcls.tw.
- 87. (kawasaki adj (disease or syndrome)).tw.

88. or/84-87
89. or/40,44,48,52,55,58,63,68,71,78,83,88
90. exp BLOOD EXAMINATION/
91. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
92. or/90-91
93. exp BLOOD CELL COUNT/
94. ((blood or platelet\$) adj (count\$ or number\$)).tw.
95. leu?ocyte\$.tw.
96. or/93-95
97. ERYTHROCYTE SEDIMENTATION RATE/
98. ((blood or erythrocyte) adj sedimentation).tw.
99. or/97-98
100. C REACTIVE PROTEIN/
101. c reactive protein\$.tw.
102. CRP.tw.
103. or/100-102
104. CALCITONIN/
105. calcitoni\$.tw.
106. PROTEIN PRECURSORS/
107. PROCALCITONIN/
108. procalcitonin.tw.
109. or/104-108
110. UROLOGIC EXAMINATION/
111. (urolog\$ adj2 exam\$).tw.
112. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
113. (urin\$ adj cytology).tw.
114. or/110-113
115. URINALYSIS/
116. ((urine or urinary) adj2 (analys\$ or test\$ or exam\$ or investigat\$ or sample\$)).tw.
117. or/115-116
118. ANALYTICAL EQUIPMENT/
119. TEST STRIP/
120. REAGENT/
121. "DYES, REAGENTS, INDICATORS, MARKERS and BUFFERS"/
122. (reagent\$ adj (kit\$ or strip\$)).tw.
123. test strip.tw.
124. (dipstick\$ or dip?stick\$).tw.
125. or/118-124
126. exp MICROSCOPY/

- 127. microscopy\$.tw.
- 128. (dipslide\$ or dip?slide\$).tw.
- 129. or/126-128
- 130. LUMBAR PUNCTURE/
- 131. ((lumbar or spinal) adj punctur\$).tw.
- 132. CEREBROSPINAL FLUID/
- 133. cerebrospinal fluid.tw.
- 134. or/130-133
- 135. X RAY/
- 136. x ray\$.tw.
- 137. or/135-136
- 138. CAPILLARY FLOW/
- 139. capillar\$.tw.
- 140. or/138-139
- 141. exp OXIMETRY/
- 142. pulse oximetry.tw.
- 143. or/141-142
- 144. BLOOD GLUCOSE MONITORING/
- 145. blood glucose.tw.
- 146. or/144-145
- 147. THORAX RADIOGRAPHY/
- 148. ((chest or thoracic) adj2 radiograph\$).tw.
- 149. or/147-148
- 150. or/92,96,99,103,109,114,117,125,129,134,137,140,143,146,149
- 151. ECONOMICS/
- 152. HEALTH ECONOMICS/
- 153. ECONOMIC EVALUATION/
- 154. COST BENEFIT ANALYSIS/
- 155. COST CONTROL/
- 156. COST EFFECTIVENESS ANALYSIS/
- 157. COST MINIMIZATION ANALYSIS/
- 158. COST OF ILLNESS/
- 159. COST UTILITY ANALYSIS/
- 160. COST/
- 161. HEALTH CARE COST/
- 162. DRUG COST/
- 163. HEALTH CARE FINANCING/
- 164. HOSPITAL COST/
- 165. SOCIOECONOMICS/

- 166. ECONOMIC ASPECT/
- 167. QUALITY-ADJUSTED LIFE YEARS/
- 168. FINANCIAL MANAGEMENT/
- 169. PHARMACOECONOMICS/
- 170. RESOURCE ALLOCATION/
- 171. (financ\$ or fiscal\$ or funding).tw.
- 172. (QALY\$ or life?year\$).tw.
- 173. (econom\$ or cost\$).tw.
- 174. pharmacoeconomic\$.tw.
- 175. or/151-174
- 176. and/37,89,150,175
- 177. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
- 178. 176 not 177

FEVER_diagnosis_health_economics_cinahl_100506

- 1. INFANT, PREMATURE/
- 2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.
- 3. INFANT, NEWBORN/
- 4. neonat\$.tw.
- 5. newborn\$.tw.
- 6. perinatal\$.tw.
- 7. postnatal\$.tw.
- 8. exp INFANT/
- 9. infan\$.tw.
- 10. (baby or babies).tw.
- 11. INFANT, LOW BIRTH WEIGHT/
- 12. INFANT, VERY LOW BIRTH WEIGHT/
- 13. INFANT, SMALL FOR GESTATIONAL AGE/
- 14. (small adj2 (date or "gestational age")).tw.
- 15. lbw.tw.
- 16. vlbw.tw.
- 17. CHILD/
- 18. CHILD, PRESCHOOL/
- 19. SCHOOL CHILD/
- 20. child\$.tw.
- 21. PREPUBERTY/
- 22. PUBERTY/
- 23. prepube\$.tw.
- 24. pubert\$.tw.
- 25. pubesc\$.tw.

26. ADOLESCENCE/

27. adolescen\$.tw.

28. "MINORS (LEGAL)"/

29. juvenile\$.tw.

30. minors.tw.

31. youth\$.tw.

32. teen\$.tw.

33. or/1-32

34. BACTERIAL INFECTIONS/

35. (bacteri\$ adj infect\$).tw.

36. or/34-35

37. exp MENINGITIS, BACTERIAL/

38. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

39. meningococc\$.tw.

40. or/37-39

41. exp SEPSIS/

42. septicemi\$.tw.

43. septicaemia\$.tw.

44. or/41-43

45. BACTEREMIA/

46. bacteremi\$.tw.

47. bacteraemia\$.tw.

48. or/45-47

49. exp PNEUMONIA/

50. pneumoni\$.tw.

51. or/49-50

52. HERPES SIMPLEX/

53. herpes simplex.tw.

54. or/52-53

55. exp ARTHRITIS, INFECTIOUS/

56. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

57. pyarthrosis.tw.

58. pyoarthritis.tw.

59. or/55-58

60. STAPHYLOCOCCAL INFECTIONS/

61. STREPTOCOCCAL INFECTIONS/

62. ((staphylococc\$ or streptococc\$) adj infect\$).tw.

63. or/60-62

- 64. OSTEOMYELITIS/
- 65. osteomyeliti\$.tw.
- 66. or/64-65
- 67. exp URINARY TRACT INFECTION/
- 68. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 69. UTI.tw.
- 70. ((upper or lower) adj5 urin\$).tw.
- 71. CYSTITIS/
- 72. cystitis\$.tw.
- 73. PYELONEPHRITIS/
- 74. pyelonephriti\$.tw.
- 75. pyonephrosi\$.tw.
- 76. pyelocystiti\$.tw.
- 77. or/67-76
- 78. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 79. (mucocutaneous adj2 lymph\$).tw.
- 80. mcls.tw.
- 81. (kawasaki adj (disease or syndrome)).tw.
- 82. or/78-81
- 83. or/36,40,44,48,51,54,59,63,66,77,82
- 84. HEMATOLOGIC TESTS/
- 85. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
- 86. or/84-85
- 87. exp BLOOD CELL COUNT/
- 88. ((blood or platelet\$) adj (count\$ or number\$)).tw.
- 89. leu?ocyte\$.tw.
- 90. or/87-89
- 91. BLOOD SEDIMENTATION/
- 92. ((blood or erythrocyte) adj sedimentation).tw.
- 93. or/91-92
- 94. C-REACTIVE PROTEIN/
- 95. c reactive protein\$.tw.
- 96. CRP.tw.
- 97. or/94-96
- 98. CALCITONIN/
- 99. calcitoni\$.tw.
- 100. PROTEIN PRECURSORS/
- 101. procalcitonin.tw.

- 102. or/98-101
- 103. DIAGNOSTIC TECHNIQUES, UROLOGICAL/
- 104. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
- 105. or/103-104
- 106. URINALYSIS/
- 107. ((urine or urinary) adj2 (analys\$ or test\$ or exam\$ or investigat\$ or sample)).tw.
- 108. or/106-107
- 109. "REAGENT KITS, DIAGNOSTIC"/
- 110. REAGENT STRIPS/
- 111. "INDICATORS AND REAGENTS"/
- 112. (reagent\$ adj (kit\$ or strip\$)).tw.
- 113. (dipstick\$ or dip?stick\$).tw.
- 114. or/109-113
- 115. exp MICROSCOPY/
- 116. microscopy\$.tw.
- 117. (dipslide\$ or dip?slide\$).tw.
- 118. or/115-117
- 119. SPINAL PUNCTURE/
- 120. ((lumbar or spinal) adj puncture\$).tw.
- 121. CEREBROSPINAL FLUID/
- 122. cerebrospinal fluid.tw.
- 123. or/119-122
- 124. X-RAYS/
- 125. x ray\$.tw.
- 126. or/124-125
- 127. capillar\$.tw.
- 128. exp OXIMETRY/
- 129. pulse oximetry.tw.
- 130. or/128-129
- 131. BLOOD GLUCOSE/
- 132. blood glucose.tw.
- 133. or/131-132
- 134. RADIOGRAPHY, THORACIC/
- 135. ((chest or thoracic) adj2 radiograph\$).tw.
- 136. or/134-135
- 137. or/86,90,93,97,102,105,108,114,118,123,126-127,130,133,136
- 138. ECONOMICS/
- 139. "COSTS AND COST ANALYSIS"/
- 140. COST BENEFIT ANALYSIS/

141. COST CONTROL/
142. COST SAVINGS/
143. COST OF ILLNESS/
144. HEALTH CARE COSTS/
145. ECONOMIC ASPECTS OF ILLNESS/
146. ECONOMICS, PHARMACEUTICAL/
147. HEALTH CARE FINANCING/
148. FINANCIAL MANAGEMENT/
149. HOSPITAL COST/
150. SOCIOECONOMIC FACTORS/
151. HEALTH RESOURCE ALLOCATION/
152. (financ\$ or fiscal\$ or funding).tw.
153. (QALY\$ or life?year\$).tw.
154. (econom\$ or cost\$).tw.
155. pharmacoeconomic\$.tw.
156. or/138-155
157. and/33,83,137,156

FEVER_diagnosis_pulse_oximetry_capillary_glucose_medline_090506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/

- 22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 23. meningococc\$.tw.
- 24. or/21-23
- 25. SEPTICEMIA/
- 26. septicemi\$.tw.
- 27. septicaemia\$.tw.
- 28. or/25-27
- 29. BACTEREMIA/
- 30. bacteremi\$.tw.
- 31. bacteraemia\$.tw.
- 32. or/29-31
- 33. exp PNEUMONIA/
- 34. pneumoni\$.tw.
- 35. or/33-34
- 36. HERPES SIMPLEX/
- 37. herpes simplex.tw.
- 38. or/36-37
- 39. exp ARTHRITIS, INFECTIOUS/
- 40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 41. pyarthrosis.tw.
- 42. pyoarthritis.tw.
- 43. or/39-42
- 44. STAPHYLOCOCCAL INFECTIONS/
- 45. STREPTOCOCCAL INFECTIONS/
- 46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 47. or/44-46
- 48. OSTEOMYELITIS/
- 49. osteomyeliti\$.tw.
- 50. or/48-49
- 51. exp URINARY TRACT INFECTIONS/
- 52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 53. UTI.tw.
- 54. ((upper or lower) adj5 urin\$).tw.
- 55. exp CYSTITIS/
- 56. cystitis\$.tw.
- 57. PYELONEPHRITIS/
- 58. pyelonephriti\$.tw.

59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp OXIMETRY/
69. pulse oximetry.tw.
70. or/68-69
71. BLOOD GLUCOSE/
72. blood glucose.tw.
73. or/71-72
74. or/70,73
75. exp "SENSITIVITY AND SPECIFICITY"/
76. (sensitivity or specificity).tw.
77. (predictive adj value\$).tw.
78. LIKELIHOOD FUNCTIONS/
79. (likelihood adj (estimate\$ or ratio\$)).tw.
80. exp DIAGNOSTIC ERRORS/
81. (false adj (negative\$ or positive\$)).tw.
82. "REPRODUCIBILITY OF RESULTS"/
83. DIAGNOSIS, DIFFERENTIAL/
84. (differential adj diagnos\$).tw.
85. or/75-84
86. and/17,67,74,85

FEVER_diagnosis_pulse_oximetry_capillary_glucose_embase_090506

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.

11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTION/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. BACTERIAL MENINGITIS/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. BACTERIAL ARTHRITIS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTION/
45. STREPTOCOCCAL INFECTION/
46. straphylococc\$.tw.
47. streptococc\$.tw.
48. or/44-47

49. OSTEOMYELITIS/
50. osteomyeliti\$.tw.
51. or/49-50
52. exp URINARY TRACT INFECTION/
53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
54. UTI.tw.
55. ((upper or lower) adj5 urin\$).tw.
56. exp CYSTITIS/
57. cystitis\$.tw.
58. or/52-57
59. PYELONEPHRITIS/
60. pyelonephriti\$.tw.
61. pyonephrosi\$.tw.
62. pyelocystiti\$.tw.
63. or/59-62
64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
65. (mucocutaneous adj2 lymph\$).tw.
66. mcls.tw.
67. (kawasaki adj (disease or syndrome)).tw.
68. or/64-67
69. or/20,24,28,32,35,38,43,48,51,58,63,68
70. exp OXIMETRY/
71. pulse oximetry.tw.
72. or/70-71
73. BLOOD GLUCOSE MONITORING/
74. blood glucose.tw.
75. or/73-74
76. or/72,75
77. exp "SENSITIVITY AND SPECIFICITY"/
78. (sensitivity or specificity).tw.
79. (predictive adj value\$).tw.
80. STATISTICAL MODEL/
81. (likelihood adj (estimate\$ or ratio\$)).tw.
82. DIAGNOSTIC ERROR/
83. (false adj (negative\$ or positive\$)).tw.
84. REPRODUCIBILITY/
85. DIFFERENTIAL DIAGNOSIS/
86. (differential adj diagnos\$).tw.

87. or/77-86

88. and/17,69,76,87

89. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

90. 88 not 89

FEVER_diagnosis_pulse_oximetry_capillary_glucose_cinahl_090506

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. exp SEPSIS/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

-
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTION/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp OXIMETRY/
69. pulse oximetry.tw.
70. or/68-69
71. BLOOD GLUCOSE/
72. blood glucose.tw.

73. or/71-72

74. or/70,73

75. and/17,67,74

FEVER_diagnosis_test_accuracy_medline_150206

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. INFANT, LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp FEVER/

19. "FEVER OF UNKNOWN ORIGIN"/

20. fever\$.tw.

21. febril\$.tw.

22. hypertherm\$.tw.

23. pyrexia\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGENS/

27. pyrogen\$.tw.

28. or/18-27

29. and/17,28

30. BACTERIAL INFECTIONS/

31. (bacteri\$ adj infect\$).tw.

32. or/30-31

33. exp MENINGITIS, BACTERIAL/

34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTIONS/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. exp CYSTITIS/
68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.

- 73. or/63-72
- 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 75. (mucocutaneous adj2 lymph\$).tw.
- 76. mcls.tw.
- 77. (kawasaki adj (disease or syndrome)).tw.
- 78. or/74-77
- 79. or/32,36,40,44,47,50,55,59,62,73,78
- 80. and/29,79
- 81. HEMATOLOGIC TESTS/
- 82. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
- 83. or/81-82
- 84. exp BLOOD CELL COUNT/
- 85. ((blood or platelet\$) adj (count\$ or number\$)).tw.
- 86. leu?ocyte\$.tw.
- 87. or/84-86
- 88. BLOOD SEDIMENTATION/
- 89. ((blood or erythrocyte) adj sedimentation).tw.
- 90. or/88-89
- 91. C-REACTIVE PROTEIN/
- 92. c reactive protein\$.tw.
- 93. CRP.tw.
- 94. or/91-93
- 95. CALCITONIN/
- 96. calcitoni\$.tw.
- 97. PROTEIN PRECURSORS/
- 98. procalcitonin.tw.
- 99. or/95-98
- 100. DIAGNOSTIC TECHNIQUES, UROLOGICAL/
- 101. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
- 102. or/100-101
- 103. URINALYSIS/
- 104. ((urine or urinary) adj2 (analys\$ or test\$)).tw.
- 105. or/103-104
- 106. REAGENT KITS, DIAGNOSTIC/
- 107. REAGENT STRIPS/
- 108. "INDICATORS AND REAGENTS"/
- 109. (reagent\$ adj (kit\$ or strip\$)).tw.
- 110. (dipstick\$ or dip?stick\$).tw.
- 111. or/106-110

- 112. exp MICROSCOPY/
- 113. microscopy\$.tw.
- 114. (dipslide\$ or dip?slide\$).tw.
- 115. or/112-114
- 116. SPINAL PUNCTURE/
- 117. ((lumbar or spinal) adj puncture\$).tw.
- 118. CEREBROSPINAL FLUID/
- 119. cerebrospinal fluid.tw.
- 120. or/116-119
- 121. X-RAYS/
- 122. x ray\$.tw.
- 123. or/121-122
- 124. or/83,87,90,94,99,102,105,111,115,120,123
- 125. and/80,124
- 126. exp "SENSITIVITY AND SPECIFICITY"/
- 127. (sensitivity or specificity).tw.
- 128. (predictive adj value\$).tw.
- 129. LIKELIHOOD FUNCTIONS/
- 130. (likelihood adj (estimate\$ or ratio\$)).tw.
- 131. exp DIAGNOSTIC ERRORS/
- 132. (false adj (negative\$ or positive\$)).tw.
- 133. "REPRODUCIBILITY OF RESULTS"/
- 134. DIAGNOSIS, DIFFERENTIAL/
- 135. (differential adj diagnos\$).tw.
- 136. or/126-135
- 137. and/125,136
- 138. animal/ not (human/ or (human/ and animal/))
- 139. 137 not 138

FEVER_diagnosis_test_accuracy_embase_150206

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.

11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTION/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. BACTERIAL MENINGITIS/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/

49. herpes simplex.tw.
50. or/48-49
51. BACTERIAL ARTHRITIS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthriti\$.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTION/
57. STREPTOCOCCAL INFECTION/
58. straphylococc\$.tw.
59. streptococc\$.tw.
60. or/56-59
61. OSTEOMYELITIS/
62. osteomyeliti\$.tw.
63. or/61-62
64. exp URINARY TRACT INFECTION/
65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
66. UTI.tw.
67. ((upper or lower) adj5 urin\$).tw.
68. exp CYSTITIS/
69. cystitis\$.tw.
70. or/64-69
71. PYELONEPHRITIS/
72. pyelonephriti\$.tw.
73. pyonephrosi\$.tw.
74. pyelocystiti\$.tw.
75. or/71-74
76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
77. (mucocutaneous adj2 lymph\$).tw.
78. mcls.tw.
79. (kawasaki adj (disease or syndrome)).tw.
80. or/76-79
81. or/32,36,40,44,47,50,55,60,63,70,75,80
82. and/29,81
83. exp BLOOD EXAMINATION/
84. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
85. or/83-84
86. exp BLOOD CELL COUNT/

- 87. ((blood or platelet\$) adj (count\$ or number\$)).tw.
- 88. leu?ocyte\$.tw.
- 89. or/86-88
- 90. ERYTHROCYTE SEDIMENTATION RATE/
- 91. ((blood or erythrocyte) adj sedimentation).tw.
- 92. or/90-91
- 93. C REACTIVE PROTEIN/
- 94. c reactive protein\$.tw.
- 95. CRP.tw.
- 96. or/93-95
- 97. CALCITONIN/
- 98. calcitoni\$.tw.
- 99. PROTEIN PRECURSORS/
- 100. PROCALCITONIN/
- 101. procalcitonin.tw.
- 102. or/97-101
- 103. UROLOGIC EXAMINATION/
- 104. (urolog\$ adj2 exam\$).tw.
- 105. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
- 106. (urin\$ adj cytology).tw.
- 107. or/103-106
- 108. URINALYSIS/
- 109. ((urine or urinary) adj2 (analys\$ or test\$ or exam\$ or investigat\$ or sample)).tw.
- 110. or/108-109
- 111. ANALYTICAL EQUIPMENT/
- 112. TEST STRIP/
- 113. REAGENT/
- 114. "DYES, REAGENTS, INDICATORS, MARKERS and BUFFERS"/
- 115. (reagent\$ adj (kit\$ or strip\$)).tw.
- 116. test strip.tw.
- 117. (dipstick\$ or dip?stick\$).tw.
- 118. or/111-117
- 119. exp MICROSCOPY/
- 120. microscopy\$.tw.
- 121. (dipslide\$ or dip?slide\$).tw.
- 122. or/119-121
- 123. LUMBAR PUNCTURE/
- 124. ((lumbar or spinal) adj punctur\$).tw.
- 125. CEREBROSPINAL FLUID/

126. cerebrospinal fluid.tw.
127. or/123-126
128. X RAY/
129. x ray\$.tw.
130. or/128-129
131. or/85,89,92,96,102,107,110,118,122,127,130
132. and/82,131
133. exp "SENSITIVITY AND SPECIFICITY"/
134. (sensitivity or specificity).tw.
135. (predictive adj value\$).tw.
136. STATISTICAL MODEL/
137. (likelihood adj (estimate\$ or ratio\$)).tw.
138. DIAGNOSTIC ERROR/
139. (false adj (negative\$ or positive\$)).tw.
140. REPRODUCIBILITY/
141. DIFFERENTIAL DIAGNOSIS/
142. (differential adj diagnos\$).tw.
143. or/133-142
144. and/132,143
145. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
146. 144 not 145

FEVER_diagnosis_test_accuracy_cinahl_150206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16

18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54

-
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTION/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. CYSTITIS/
68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79
81. HEMATOLOGIC TESTS/
82. ((blood or hematolog\$) adj (analys\$ or examin\$ or test\$)).tw.
83. or/81-82
84. exp BLOOD CELL COUNT/
85. ((blood or platelet\$) adj (count\$ or number\$)).tw.
86. leu?ocyte\$.tw.
87. or/84-86
88. BLOOD SEDIMENTATION/
89. ((blood or erythrocyte) adj sedimentation).tw.
90. or/88-89
91. C-REACTIVE PROTEIN/
92. c reactive protein\$.tw.
93. CRP.tw.

- 94. or/91-93
- 95. CALCITONIN/
- 96. calcitoni\$.tw.
- 97. PROTEIN PRECURSORS/
- 98. procalcitonin.tw.
- 99. or/95-98
- 100. DIAGNOSTIC TECHNIQUES, UROLOGICAL/
- 101. (urolog\$ adj2 (diagnostic\$ or technic\$ or technique\$)).tw.
- 102. or/100-101
- 103. URINALYSIS/
- 104. ((urine or urinary) adj2 (analys\$ or test\$ or exam\$ or investigat\$ or sample)).tw.
- 105. or/103-104
- 106. "REAGENT KITS, DIAGNOSTIC"/
- 107. REAGENT STRIPS/
- 108. "INDICATORS AND REAGENTS"/
- 109. (reagent\$ adj (kit\$ or strip\$)).tw.
- 110. (dipstick\$ or dip?stick\$).tw.
- 111. or/106-110
- 112. exp MICROSCOPY/
- 113. microscopy\$.tw.
- 114. (dipslide\$ or dip?slide\$).tw.
- 115. or/112-114
- 116. SPINAL PUNCTURE/
- 117. ((lumbar or spinal) adj puncture\$).tw.
- 118. CEREBROSPINAL FLUID/
- 119. cerebrospinal fluid.tw.
- 120. or/116-119
- 121. X-RAYS/
- 122. x ray\$.tw.
- 123. or/121-122
- 124. or/83,87,90,94,99,102,105,111,115,120,123
- 125. and/80,124

FEVER_diagnosis_thoracic_radiography_pneumonia_medline_260406

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp PNEUMONIA/
19. pneumoni\$.tw.
20. or/18-19
21. RADIOGRAPHY, THORACIC/
22. ((chest or thoracic) adj2 radiograph\$).tw.
23. or/21-22
24. X-RAYS/
25. x ray\$.tw.
26. or/24-25
27. or/23,26
28. exp "SENSITIVITY AND SPECIFICITY"/
29. (sensitivity or specificity).tw.
30. (predictive adj value\$).tw.
31. LIKELIHOOD FUNCTIONS/
32. (likelihood adj (estimate\$ or ratio\$)).tw.
33. exp DIAGNOSTIC ERRORS/
34. (false adj (negative\$ or positive\$)).tw.
35. "REPRODUCIBILITY OF RESULTS"/
36. DIAGNOSIS, DIFFERENTIAL/
37. (differential adj diagnos\$).tw.
38. or/28-37
39. and/17,20,27,38
40. animal/ not (human/ or (human/ and animal/))
41. 39 not 40

FEVER_diagnosis_thoracic_radiography_pneumonia_embase_260406

1. PREMATUREITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp PNEUMONIA/
19. pneumoni\$.tw.
20. or/18-19
21. THORAX RADIOGRAPHY/
22. ((chest or thoracic) adj2 radiograph\$).tw.
23. or/21-22
24. X RAY/
25. x ray\$.tw.
26. or/24-25
27. or/23,26
28. exp "SENSITIVITY AND SPECIFICITY"/
29. (sensitivity or specificity).tw.
30. (predictive adj value\$).tw.
31. STATISTICAL MODEL/
32. (likelihood adj (estimate\$ or ratio\$)).tw.
33. DIAGNOSTIC ERROR/
34. (false adj (negative\$ or positive\$)).tw.
35. REPRODUCIBILITY/
36. DIFFERENTIAL DIAGNOSIS/
37. (differential adj diagnos\$).tw.
38. or/28-37
39. and/17,20,27,38
40. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
41. 39 not 40

FEVER_diagnosis_thoracic_radiography_pneumonia_cinahl_260406

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp PNEUMONIA/
19. pneumoni\$.tw.
20. or/18-19
21. RADIOGRAPHY, THORACIC/
22. ((chest or thoracic) adj2 radiograph\$).tw.
23. or/21-22
24. X-RAYS/
25. x ray\$.tw.
26. or/24-25
27. or/23,26
28. and/17,20,27

FEVER_febrile_convulsions_antipyretics_medline_020506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.

10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. ANALGESICS/
19. ANALGESICS, NON-NARCOTIC/
20. (analges\$ or analget\$ or anodyne\$).tw.
21. anti?pyretic\$.tw.
22. (antinociceptive adj (agent\$ or drug\$)).tw.
23. or/18-22
24. ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
25. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
26. NSAID\$.tw.
27. or/24-26
28. IBUPROFEN/
29. ibuprofen\$.tw.
30. or/28-29
31. ACETAMINOPHEN/
32. acetaminophen\$.tw.
33. paracetamol\$.tw.
34. or/31-33
35. or/23,27,30,34
36. CRYOTHERAPY/
37. cryother\$.tw.
38. cryotreatment\$.tw.
39. cryoanalgesi\$.tw.
40. cyroanalgesi\$.tw.
41. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.
42. or/36-41
43. BATHS/
44. bath\$.tw.
45. spong\$.tw.
46. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.
47. or/43-46
48. WATER/

49. DRINKING/

50. FLUID THERAPY/

51. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.

52. hydrat\$.tw.

53. rehydrat\$.tw.

54. or/48-53

55. CLOTHING/

56. ((light\$ or remov\$) adj2 cloth\$).tw.

57. or/55-56

58. climatotherap\$.tw.

59. (climat\$ adj (therap\$ or treat\$)).tw.

60. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.

61. fan\$.tw.

62. or/58-61

63. HYPOTHERMIA, INDUCED/

64. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.

65. (blanket adj treatment\$).tw.

66. swaddling.tw.

67. or/63-66

68. COMBINED MODALITY THERAPY/

69. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.

70. or/68-69

71. or/35,42,47,54,57,62,67,70

72. SEIZURES, FEBRILE/

73. ((febrile or fever or pyrexial) adj (convulsion\$ or fit\$ or seizure\$)).tw.

74. or/72-73

75. and/17,71,74

76. animal/ not (human/ or (human/ and animal/))

77. 75 not 76

FEVER_febrile_convulsions_antipyretics_embase_020506

1. PREMATURITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. NEWBORN/

9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. ANALGESIA/
19. ANALGESIC AGENT/
20. (analges\$ or analget\$ or anodyne\$).tw.
21. (antinociceptive adj (agent\$ or drug\$)).tw.
22. ANTIPYRETIC AGENT/
23. anti?pyretic\$.tw.
24. or/18-23
25. NONSTEROID ANTIINFLAMMATORY AGENT/
26. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
27. NSAID\$.tw.
28. or/25-27
29. IBUPROFEN/
30. ibuprofen\$.tw.
31. or/29-30
32. PARACETAMOL/
33. paracetamol\$.tw.
34. acetaminophen\$.tw.
35. or/32-34
36. or/24,28,31,35
37. CRYOTHERAPY/
38. cryother\$.tw.
39. cryotreatment\$.tw.
40. CRYOANESTHESIA/
41. cryoanalgesi\$.tw.
42. cyroanalgesi\$.tw.
43. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.
44. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.
45. (blanket adj treatment\$).tw.
46. swaddling.tw.
47. or/37-46

48. BATH/
49. bath\$.tw.
50. spong\$.tw.
51. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.
52. or/48-51
53. WATER/
54. FLUID THERAPY/
55. FLUID INTAKE/
56. FLUID BALANCE/
57. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.
58. HYDRATION/
59. REHYDRATION/
60. hydrat\$.tw.
61. rehydrat\$.tw.
62. or/53-61
63. CLOTHING/
64. ((light\$ or remov\$) adj2 cloth\$).tw.
65. or/63-64
66. CLIMATOTHERAPY/
67. climatotherap\$.tw.
68. (climat\$ adj (therap\$ or treat\$)).tw.
69. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.
70. fan\$.tw.
71. or/66-70
72. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.
73. or/36,47,52,62,65,71-72
74. FEBRILE CONVULSION/
75. ((febrile or fever or pyrexial) adj (convulsion\$ or fit\$ or seizure\$)).tw.
76. or/74-75
77. and/17,73,76
78. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
79. 77 not 78

FEVER_febrile_convulsions_antipyretics_cinahl_020506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. ANALGESIA/

19. ANALGESICS/

20. ANALGESICS, NONNARCOTIC/

21. (analges\$ or analget\$ or anodyne\$).tw.

22. (antinociceptive adj (agent\$ or drug\$)).tw.

23. (anti-pyretic\$ or antipyretic\$).tw.

24. or/18-23

25. ANTIINFLAMMATORY AGENTS, NON-STEROIDAL/

26. ((non-steroid\$ or nonsteroid\$) adj (anti-inflammatory or antiinflammatory) adj (agent\$ or drug\$)).tw.

27. NSAID\$.tw.

28. or/25-27

29. IBUPROFEN/

30. ibuprofen\$.tw.

31. or/29-30

32. ACETAMINOPHEN/

33. acetaminophen\$.tw.

34. paracetamol\$.tw.

35. or/32-34

36. or/24,28,31,35

37. CRYOTHERAPY/

38. cryother\$.tw.

39. cryotreatment\$.tw.

40. cryoanalgesi\$.tw.

41. cyroanalgesi\$.tw.

42. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.

43. or/37-42

44. BATHS/
45. bath\$.tw.
46. spong\$.tw.
47. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.
48. or/44-47
49. WATER/
50. DRINKING BEHAVIOR/
51. FLUID THERAPY/
52. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.
53. hydrat\$.tw.
54. rehydrat\$.tw.
55. or/49-54
56. CLOTHING/
57. ((light\$ or remov\$) adj2 cloth\$).tw.
58. or/56-57
59. climatotherap\$.tw.
60. (climat\$ adj (therap\$ or treat\$)).tw.
61. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.
62. fan\$.tw.
63. or/59-62
64. HYPOTHERMIA, INDUCED/
65. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.
66. (blanket adj treatment\$).tw.
67. swaddling.tw.
68. or/64-67
69. COMBINED MODALITY THERAPY/
70. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.
71. or/69-70
72. or/36,43,48,55,58,63,68,71
73. CONVULSIONS, FEBRILE/
74. ((febrile or fever or pyrexial) adj (convulsion\$ or fit\$ or seizure\$)).tw.
75. or/73-74
76. and/17,72,75

FEVER_health_economic_filter_medline_021205

1. ECONOMICS/
2. "COSTS AND COST ANALYSIS"/
3. COST ALLOCATION/
4. COST-BENEFIT ANALYSIS/

5. COST CONTROL/
6. COST SAVINGS/
7. COST OF ILLNESS/
8. COST SHARING/
9. HEALTH CARE COSTS/
10. DIRECT SERVICE COSTS/
11. DRUG COSTS/
12. EMPLOYER HEALTH COSTS/
13. HOSPITAL COSTS/
14. HEALTH RESOURCES/
15. "HEALTH SERVICES NEEDS AND DEMAND"/
16. HEALTH PRIORITIES/
17. HEALTH EXPENDITURES/
18. CAPITAL EXPENDITURES/
19. FINANCIAL MANAGEMENT/
20. FINANCIAL MANAGEMENT, HOSPITAL/
21. QUALITY-ADJUSTED LIFE YEARS/
22. "DEDUCTIBLES AND COINSURANCE"/
23. MEDICAL SAVINGS ACCOUNTS/
24. ECONOMICS, HOSPITAL/
25. ECONOMICS, MEDICAL/
26. ECONOMICS, NURSING/
27. ECONOMICS, PHARMACEUTICAL/
28. MODELS, ECONOMIC/
29. MODELS, ECONOMETRIC/
30. RESOURCE ALLOCATION/
31. HEALTH CARE RATIONING/
32. "FEES AND CHARGES"/
33. BUDGETS/
34. VALUE OF LIFE/
35. (financ\$ or fiscal\$ or funding).tw.
36. (QALY\$ or life?year\$).tw.
37. (econom\$ or cost\$).tw.
38. pharmacoeconomic\$.tw.
39. ec.fs.
40. or/1-39
41. INFANT, PREMATURE/
42. INFANT, POSTMATURE/
43. INFANT, LOW BIRTH WEIGHT/

44. (low adj birth adj weight).tw.
45. lbw.tw.
46. INFANT, VERY LOW BIRTH WEIGHT/
47. vlbw.tw.
48. INFANT, NEWBORN/
49. neonat\$.tw.
50. newborn\$.tw.
51. exp INFANT/
52. infan\$.tw.
53. CHILD, PRESCHOOL/
54. (baby or babies).tw.
55. (child\$ adj5 pre?school).tw.
56. toddler\$.tw.
57. or/41-56
58. exp FEVER/
59. "FEVER OF UNKNOWN ORIGIN"/
60. fever\$.tw.
61. febril\$.tw.
62. hypertherm\$.tw.
63. pyrexia\$.tw.
64. MALIGNANT HYPERTHERMIA/
65. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
66. exp PYROGENS/
67. pyrogen\$.tw.
68. or/58-67
69. and/57,68
70. and/40,69
71. animal/ not (human/ or (human/ and animal/))
72. 70 not 71

FEVER_health_economic_filter_embase_021205

1. ECONOMICS/
2. HEALTH ECONOMICS/
3. ECONOMIC EVALUATION/
4. COST BENEFIT ANALYSIS/
5. COST CONTROL/
6. COST EFFECTIVENESS ANALYSIS/
7. COST MINIMIZATION ANALYSIS/
8. COST OF ILLNESS/
9. COST UTILITY ANALYSIS/

10. COST/
11. HEALTH CARE COST/
12. DRUG COST/
13. HEALTH CARE FINANCING/
14. HOSPITAL COST/
15. SOCIOECONOMICS/
16. ECONOMIC ASPECT/
17. QUALITY-ADJUSTED LIFE YEARS/
18. FINANCIAL MANAGEMENT/
19. PHARMACOECONOMICS/
20. RESOURCE ALLOCATION/
21. (financ\$ or fiscal\$ or funding).tw.
22. (QALY\$ or life?year\$).tw.
23. (econom\$ or cost\$).tw.
24. pharmacoeconomic\$.tw.
25. or/1-24
26. PREMATURITY/
27. POSTMATURITY/
28. LOW BIRTH WEIGHT/
29. (low adj birth adj weight).tw.
30. lbw.tw.
31. VERY LOW BIRTH WEIGHT/
32. vlbw.tw.
33. NEWBORN/
34. neonat\$.tw.
35. newborn\$.tw.
36. exp INFANT/
37. infan\$.tw.
38. PRESCHOOL CHILD/
39. (baby or babies).tw.
40. (child\$ adj5 pre?school).tw.
41. toddler\$.tw.
42. or/26-41
43. exp FEVER/
44. PYREXIA IDIOPATHICA/
45. fever\$.tw.
46. febril\$.tw.
47. hypertherm\$.tw.
48. pyrexia\$.tw.

49. MALIGNANT HYPERTHERMIA/
50. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
51. exp PYROGEN/
52. pyrogen\$.tw.
53. or/43-52
54. and/42,53
55. and/25,54
56. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
57. 55 not 56

FEVER_health_economic_filter_cinahl_021205

1. ECONOMICS/
2. "COSTS AND COST ANALYSIS"/
3. COST BENEFIT ANALYSIS/
4. COST CONTROL/
5. COST SAVINGS/
6. COST OF ILLNESS/
7. HEALTH CARE COSTS/
8. ECONOMIC ASPECTS OF ILLNESS/
9. ECONOMICS, PHARMACEUTICAL/
10. HEALTH CARE FINANCING/
11. FINANCIAL MANAGEMENT/
12. HOSPITAL COST/
13. SOCIOECONOMIC FACTORS/
14. HEALTH RESOURCE ALLOCATION/
15. (financ\$ or fiscal\$ or funding).tw.
16. (QALY\$ or life?year\$).tw.
17. (econom\$ or cost\$).tw.
18. pharmacoeconomic\$.tw.
19. or/1-18
20. INFANT, PREMATURE/
21. INFANT, POSTMATURE/
22. LOW BIRTH WEIGHT/
23. (low adj birth adj weight).tw.
24. lbw.tw.
25. VERY LOW BIRTH WEIGHT/
26. vlbw.tw.
27. INFANT, NEWBORN/
28. neonat\$.tw.
29. newborn\$.tw.

- 30. exp INFANT/
- 31. infan\$.tw.
- 32. PRESCHOOL CHILD/
- 33. (baby or babies).tw.
- 34. (child\$ adj5 pre?school).tw.
- 35. toddler\$.tw.
- 36. or/20-35
- 37. exp FEVER/
- 38. "FEVER OF UNKNOWN ORIGIN"/
- 39. fever\$.tw.
- 40. febril\$.tw.
- 41. hypertherm\$.tw.
- 42. pyrexia\$.tw.
- 43. MALIGNANT HYPERTHERMIA/
- 44. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 45. exp PYROGENS/
- 46. pyrogen\$.tw.
- 47. or/37-46
- 48. and/36,47
- 49. and/19,48

FEVER_heart_monitoring_medline_280206

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. INFANT, VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. CHILD, PRESCHOOL/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/

19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/

57. STREPTOCOCCAL INFECTIONS/

58. ((straphylococc\$ or streptococc\$) adj infect\$).tw.

59. or/56-58

60. OSTEOMYELITIS/

61. osteomyeliti\$.tw.

62. or/60-61

63. exp URINARY TRACT INFECTIONS/

64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

65. UTI.tw.

66. ((upper or lower) adj5 urin\$).tw.

67. exp CYSTITIS/

68. cystitis\$.tw.

69. PYELONEPHRITIS/

70. pyelonephriti\$.tw.

71. pyonephrosi\$.tw.

72. pyelocystiti\$.tw.

73. or/63-72

74. MUCOCUTANEOUS LYMPH NODE SYNDROME/

75. (mucocutaneous adj2 lymph\$).tw.

76. mcls.tw.

77. (kawasaki adj (disease or syndrome)).tw.

78. or/74-77

79. or/32,36,40,44,47,50,55,59,62,73,78

80. and/29,79

81. HEART RATE/

82. exp TACHYCARDIA/

83. ((cardiac or heart or pulse) adj (rate\$ or monitor\$)).tw.

84. or/81-83

85. and/80,84

86. animal/ not (human/ or (human/ and animal/))

87. 85 not 86

FEVER_heart_monitoring_embase_280206

1. PREMATURITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTION/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. BACTERIAL MENINGITIS/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43

- 45. exp PNEUMONIA/
- 46. pneumoni\$.tw.
- 47. or/45-46
- 48. HERPES SIMPLEX/
- 49. herpes simplex.tw.
- 50. or/48-49
- 51. BACTERIAL ARTHRITIS/
- 52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 53. pyarthrosis.tw.
- 54. pyoarthritis.tw.
- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTION/
- 57. STREPTOCOCCAL INFECTION/
- 58. straphylococc\$.tw.
- 59. streptococc\$.tw.
- 60. or/56-59
- 61. OSTEOMYELITIS/
- 62. osteomyeliti\$.tw.
- 63. or/61-62
- 64. exp URINARY TRACT INFECTION/
- 65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 66. UTI.tw.
- 67. ((upper or lower) adj5 urin\$).tw.
- 68. exp CYSTITIS/
- 69. cystitis\$.tw.
- 70. or/64-69
- 71. PYELONEPHRITIS/
- 72. pyelonephriti\$.tw.
- 73. pyonephrosi\$.tw.
- 74. pyelocystiti\$.tw.
- 75. or/71-74
- 76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 77. (mucocutaneous adj2 lymph\$).tw.
- 78. mcls.tw.
- 79. (kawasaki adj (disease or syndrome)).tw.
- 80. or/76-79
- 81. or/32,36,40,44,47,50,55,60,63,70,75,80
- 82. and/29,81

83. HEART RATE/
84. PULSE RATE/
85. exp TACHYCARDIA/
86. ((cardiac or heart or pulse) adj (rate\$ or monitor\$)).tw.
87. or/83-86
88. and/82,87
89. animal/ not (human/ or (human/ and animal/))
90. 88 not 89

FEVER_heart_monitoring_cinahl_280206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/

31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTION/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. CYSTITIS/

68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79
81. HEART RATE/
82. exp TACHYCARDIA/
83. ((cardiac or heart or pulse) adj (rate\$ or monitor\$)).tw.
84. or/81-83
85. and/80,84

FEVER_hospitalisation_medline_280206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.

21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrex\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. PATIENT ADMISSION/
31. CHILD, HOSPITALIZED/
32. or/30-31
33. and/29,32
34. animal/ not (human/ or (human/ and animal/))
35. 33 not 34

FEVER_hospitalisation_embase_280206

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrex\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGEN/

27. pyrogen\$.tw.

28. or/18-27

29. and/17,28

30. BACTERIAL INFECTION/

31. (bacteri\$ adj infect\$).tw.

32. or/30-31

33. BACTERIAL MENINGITIS/

34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

35. meningococc\$.tw.

36. or/33-35

37. SEPTICEMIA/

38. septicemi\$.tw.

39. septicaemia\$.tw.

40. or/37-39

41. BACTEREMIA/

42. bacteremi\$.tw.

43. bacteraemia\$.tw.

44. or/41-43

45. exp PNEUMONIA/

46. pneumoni\$.tw.

47. or/45-46

48. HERPES SIMPLEX/

49. herpes simplex.tw.

50. or/48-49

51. BACTERIAL ARTHRITIS/

52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

53. pyarthrosis.tw.

54. pyoarthritis.tw.

55. or/51-54

56. STAPHYLOCOCCAL INFECTION/

57. STREPTOCOCCAL INFECTION/

58. straphylococc\$.tw.

59. streptococc\$.tw.

60. or/56-59

61. OSTEOMYELITIS/

- 62. osteomyeliti\$.tw.
- 63. or/61-62
- 64. exp URINARY TRACT INFECTION/
- 65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 66. UTI.tw.
- 67. ((upper or lower) adj5 urin\$).tw.
- 68. exp CYSTITIS/
- 69. cystitis\$.tw.
- 70. or/64-69
- 71. PYELONEPHRITIS/
- 72. pyelonephriti\$.tw.
- 73. pyonephrosi\$.tw.
- 74. pyelocystiti\$.tw.
- 75. or/71-74
- 76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 77. (mucocutaneous adj2 lymph\$).tw.
- 78. mcls.tw.
- 79. (kawasaki adj (disease or syndrome)).tw.
- 80. or/76-79
- 81. or/32,36,40,44,47,50,55,60,63,70,75,80
- 82. and/29,81
- 83. HOSPITAL ADMISSION/
- 84. CHILD HOSPITALIZATION/
- 85. or/83-84
- 86. and/82,85
- 87. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
- 88. 86 not 87

FEVER_hospitalisation_cinahl_280206

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.

11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/

- 49. herpes simplex.tw.
- 50. or/48-49
- 51. exp ARTHRITIS, INFECTIOUS/
- 52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 53. pyarthrosis.tw.
- 54. pyoarthritis.tw.
- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTIONS/
- 57. STREPTOCOCCAL INFECTIONS/
- 58. ((straphylococc\$ or streptococc\$) adj infect\$).tw.
- 59. or/56-58
- 60. OSTEOMYELITIS/
- 61. osteomyeliti\$.tw.
- 62. or/60-61
- 63. exp URINARY TRACT INFECTION/
- 64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 65. UTI.tw.
- 66. ((upper or lower) adj5 urin\$).tw.
- 67. CYSTITIS/
- 68. cystitis\$.tw.
- 69. PYELONEPHRITIS/
- 70. pyelonephriti\$.tw.
- 71. pyonephrosi\$.tw.
- 72. pyelocystiti\$.tw.
- 73. or/63-72
- 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 75. (mucocutaneous adj2 lymph\$).tw.
- 76. mcls.tw.
- 77. (kawasaki adj (disease or syndrome)).tw.
- 78. or/74-77
- 79. or/32,36,40,44,47,50,55,59,62,73,78
- 80. and/29,79
- 81. PATIENT ADMISSION/
- 82. CHILD, HOSPITALIZED/
- 83. or/81-82
- 84. and/80,83

FEVER_ibuprofen_paracetamol_adverse_effects_medline_091105

- 1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANALGESICS/
31. ANALGESICS, NON-NARCOTIC/
32. (analges\$ or analget\$ or anodyne\$).tw.
33. anti?pyretic\$.tw.
34. (antinociceptive adj (agent\$ or drug\$)).tw.
35. or/30-34
36. ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
37. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
38. NSAID\$.tw.
39. or/36-38
40. IBUPROFEN/

- 41. ibuprofen\$.tw.
- 42. or/40-41
- 43. ACETAMINOPHEN/
- 44. acetaminophen\$.tw.
- 45. paracetamol\$.tw.
- 46. or/43-45
- 47. or/35,39,42,46
- 48. and/29,47
- 49. ANALGESICS, NON-NARCOTIC/ae
- 50. ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/ae
- 51. IBUPROFEN/ae
- 52. ACETAMINOPHEN/ae
- 53. (adverse adj (effect\$ or outcome\$ or react\$)).tw.
- 54. side effect\$.tw.
- 55. or/49-54
- 56. and/48,55
- 57. animal/ not (human/ or (human/ and animal/))
- 58. 56 not 57

FEVER_ibuprofen_paracetamol_adverse_effects_embase_091105

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/
- 20. fever\$.tw.

21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrex\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANALGESIA/
31. ANALGESIC AGENT/
32. (analges\$ or analget\$ or anodyne\$).tw.
33. (antinociceptive adj (agent\$ or drug\$)).tw.
34. ANTIPYRETIC AGENT/
35. anti?pyretic\$.tw.
36. or/30-35
37. NONSTEROID ANTIINFLAMMATORY AGENT/
38. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
39. NSAID\$.tw.
40. or/37-39
41. IBUPROFEN/
42. ibuprofen\$.tw.
43. or/41-42
44. PARACETAMOL/
45. paracetamol\$.tw.
46. acetaminophen\$.tw.
47. or/44-46
48. or/36,40,43,47
49. and/29,48
50. ANALGESIC AGENT/ae
51. ANTIPYRETIC AGENT/ae
52. NONSTEROID ANTIINFLAMMATORY AGENT/ae
53. IBUPROFEN/ae
54. PARACETAMOL/ae
55. ADVERSE DRUG REACTION/
56. (adverse adj (effect\$ or outcome\$ or react\$)).tw.
57. side effect\$.tw.
58. or/50-57
59. and/49,58

FEVER_ibuprofen_paracetamol_adverse_effects_cinahl_091105

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANALGESIA/
31. ANALGESICS/
32. ANALGESICS, NONNARCOTIC/
33. (analges\$ or analget\$ or anodyne\$).tw.
34. (antinociceptive adj (agent\$ or drug\$)).tw.
35. (anti-pyretic\$ or antipyretic\$).tw.
36. or/30-35
37. ANTIINFLAMMATORY AGENTS, NON-STEROIDAL/

38. ((non-steroid\$ or nonsteroid\$) adj (anti-inflammatory or antiinflammatory) adj (agent\$ or drug\$)).tw.
39. NSAID\$.tw.
40. or/37-39
41. IBUPROFEN/
42. ibuprofen\$.tw.
43. or/41-42
44. ACETAMINOPHEN/
45. acetaminophen\$.tw.
46. paracetamol\$.tw.
47. or/44-46
48. or/36,40,43,47
49. and/29,48
50. ANALGESICS/ae
51. ANALGESICS, NONNARCOTIC/ae
52. ANTIINFLAMMATORY AGENTS, NON-STEROIDAL/ae
53. IBUPROFEN/ae
54. ACETAMINOPHEN/ae
55. ADVERSE DRUG EVENT/
56. (adverse adj (effect\$ or event\$ or outcome\$ or react\$)).tw.
57. side effect\$.tw.
58. or/50-57
59. and/49,58

FEVER_influenza_rsv_medline_150506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. INFLUENZA, HUMAN/
30. influenza.tw.
31. flu.tw.
32. or/29-31
33. RESPIRATORY SYNCYTIAL VIRUSES/
34. respiratory syncytial virus\$.tw.
35. rsv.tw.
36. or/33-35
37. and/17,28,32,36
38. animal/ not (human/ or (human/ and animal/))
39. 37 not 38

FEVER_influenza_rsv_embase_150506

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. INFLUENZA/
30. influenza.tw.
31. flu.tw.
32. or/29-31
33. RESPIRATORY SYNCYTIAL PNEUMOVIRUS/
34. respiratory syncytial virus\$.tw.
35. rsv.tw.
36. or/33-35
37. and/17,28,32,36

FEVER_influenza_rsv_cinahl_150506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. INFLUENZA/
30. influenza.tw.
31. flu.tw.
32. or/29-31
33. RESPIRATORY SYNCYTIAL VIRUSES/
34. respiratory syncytial virus\$.tw.
35. rsv.tw.
36. or/33-35
37. and/17,28,32,36

FEVER_oxygen_medline_210206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.

17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.

- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTIONS/
- 57. STREPTOCOCCAL INFECTIONS/
- 58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 59. or/56-58
- 60. OSTEOMYELITIS/
- 61. osteomyeliti\$.tw.
- 62. or/60-61
- 63. exp URINARY TRACT INFECTIONS/
- 64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 65. UTI.tw.
- 66. ((upper or lower) adj5 urin\$).tw.
- 67. exp CYSTITIS/
- 68. cystitis\$.tw.
- 69. PYELONEPHRITIS/
- 70. pyelonephriti\$.tw.
- 71. pyonephrosi\$.tw.
- 72. pyelocystiti\$.tw.
- 73. or/63-72
- 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 75. (mucocutaneous adj2 lymph\$).tw.
- 76. mcls.tw.
- 77. (kawasaki adj (disease or syndrome)).tw.
- 78. or/74-77
- 79. or/32,36,40,44,47,50,55,59,62,73,78
- 80. and/29,79
- 81. exp ANOXIA/
- 82. anoxi\$.tw.
- 83. hypoxi\$.tw.
- 84. ((oxygen or O2) adj deficien\$).tw.
- 85. or/81-84
- 86. OXYGEN CONSUMPTION/
- 87. (oxygen adj (consumption or saturat\$)).tw.
- 88. or/86-87
- 89. OXIMETRY/
- 90. oximetry.tw.
- 91. or/89-90
- 92. OXYGEN INHALATION THERAPY/

- 93. (oxygen\$ adj (administer or administration or therap\$)).tw.
- 94. or/92-93
- 95. or/85,88,91,94
- 96. and/80,95
- 97. animal/ not (human/ or (human/ and animal/))
- 98. 96 not 97

FEVER_oxygen_embase_210206

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 26. exp PYROGEN/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. BACTERIAL INFECTION/
- 31. (bacteri\$ adj infect\$).tw.
- 32. or/30-31

33. BACTERIAL MENINGITIS/

34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

35. meningococc\$.tw.

36. or/33-35

37. SEPTICEMIA/

38. septicemi\$.tw.

39. septicaemia\$.tw.

40. or/37-39

41. BACTEREMIA/

42. bacteremi\$.tw.

43. bacteraemia\$.tw.

44. or/41-43

45. exp PNEUMONIA/

46. pneumoni\$.tw.

47. or/45-46

48. HERPES SIMPLEX/

49. herpes simplex.tw.

50. or/48-49

51. BACTERIAL ARTHRITIS/

52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

53. pyarthrosis.tw.

54. pyoarthritis.tw.

55. or/51-54

56. STAPHYLOCOCCAL INFECTION/

57. STREPTOCOCCAL INFECTION/

58. straphylococc\$.tw.

59. streptococc\$.tw.

60. or/56-59

61. OSTEOMYELITIS/

62. osteomyeliti\$.tw.

63. or/61-62

64. exp URINARY TRACT INFECTION/

65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

66. UTI.tw.

67. ((upper or lower) adj5 urin\$).tw.

68. exp CYSTITIS/

69. cystitis\$.tw.

70. or/64-69
71. PYELONEPHRITIS/
72. pyelonephriti\$.tw.
73. pyonephrosi\$.tw.
74. pyelocystiti\$.tw.
75. or/71-74
76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
77. (mucocutaneous adj2 lymph\$).tw.
78. mcls.tw.
79. (kawasaki adj (disease or syndrome)).tw.
80. or/76-79
81. or/32,36,40,44,47,50,55,60,63,70,75,80
82. and/29,81
83. exp ANOXIA/
84. anoxi\$.tw.
85. hypoxi\$.tw.
86. ((oxygen or O2) adj deficien\$).tw.
87. or/83-86
88. OXYGEN THERAPY/
89. (oxygen adj (administer or administration or therap\$)).tw.
90. or/88-89
91. OXYGEN CONSUMPTION/
92. (oxygen adj consumption).tw.
93. or/91-92
94. OXYGEN SATURATION/
95. (oxygen adj saturat\$).tw.
96. or/94-95
97. exp OXIMETRY/
98. oximetry.tw.
99. or/97-98
100. or/87,90,93,96,99
101. and/82,100
102. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
103. 101 not 102

FEVER_oxygen_cinahl_210206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.

5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.

43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTION/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. CYSTITIS/
68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79

81. exp ANOXIA/
82. anoxi\$.tw.
83. hypoxi\$.tw.
84. ((oxygen or O2) adj deficien\$).tw.
85. or/81-84
86. OXYGEN INHALATION THERAPY/
87. (oxygen\$ adj (administer or administration or therap\$)).tw.
88. or/86-87
89. OXYGEN CONSUMPTION/
90. (oxygen adj consumption).tw.
91. or/89-90
92. OXYGEN SATURATION/
93. (oxygen adj saturat\$).tw.
94. or/92-93
95. OXIMETRY/
96. oximetry.tw.
97. or/95-96
98. or/85,88,91,94,97
99. and/80,98

FEVER_patient_observation_medline_210206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/

20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/

- 58. ((straphylococc\$ or streptococc\$) adj infect\$).tw.
- 59. or/56-58
- 60. OSTEOMYELITIS/
- 61. osteomyeliti\$.tw.
- 62. or/60-61
- 63. exp URINARY TRACT INFECTIONS/
- 64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 65. UTI.tw.
- 66. ((upper or lower) adj5 urin\$).tw.
- 67. exp CYSTITIS/
- 68. cystitis\$.tw.
- 69. PYELONEPHRITIS/
- 70. pyelonephriti\$.tw.
- 71. pyonephrosi\$.tw.
- 72. pyelocystiti\$.tw.
- 73. or/63-72
- 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 75. (mucocutaneous adj2 lymph\$).tw.
- 76. mcls.tw.
- 77. (kawasaki adj (disease or syndrome)).tw.
- 78. or/74-77
- 79. or/32,36,40,44,47,50,55,59,62,73,78
- 80. and/29,79
- 81. MONITORING, PHYSIOLOGIC/
- 82. ((patient\$ or physical\$ or physiologic\$) adj2 (assess\$ or monitor\$)).tw.
- 83. or/81-82
- 84. RISK ASSESSMENT/
- 85. risk\$.tw.
- 86. TIME FACTORS/
- 87. or/84-86
- 88. OBSERVATION/
- 89. observ\$.tw.
- 90. or/88-89
- 91. and/87,90
- 92. or/83,91
- 93. and/80,92
- 94. animal/ not (human/ or (human/ and animal/))
- 95. 93 not 94

FEVER_patient_observation_embase_210206

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTION/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. BACTERIAL MENINGITIS/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/

- 38. septicemi\$.tw.
- 39. septicaemia\$.tw.
- 40. or/37-39
- 41. BACTEREMIA/
- 42. bacteremi\$.tw.
- 43. bacteraemia\$.tw.
- 44. or/41-43
- 45. exp PNEUMONIA/
- 46. pneumoni\$.tw.
- 47. or/45-46
- 48. HERPES SIMPLEX/
- 49. herpes simplex.tw.
- 50. or/48-49
- 51. BACTERIAL ARTHRITIS/
- 52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 53. pyarthrosis.tw.
- 54. pyoarthritis.tw.
- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTION/
- 57. STREPTOCOCCAL INFECTION/
- 58. straphylococc\$.tw.
- 59. streptococc\$.tw.
- 60. or/56-59
- 61. OSTEOMYELITIS/
- 62. osteomyeliti\$.tw.
- 63. or/61-62
- 64. exp URINARY TRACT INFECTION/
- 65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 66. UTI.tw.
- 67. ((upper or lower) adj5 urin\$).tw.
- 68. exp CYSTITIS/
- 69. cystitis\$.tw.
- 70. or/64-69
- 71. PYELONEPHRITIS/
- 72. pyelonephriti\$.tw.
- 73. pyonephrosi\$.tw.
- 74. pyelocystiti\$.tw.
- 75. or/71-74

76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
77. (mucocutaneous adj2 lymph\$).tw.
78. mcls.tw.
79. (kawasaki adj (disease or syndrome)).tw.
80. or/76-79
81. or/32,36,40,44,47,50,55,60,63,70,75,80
82. and/29,81
83. exp PATIENT MONITORING/
84. ((patient\$ or physical\$ or physiologic\$) adj2 (assess\$ or monitor\$)).tw.
85. or/83-84
86. RISK ASSESSMENT/
87. risk\$.tw.
88. TIME/
89. or/86-88
90. CLINICAL OBSERVATION/
91. observ\$.tw.
92. or/90-91
93. and/89,92
94. or/85,93
95. and/82,94
96. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
97. 95 not 96

FEVER_patient_observation_cinahl_210206

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.

17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTIONS/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.

-
55. or/51-54
 56. STAPHYLOCOCCAL INFECTIONS/
 57. STREPTOCOCCAL INFECTIONS/
 58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
 59. or/56-58
 60. OSTEOMYELITIS/
 61. osteomyeliti\$.tw.
 62. or/60-61
 63. exp URINARY TRACT INFECTION/
 64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
 65. UTI.tw.
 66. ((upper or lower) adj5 urin\$).tw.
 67. CYSTITIS/
 68. cystitis\$.tw.
 69. PYELONEPHRITIS/
 70. pyelonephriti\$.tw.
 71. pyonephrosi\$.tw.
 72. pyelocystiti\$.tw.
 73. or/63-72
 74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
 75. (mucocutaneous adj2 lymph\$).tw.
 76. mcls.tw.
 77. (kawasaki adj (disease or syndrome)).tw.
 78. or/74-77
 79. or/32,36,40,44,47,50,55,59,62,73,78
 80. and/29,79
 81. MONITORING, PHYSIOLOGIC/
 82. ((patient\$ or physical\$ or physiologic\$) adj2 (assess\$ or monitor\$)).tw.
 83. or/81-82
 84. RISK ASSESSMENT/
 85. risk\$.tw.
 86. TIME FACTORS/
 87. or/84-86
 88. OBSERVATION UNITS/
 89. observ\$.tw.
 90. or/88-89
 91. and/87,90
 92. or/83,91

93. and/80,92

FEVER_perception_medline_010306

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. INFANT, LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. ACUTE DISEASE/

19. (acute adj (disease\$ or illness\$)).tw.

20. or/18-19

21. BACTERIAL INFECTIONS/

22. (bacteri\$ adj infect\$).tw.

23. or/21-22

24. exp MENINGITIS, BACTERIAL/

25. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

26. meningococc\$.tw.

27. or/24-26

28. SEPTICEMIA/

29. septicemi\$.tw.

30. septicemia\$.tw.

31. or/28-30

32. BACTEREMIA/

33. bacteremi\$.tw.

34. bacteraemia\$.tw.

35. or/32-34

36. exp PNEUMONIA/

37. pneumoni\$.tw.
38. or/36-37
39. HERPES SIMPLEX/
40. herpes simplex.tw.
41. or/39-40
42. exp ARTHRITIS, INFECTIOUS/
43. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
44. pyarthrosis.tw.
45. pyoarthritis.tw.
46. or/42-45
47. STAPHYLOCOCCAL INFECTIONS/
48. STREPTOCOCCAL INFECTIONS/
49. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
50. or/47-49
51. OSTEOMYELITIS/
52. osteomyeliti\$.tw.
53. or/51-52
54. exp URINARY TRACT INFECTIONS/
55. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
56. UTI.tw.
57. ((upper or lower) adj5 urin\$).tw.
58. exp CYSTITIS/
59. cystitis\$.tw.
60. PYELONEPHRITIS/
61. pyelonephriti\$.tw.
62. pyonephrosi\$.tw.
63. pyelocystiti\$.tw.
64. or/54-63
65. MUCOCUTANEOUS LYMPH NODE SYNDROME/
66. (mucocutaneous adj2 lymph\$).tw.
67. mcls.tw.
68. (kawasaki adj (disease or syndrome)).tw.
69. or/65-68
70. or/20,23,27,31,35,38,41,46,50,53,64,69
71. "ATTITUDE OF HEALTH PERSONNEL"/
72. PERCEPTION/
73. perception.tw.
74. perceive\$.tw.

75. or/71-74

76. and/17,70,75

77. animal/ not (human/ or (human/ and animal/))

78. 76 not 77

FEVER_perception_embase_010306

1. PREMATUREITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. ACUTE DISEASE/

19. (acute adj (disease\$ or illness\$)).tw.

20. or/18-19

21. BACTERIAL INFECTION/

22. (bacteri\$ adj infect\$).tw.

23. or/21-22

24. BACTERIAL MENINGITIS/

25. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

26. meningococc\$.tw.

27. or/24-26

28. SEPTICEMIA/

29. septicemi\$.tw.

30. septicaemia\$.tw.

31. or/28-30

32. BACTEREMIA/

33. bacteremi\$.tw.

34. bacteraemia\$.tw.
35. or/32-34
36. exp PNEUMONIA/
37. pneumoni\$.tw.
38. or/36-37
39. HERPES SIMPLEX/
40. herpes simplex.tw.
41. or/39-40
42. BACTERIAL ARTHRITIS/
43. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
44. pyarthrosis.tw.
45. pyoarthritis.tw.
46. or/42-45
47. STAPHYLOCOCCAL INFECTION/
48. STREPTOCOCCAL INFECTION/
49. straphylococc\$.tw.
50. streptococc\$.tw.
51. or/47-50
52. OSTEOMYELITIS/
53. osteomyeliti\$.tw.
54. or/52-53
55. exp URINARY TRACT INFECTION/
56. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
57. UTI.tw.
58. ((upper or lower) adj5 urin\$).tw.
59. exp CYSTITIS/
60. cystitis\$.tw.
61. or/55-60
62. PYELONEPHRITIS/
63. pyelonephriti\$.tw.
64. pyonephrosi\$.tw.
65. pyelocystiti\$.tw.
66. or/62-65
67. MUCOCUTANEOUS LYMPH NODE SYNDROME/
68. (mucocutaneous adj2 lymph\$).tw.
69. mcls.tw.
70. (kawasaki adj (disease or syndrome)).tw.
71. or/67-70

72. or/20,23,27,31,35,38,41,46,51,54,61,66,71

73. "HEALTH PERSONNEL ATTITUDE"/

74. PERCEPTION/

75. perception.tw.

76. perceive\$.tw.

77. or/73-76

78. and/17,72,77

79. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

80. 78 not 79

FEVER_perception_cinahl_010306

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. ACUTE DISEASE/

19. (acute adj (disease\$ or illness\$)).tw.

20. or/18-19

21. BACTERIAL INFECTIONS/

22. (bacteri\$ adj infect\$).tw.

23. or/21-22

24. exp MENINGITIS, BACTERIAL/

25. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

26. meningococc\$.tw.

27. or/24-26

28. exp SEPSIS/

29. septicemi\$.tw.
30. septicaemia\$.tw.
31. or/28-30
32. BACTEREMIA/
33. bacteremi\$.tw.
34. bacteraemia\$.tw.
35. or/32-34
36. exp PNEUMONIA/
37. pneumoni\$.tw.
38. or/36-37
39. HERPES SIMPLEX/
40. herpes simplex.tw.
41. or/39-40
42. exp ARTHRITIS, INFECTIOUS/
43. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
44. pyarthrosis.tw.
45. pyoarthritis.tw.
46. or/42-45
47. STAPHYLOCOCCAL INFECTIONS/
48. STREPTOCOCCAL INFECTIONS/
49. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
50. or/47-49
51. OSTEOMYELITIS/
52. osteomyeliti\$.tw.
53. or/51-52
54. exp URINARY TRACT INFECTION/
55. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
56. UTI.tw.
57. ((upper or lower) adj5 urin\$).tw.
58. CYSTITIS/
59. cystitis\$.tw.
60. PYELONEPHRITIS/
61. pyelonephriti\$.tw.
62. pyonephrosi\$.tw.
63. pyelocystiti\$.tw.
64. or/54-63
65. MUCOCUTANEOUS LYMPH NODE SYNDROME/
66. (mucocutaneous adj2 lymph\$).tw.

- 67. mcls.tw.
- 68. (kawasaki adj (disease or syndrome)).tw.
- 69. or/65-68
- 70. or/20,23,27,31,35,38,41,46,50,53,64,69
- 71. "ATTITUDE OF HEALTH PERSONNEL"/
- 72. PERCEPTION/
- 73. perception.tw.
- 74. perceive\$.tw.
- 75. or/71-74
- 76. and/17,70,75

FEVER_prediction_severity_illness_medline_270905

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. INFANT, VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. CHILD, PRESCHOOL/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. "FEVER OF UNKNOWN ORIGIN"/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 26. exp PYROGENS/
- 27. pyrogen\$.tw.
- 28. or/18-27

29. and/17,28
30. "SEVERITY OF ILLNESS INDEX"/
31. (sever\$ adj3 (disease\$ or illness\$ or infect\$)).tw.
32. or/30-31
33. (temperature\$ adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
34. ((fever\$ or febrile\$ or hypertherm\$ or pyre\$) adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
35. or/33,34
36. and/32,35
37. and/29,36
38. animal/ not (human/ or (human/ and animal/))
39. 37 not 38

FEVER_prediction_severity_illness_embase_270905

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

- 26. exp PYROGEN/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. HOSPITALIZATION/
- 31. (sever\$ adj3 (disease\$ or illness\$ or infect\$)).tw.
- 32. or/30-31
- 33. (temperature\$ adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
- 34. (fever\$ adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
- 35. or/33-34
- 36. and/32,35
- 37. and/29,36
- 38. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
- 39. 37 not 38

FEVER_prediction_severity_illness_cinahl_270905

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. "FEVER OF UNKNOWN ORIGIN"/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.

23. pyrex\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. "SEVERITY OF ILLNESS INDICES"/
31. (sever\$ adj3 (disease\$ or illness\$ or infect\$)).tw.
32. or/30-31
33. (temperature\$ adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
34. (fever\$ adj3 (classif\$ or correlat\$ or degree\$ or height\$ or indicat\$ or magnitude\$ or predict\$ or sever\$ or stratif\$)).tw.
35. or/33-34
36. and/32,35
37. and/29,36

FEVER_procalcitonin_medline_120406

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/

- 22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 23. meningococc\$.tw.
- 24. or/21-23
- 25. SEPTICEMIA/
- 26. septicemi\$.tw.
- 27. septicaemia\$.tw.
- 28. or/25-27
- 29. BACTEREMIA/
- 30. bacteremi\$.tw.
- 31. bacteraemia\$.tw.
- 32. or/29-31
- 33. exp PNEUMONIA/
- 34. pneumoni\$.tw.
- 35. or/33-34
- 36. HERPES SIMPLEX/
- 37. herpes simplex.tw.
- 38. or/36-37
- 39. exp ARTHRITIS, INFECTIOUS/
- 40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 41. pyarthrosis.tw.
- 42. pyoarthritis.tw.
- 43. or/39-42
- 44. STAPHYLOCOCCAL INFECTIONS/
- 45. STREPTOCOCCAL INFECTIONS/
- 46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 47. or/44-46
- 48. OSTEOMYELITIS/
- 49. osteomyeliti\$.tw.
- 50. or/48-49
- 51. exp URINARY TRACT INFECTIONS/
- 52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 53. UTI.tw.
- 54. ((upper or lower) adj5 urin\$).tw.
- 55. exp CYSTITIS/
- 56. cystitis\$.tw.
- 57. PYELONEPHRITIS/
- 58. pyelonephriti\$.tw.

59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. CALCITONIN/
69. calcitoni\$.tw.
70. PROTEIN PRECURSORS/
71. procalcitonin.tw.
72. or/68-71
73. exp "SENSITIVITY AND SPECIFICITY"/
74. (sensitivity or specificity).tw.
75. (predictive adj value\$).tw.
76. LIKELIHOOD FUNCTIONS/
77. (likelihood adj (estimate\$ or ratio\$)).tw.
78. exp DIAGNOSTIC ERRORS/
79. (false adj (negative\$ or positive\$)).tw.
80. "REPRODUCIBILITY OF RESULTS"/
81. DIAGNOSIS, DIFFERENTIAL/
82. (differential adj diagnos\$).tw.
83. or/73-82
84. and/17,67,72,83
85. animal/ not (human/ or (human/ and animal/))
86. 84 not 85

FEVER_procalcitonin_embase_120406

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.

11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTION/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. BACTERIAL MENINGITIS/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. BACTERIAL ARTHRITIS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTION/
45. STREPTOCOCCAL INFECTION/
46. straphylococc\$.tw.
47. streptococc\$.tw.
48. or/44-47

49. OSTEOMYELITIS/
50. osteomyeliti\$.tw.
51. or/49-50
52. exp URINARY TRACT INFECTION/
53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
54. UTI.tw.
55. ((upper or lower) adj5 urin\$).tw.
56. exp CYSTITIS/
57. cystitis\$.tw.
58. or/52-57
59. PYELONEPHRITIS/
60. pyelonephriti\$.tw.
61. pyonephrosi\$.tw.
62. pyelocystiti\$.tw.
63. or/59-62
64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
65. (mucocutaneous adj2 lymph\$).tw.
66. mcls.tw.
67. (kawasaki adj (disease or syndrome)).tw.
68. or/64-67
69. or/20,24,28,32,35,38,43,48,51,58,63,68
70. CALCITONIN/
71. calcitoni\$.tw.
72. PROTEIN PRECURSORS/
73. PROCALCITONIN/
74. procalcitonin.tw.
75. or/70-74
76. exp "SENSITIVITY AND SPECIFICITY"/
77. (sensitivity or specificity).tw.
78. (predictive adj value\$).tw.
79. STATISTICAL MODEL/
80. (likelihood adj (estimate\$ or ratio\$)).tw.
81. DIAGNOSTIC ERROR/
82. (false adj (negative\$ or positive\$)).tw.
83. REPRODUCIBILITY/
84. DIFFERENTIAL DIAGNOSIS/
85. (differential adj diagnos\$).tw.
86. or/76-85

87. and/17,69,75,86

88. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

89. 87 not 88

FEVER_procalcitonin_cinahl_120406

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. exp SEPSIS/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

-
35. or/33-34
 36. HERPES SIMPLEX/
 37. herpes simplex.tw.
 38. or/36-37
 39. exp ARTHRITIS, INFECTIOUS/
 40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
 41. pyarthrosis.tw.
 42. pyoarthritis.tw.
 43. or/39-42
 44. STAPHYLOCOCCAL INFECTIONS/
 45. STREPTOCOCCAL INFECTIONS/
 46. ((straphylococc\$ or streptococc\$) adj infect\$).tw.
 47. or/44-46
 48. OSTEOMYELITIS/
 49. osteomyeliti\$.tw.
 50. or/48-49
 51. exp URINARY TRACT INFECTION/
 52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
 53. UTI.tw.
 54. ((upper or lower) adj5 urin\$).tw.
 55. CYSTITIS/
 56. cystitis\$.tw.
 57. PYELONEPHRITIS/
 58. pyelonephriti\$.tw.
 59. pyonephrosi\$.tw.
 60. pyelocystiti\$.tw.
 61. or/51-60
 62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
 63. (mucocutaneous adj2 lymph\$).tw.
 64. mcls.tw.
 65. (kawasaki adj (disease or syndrome)).tw.
 66. or/62-65
 67. or/20,24,28,32,35,38,43,47,50,61,66
 68. CALCITONIN/
 69. calcitoni\$.tw.
 70. PROTEIN PRECURSORS/
 71. procalcitonin.tw.
 72. or/68-71

73. and/17,67,72

FEVER_prognosis_medline_251105

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. INFANT, LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp FEVER/

19. "FEVER OF UNKNOWN ORIGIN"/

20. fever\$.tw.

21. febril\$.tw.

22. hypertherm\$.tw.

23. pyrexia\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGENS/

27. pyrogen\$.tw.

28. or/18-27

29. and/17,28

30. BACTERIAL INFECTIONS/

31. (bacteri\$ adj infect\$).tw.

32. or/30-31

33. exp MENINGITIS, BACTERIAL/

34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

35. meningococc\$.tw.

36. or/33-35

37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTIONS/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. exp CYSTITIS/
68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/

75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79
81. exp COHORT STUDIES/
82. exp MORTALITY/
83. exp MORBIDITY/
84. natural history.ti,ab.
85. prognos\$.ti,ab.
86. course.ti,ab.
87. predict\$.ti,ab.
88. exp "OUTCOME ASSESSMENT (HEALTH CARE)"/
89. outcome\$.ti,ab.
90. (inception adj cohort\$).ti,ab.
91. DISEASE PROGRESSION/
92. exp SURVIVAL ANALYSIS/
93. exp PROGNOSIS/
94. or/81-93
95. and/80,94
96. animal/ not (human/ or (human/ and animal/))
97. 95 not 96

FEVER_prognosis_embase_251105

1. PREMATURITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BACTERIAL INFECTION/
31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. BACTERIAL MENINGITIS/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. BACTERIAL ARTHRITIS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.

- 54. pyoarthritis.tw.
- 55. or/51-54
- 56. STAPHYLOCOCCAL INFECTION/
- 57. STREPTOCOCCAL INFECTION/
- 58. straphylococc\$.tw.
- 59. streptococc\$.tw.
- 60. or/56-59
- 61. OSTEOMYELITIS/
- 62. osteomyeliti\$.tw.
- 63. or/61-62
- 64. exp URINARY TRACT INFECTION/
- 65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 66. UTI.tw.
- 67. ((upper or lower) adj5 urin\$).tw.
- 68. exp CYSTITIS/
- 69. cystitis\$.tw.
- 70. or/64-69
- 71. PYELONEPHRITIS/
- 72. pyelonephriti\$.tw.
- 73. pyonephrosi\$.tw.
- 74. pyelocystiti\$.tw.
- 75. or/71-74
- 76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 77. (mucocutaneous adj2 lymph\$).tw.
- 78. mcls.tw.
- 79. (kawasaki adj (disease or syndrome)).tw.
- 80. or/76-79
- 81. or/32,36,40,44,47,50,55,60,63,70,75,80
- 82. and/29,81
- 83. exp COHORT STUDIES/
- 84. exp MORTALITY/
- 85. exp MORBIDITY/
- 86. natural history.ti,ab.
- 87. prognos\$.ti,ab.
- 88. course.ti,ab.
- 89. predict\$.ti,ab.
- 90. exp "OUTCOME ASSESSMENT (HEALTH CARE)"/
- 91. outcome\$.ti,ab.

- 92. (inception adj cohort\$).ti,ab.
- 93. DISEASE PROGRESSION/
- 94. exp SURVIVAL ANALYSIS/
- 95. exp PROGNOSIS/
- 96. or/83-95
- 97. and/82,96
- 98. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
- 99. 97 not 98

FEVER_prognosis_cinahl_251105

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. "FEVER OF UNKNOWN ORIGIN"/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 26. exp PYROGENS/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. BACTERIAL INFECTIONS/

31. (bacteri\$ adj infect\$).tw.
32. or/30-31
33. exp MENINGITIS, BACTERIAL/
34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. exp SEPSIS/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. exp ARTHRITIS, INFECTIOUS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTIONS/
57. STREPTOCOCCAL INFECTIONS/
58. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
59. or/56-58
60. OSTEOMYELITIS/
61. osteomyeliti\$.tw.
62. or/60-61
63. exp URINARY TRACT INFECTION/
64. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
65. UTI.tw.
66. ((upper or lower) adj5 urin\$).tw.
67. CYSTITIS/

68. cystitis\$.tw.
69. PYELONEPHRITIS/
70. pyelonephriti\$.tw.
71. pyonephrosi\$.tw.
72. pyelocystiti\$.tw.
73. or/63-72
74. MUCOCUTANEOUS LYMPH NODE SYNDROME/
75. (mucocutaneous adj2 lymph\$).tw.
76. mcls.tw.
77. (kawasaki adj (disease or syndrome)).tw.
78. or/74-77
79. or/32,36,40,44,47,50,55,59,62,73,78
80. and/29,79
81. exp COHORT STUDIES/
82. exp MORTALITY/
83. exp MORBIDITY/
84. natural history.ti,ab.
85. prognos\$.ti,ab.
86. course.ti,ab.
87. predict\$.ti,ab.
88. OUTCOME ASSESSMENT/
89. outcome\$.ti,ab.
90. (inception adj cohort\$).ti,ab.
91. DISEASE PROGRESSION/
92. exp SURVIVAL ANALYSIS/
93. exp PROGNOSIS/
94. or/81-93
95. and/80,94

FEVER_serious_bacterial_infections_epidemiology_medline_101105

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.

11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/

49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTIONS/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. exp CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. and/17,67
69. EPIDEMIOLOGY/
70. epidemiolog\$.tw.
71. BACTERIAL INFECTIONS/ep
72. MENINGITIS, BACTERIAL/ep
73. SEPTICEMIA/ep
74. BACTEREMIA/ep
75. PNEUMONIA/ep
76. HERPES SIMPLEX/ep
77. ARTHRITIS, INFECTIOUS/ep
78. STAPHYLOCOCCAL INFECTIONS/ep
79. STREPTOCOCCAL INFECTIONS/ep
80. OSTEOMYELITIS/ep
81. URINARY TRACT INFECTIONS/ep
82. CYSTITIS/ep
83. PYELONEPHRITIS/ep
84. MUCOCUTANEOUS LYMPH NODE SYNDROME/ep
85. or/69-84
86. and/68,85

- 87. exp GREAT BRITAIN/
- 88. (britain or england or northern ireland or scotland or united kingdom or wales).tw.
- 89. or/87-88
- 90. and/86,89
- 91. limit 90 to yr="1992 - 2006"

FEVER_serious_bacterial_infections_epidemiology_embase_101105

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
- 26. exp PYROGEN/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. BACTERIAL INFECTION/
- 31. (bacteri\$ adj infect\$).tw.
- 32. or/30-31
- 33. BACTERIAL MENINGITIS/

34. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
35. meningococc\$.tw.
36. or/33-35
37. SEPTICEMIA/
38. septicemi\$.tw.
39. septicaemia\$.tw.
40. or/37-39
41. BACTEREMIA/
42. bacteremi\$.tw.
43. bacteraemia\$.tw.
44. or/41-43
45. exp PNEUMONIA/
46. pneumoni\$.tw.
47. or/45-46
48. HERPES SIMPLEX/
49. herpes simplex.tw.
50. or/48-49
51. BACTERIAL ARTHRITIS/
52. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
53. pyarthrosis.tw.
54. pyoarthritis.tw.
55. or/51-54
56. STAPHYLOCOCCAL INFECTION/
57. STREPTOCOCCAL INFECTION/
58. staphylococc\$.tw.
59. streptococc\$.tw.
60. or/56-59
61. OSTEOMYELITIS/
62. osteomyeliti\$.tw.
63. or/61-62
64. exp URINARY TRACT INFECTION/
65. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
66. UTI.tw.
67. ((upper or lower) adj5 urin\$).tw.
68. exp CYSTITIS/
69. cystitis\$.tw.
70. or/64-69

71. PYELONEPHRITIS/
72. pyelonephriti\$.tw.
73. pyonephrosi\$.tw.
74. pyelocystiti\$.tw.
75. or/71-74
76. MUCOCUTANEOUS LYMPH NODE SYNDROME/
77. (mucocutaneous adj2 lymph\$).tw.
78. mcls.tw.
79. (kawasaki adj (disease or syndrome)).tw.
80. or/76-79
81. or/32,36,40,44,47,50,55,60,63,70,75,80
82. and/29,81
83. EPIDEMIOLOGY/
84. epidemiolog\$.tw.
85. BACTERIAL INFECTION/ep
86. BACTERIAL MENINGITIS/ep
87. PNEUMONIA/ep
88. HERPES SIMPLEX/ep
89. BACTERIAL ARTHRITIS/ep
90. STAPHYLOCOCCAL INFECTION/ep
91. STREPTOCOCCAL INFECTION/ep
92. OSTEOMYELITIS/ep
93. URINARY TRACT INFECTION/ep
94. CYSTITIS/ep
95. PYELONEPHRITIS/ep
96. MUCOCUTANEOUS LYMPH NODE SYNDROME/ep
97. or/83-96
98. and/82,97
99. exp UNITED KINGDOM/
100. (britain or england or northern ireland or scotland or united kingdom or wales).tw.
101. or/99-100
102. and/98,101
103. limit 102 to yr="1992 - 2006"

FEVER_serious_bacterial_infections_epidemiology_cinahl_101105

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. exp SEPSIS/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34

36. HERPES SIMPLEX/

37. herpes simplex.tw.

38. or/36-37

39. exp ARTHRITIS, INFECTIOUS/

40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

41. pyarthrosis.tw.

42. pyoarthritis.tw.

43. or/39-42

- 44. STAPHYLOCOCCAL INFECTIONS/
- 45. STREPTOCOCCAL INFECTIONS/
- 46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 47. or/44-46
- 48. OSTEOMYELITIS/
- 49. osteomyeliti\$.tw.
- 50. or/48-49
- 51. exp URINARY TRACT INFECTION/
- 52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 53. UTI.tw.
- 54. ((upper or lower) adj5 urin\$).tw.
- 55. CYSTITIS/
- 56. cystitis\$.tw.
- 57. PYELONEPHRITIS/
- 58. pyelonephriti\$.tw.
- 59. pyonephrosi\$.tw.
- 60. pyelocystiti\$.tw.
- 61. or/51-60
- 62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 63. (mucocutaneous adj2 lymph\$).tw.
- 64. mcls.tw.
- 65. (kawasaki adj (disease or syndrome)).tw.
- 66. or/62-65
- 67. or/20,24,28,32,35,38,43,47,50,61,66
- 68. and/17,67
- 69. EPIDEMIOLOGY/
- 70. epidemiolog\$.tw.
- 71. BACTERIAL INFECTIONS/ep
- 72. MENINGITIS, BACTERIAL/ep
- 73. SEPSIS/ep
- 74. BACTEREMIA/ep
- 75. PNEUMONIA/ep
- 76. HERPES SIMPLEX/ep
- 77. ARTHRITIS, INFECTIOUS/ep
- 78. STAPHYLOCOCCAL INFECTIONS/ep
- 79. STREPTOCOCCAL INFECTIONS/ep
- 80. OSTEOMYELITIS/ep
- 81. URINARY TRACT INFECTION/ep

82. CYSTITIS/ep
83. PYELONEPHRITIS/ep
84. MUCOCUTANEOUS LYMPH NODE SYNDROME/ep
85. or/69-84
86. and/68,85
87. exp GREAT BRITAIN/
88. (britain or england or northern ireland or scotland or united kingdom or wales).tw.
89. or/87-88
90. and/86,89
91. limit 90 to yr="1992 - 2005"

FEVER_severity_of_illness_indices_medline_250106

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.

- 28. or/18-27
- 29. and/17,28
- 30. "SEVERITY OF ILLNESS INDEX"/
- 31. ((illness or severity) adj3 (classif\$ or criteria or index or indice\$ or scale\$)).tw.
- 32. (yale adj2 (observation or scale)).tw.
- 33. (rochester adj2(criteria or scale)).tw.
- 34. RISK ASSESSMENT/
- 35. (risk adj (assess\$ or criteria\$)).tw.
- 36. or/30-35
- 37. and/29,36
- 38. animal/ not (human/ or (human/ and animal/))
- 39. 37 not 38

FEVER_severity_of_illness_indices_embase_250106

- 1. PREMATUREITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. HOSPITALIZATION/
31. ((illness or severity) adj3 (classif\$ or criteria or index or indice\$ or scale\$)).tw.
32. (yale adj2 (observation or scale)).tw.
33. (rochester adj (criteria or scale)).tw.
34. SCORING SYSTEM/
35. RISK ASSESSMENT/
36. (risk adj (assess\$ or criteria\$)).tw.
37. or/30-36
38. and/29,37
39. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
40. 38 not 39

FEVER_severity_of_illness_indices_cinahl_250106

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.

23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignant adj3 (hyperthermia\$ or hyperpyrexia\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. "SEVERITY OF ILLNESS INDEX"/
31. ((illness or severity) adj3 (classification\$ or criteria or index or indices\$ or scale\$)).tw.
32. (yale adj2 (observation or scale)).tw.
33. (rochester adj (criteria or scale)).tw.
34. RISK ASSESSMENT/
35. (risk adj (assessment\$ or criteria\$)).tw.
36. or/30-35
37. and/29,36

FEVER_signs_symptoms_prospective_medline_200306

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonate\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteria\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/
22. (meningitis\$ adj2 (bacteria\$ or coli or escheichia or listeria or pneumococcus\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTIONS/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. exp CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.

61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp "SIGNS AND SYMPTOMS"/
69. (sign\$ adj2 symptom\$).tw.
70. or/68-69
71. COHORT STUDIES/
72. LONGITUDINAL STUDIES/
73. FOLLOW-UP STUDIES/
74. PROSPECTIVE STUDIES/
75. ((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
76. or/71-75
77. and/17,67,70,76
78. animal/ not (human/ or (human/ and animal/))
79. 77 not 78
80. limit 79 to yr="1985 - 2006"
- FEVER_signs_symptoms_prospective_embase_200306
1. PREMATUREITY/
2. POSTMATURITY/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16

18. BACTERIAL INFECTION/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. BACTERIAL MENINGITIS/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. SEPTICEMIA/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34

36. HERPES SIMPLEX/

37. herpes simplex.tw.

38. or/36-37

39. BACTERIAL ARTHRITIS/

40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

41. pyarthrosis.tw.

42. pyoarthritis.tw.

43. or/39-42

44. STAPHYLOCOCCAL INFECTION/

45. STREPTOCOCCAL INFECTION/

46. straphylococc\$.tw.

47. streptococc\$.tw.

48. or/44-47

49. OSTEOMYELITIS/

50. osteomyeliti\$.tw.

51. or/49-50

52. exp URINARY TRACT INFECTION/

53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

54. UTI.tw.

55. ((upper or lower) adj5 urin\$).tw.
56. exp CYSTITIS/
57. cystitis\$.tw.
58. or/52-57
59. PYELONEPHRITIS/
60. pyelonephriti\$.tw.
61. pyonephrosi\$.tw.
62. pyelocystiti\$.tw.
63. or/59-62
64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
65. (mucocutaneous adj2 lymph\$).tw.
66. mcls.tw.
67. (kawasaki adj (disease or syndrome)).tw.
68. or/64-67
69. or/20,24,28,32,35,38,43,48,51,58,63,68
70. exp "PHYSICAL DISEASE BY BODY FUNCTION"/
71. (sign\$ adj2 symptom\$).tw.
72. or/70-71
73. COHORT STUDIES/
74. LONGITUDINAL STUDIES/
75. FOLLOW-UP STUDIES/
76. PROSPECTIVE STUDIES/
77. ((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
78. or/73-77
79. and/17,69,72,78
80. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
81. 79 not 80
82. limit 81 to yr="1985 - 2006"

FEVER_signs_symptoms_prospective_cinahl_200306

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.

10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. exp SEPSIS/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46

48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTION/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp "SIGNS AND SYMPTOMS"/
69. (sign\$ adj2 symptom\$).tw.
70. or/68-69
71. COHORT STUDIES/
72. LONGITUDINAL STUDIES/
73. FOLLOW-UP STUDIES/
74. PROSPECTIVE STUDIES/
75. ((cohort\$ or follow-up or follow?up or inciden\$ or longitudinal or prospective) adj1 (stud\$ or research or analys\$)).tw.
76. or/71-75
77. and/17,67,70,76
78. limit 77 to yr="1985 - 2006"

FEVER_signs_symptoms_retrospective_medline_090506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. SEPTICEMIA/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34

36. HERPES SIMPLEX/

37. herpes simplex.tw.

38. or/36-37

39. exp ARTHRITIS, INFECTIOUS/

40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

41. pyarthrosis.tw.

42. pyoarthritis.tw.

43. or/39-42

44. STAPHYLOCOCCAL INFECTIONS/

45. STREPTOCOCCAL INFECTIONS/

46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.

47. or/44-46

48. OSTEOMYELITIS/

49. osteomyeliti\$.tw.

50. or/48-49

51. exp URINARY TRACT INFECTIONS/

52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

53. UTI.tw.

54. ((upper or lower) adj5 urin\$).tw.

55. exp CYSTITIS/

56. cystitis\$.tw.

57. PYELONEPHRITIS/

58. pyelonephriti\$.tw.

59. pyonephrosi\$.tw.

60. pyelocystiti\$.tw.

61. or/51-60

62. MUCOCUTANEOUS LYMPH NODE SYNDROME/

63. (mucocutaneous adj2 lymph\$).tw.

64. mcls.tw.

65. (kawasaki adj (disease or syndrome)).tw.

66. or/62-65

67. or/20,24,28,32,35,38,43,47,50,61,66

68. exp "SIGNS AND SYMPTOMS"/

69. (sign\$ adj2 symptom\$).tw.

70. or/68-69

71. RETROSPECTIVE STUDIES/

72. retrospective\$.tw.

73. or/71-72

74. and/17,67,70,73

75. animal/ not (human/ or (human/ and animal/))

76. 74 not 75

77. limit 76 to yr="1985 - 2006"

FEVER_signs_symptoms_retrospective_embase_090506

1. PREMATURITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTION/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. BACTERIAL MENINGITIS/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. SEPTICEMIA/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. BACTERIAL ARTHRITIS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.

42. pyoarthriti\$.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTION/
45. STREPTOCOCCAL INFECTION/
46. straphylococc\$.tw.
47. streptococc\$.tw.
48. or/44-47
49. OSTEOMYELITIS/
50. osteomyeliti\$.tw.
51. or/49-50
52. exp URINARY TRACT INFECTION/
53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
54. UTI.tw.
55. ((upper or lower) adj5 urin\$).tw.
56. exp CYSTITIS/
57. cystitis\$.tw.
58. or/52-57
59. PYELONEPHRITIS/
60. pyelonephriti\$.tw.
61. pyonephrosi\$.tw.
62. pyelocystiti\$.tw.
63. or/59-62
64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
65. (mucocutaneous adj2 lymph\$).tw.
66. mcls.tw.
67. (kawasaki adj (disease or syndrome)).tw.
68. or/64-67
69. or/20,24,28,32,35,38,43,48,51,58,63,68
70. exp "PHYSICAL DISEASE BY BODY FUNCTION"/
71. (sign\$ adj2 symptom\$).tw.
72. or/70-71
73. RETROSPECTIVE STUDY/
74. retrospective\$.tw.
75. or/73-74
76. and/17,69,72,75
77. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
78. 76 not 77
79. limit 78 to yr="1985 - 2006"

FEVER_signs_symptoms_retrospective_cinahl_090506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BACTERIAL INFECTIONS/
19. (bacteri\$ adj infect\$).tw.
20. or/18-19
21. exp MENINGITIS, BACTERIAL/
22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
23. meningococc\$.tw.
24. or/21-23
25. exp SEPSIS/
26. septicemi\$.tw.
27. septicaemia\$.tw.
28. or/25-27
29. BACTEREMIA/
30. bacteremi\$.tw.
31. bacteraemia\$.tw.
32. or/29-31
33. exp PNEUMONIA/
34. pneumoni\$.tw.
35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.

38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTION/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. exp "SIGNS AND SYMPTOMS"/
69. (sign\$ adj2 symptom\$).tw.
70. or/68-69
71. RETROSPECTIVE DESIGN/
72. retrospective\$.tw.
73. or/71-72
74. and/17,67,70,73
75. limit 74 to yr="1985 - 2006"

FEVER_subjective_diagnosis_medline_050905

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. (carer\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
31. ((maternal\$ or mother\$) adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
32. (parent\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
33. (subjective\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
34. or/30-33
35. PALPATION/

- 36. (palpation adj5 (fever\$ or febril\$ or hypertherm\$ or pyrexia\$)).tw.
- 37. ((tactile or touch) adj2 examin\$).tw.
- 38. or/35-37
- 39. or/34,38
- 40. and/29,39
- 41. animal/ not (human/ or (human/ and animal/))
- 42. 40 not 41

FEVER_subjective_diagnosis_embase_060905

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/
- 20. fever\$.tw.
- 21. febril\$.tw.
- 22. hypertherm\$.tw.
- 23. pyrexia\$.tw.
- 24. MALIGNANT HYPERTHERMIA/
- 25. (malignan\$ adj3 (hypertherm\$ or hyperpyrexia\$)).tw.
- 26. exp PYROGEN/
- 27. pyrogen\$.tw.
- 28. or/18-27
- 29. and/17,28
- 30. (carer\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.

31. ((maternal\$ or mother\$) adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
32. (parent\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
33. (subjective\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
34. or/30-33
35. PALPATATION/
36. (palpation adj5 (fever\$ or febril\$ or hypertherm\$ or pyrexia\$)).tw.
37. ((tactile or touch) adj2 examin\$).tw.
38. or/35-37
39. or/34,38
40. and/29,39
41. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
42. 40 not 41

FEVER_subjective_diagnosis_cinahl_060905

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. (carer\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
31. ((maternal\$ or mother\$) adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
32. (parent\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
33. (subjective\$ adj2 (assess\$ or detect\$ or determin\$ or diagnos\$ or evaluat\$ or measur\$ or perceive\$ or perception\$ or presence\$)).tw.
34. or/30-33
35. PALPATION/
36. (palpation adj5 (fever\$ or febril\$ or hypertherm\$ or pyrexia\$)).tw.
37. ((tactile or touch) adj2 examin\$).tw.
38. or/35-37
39. or/34,38
40. and/29,39
41. animal/ not (human/ or (human/ and animal/))
42. 40 not 41

FEVER_temperature_measurement_medline_050805

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16

18. BODY TEMPERATURE/

19. ((bodies or body\$) adj2 temperature\$).tw.

20. ((axillar\$ or forehead\$ or oral\$ or rect\$ or skin\$ or surface\$ or topical\$) adj2 temperature\$).tw.

21. or/18-20

22. THERMOMETERS/

23. THERMOGRAPHY/mt

24. thermomet\$.tw.

25. thermograph\$.tw.

26. ((chemical\$ or crystal\$ or digital\$ or dispos\$ or electr\$ or forehead\$ or infrared\$ or glass\$ or mercury\$ or tympanic\$) adj5 thermomet\$).tw.

27. (pulmonary adj2 artery adj5 temperature).tw.

28. *TYMPANIC MEMBRANE/

29. INFRARED RAYS/du

30. or/22-29

31. and/21,30

32. and/17,31

33. animal/ not (human/ or (human/ and animal/))

34. 32 not 33

FEVER_temperature_measurement_embase_050805

1. PREMATUREITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BODY TEMPERATURE/

19. ((bodies or body\$) adj2 temperature\$).tw.

20. ((axillar\$ or forehead\$ or oral\$ or rect\$ or skin\$ or surface\$ or topical\$) adj2 temperature\$).tw.

21. or/18-20
22. THERMOMETER/
23. THERMOGRAPHY/
24. thermomet\$.tw.
25. thermograph\$.tw.
26. ((chemical\$ or crystal\$ or digital\$ or dispos\$ or electr\$ or forehead\$ or infrared\$ or glass\$ or mercury\$ or tympanic\$) adj5 thermomet\$).tw.
27. (pulmonary adj2 artery adj5 temperature).tw.
28. *EARDRUM/
29. INFRARED RADIATION/du
30. or/22-29
31. and/21,30
32. and/17,31
33. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
34. 32 not 33

FEVER_temperature_measurement_cinahl_050805

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. BODY TEMPERATURE/
19. ((bodies or body\$) adj2 temperature\$).tw.
20. ((axillar\$ or forehead\$ or oral\$ or rect\$ or skin\$ or surface\$ or topical\$) adj2 temperature\$).tw.
21. or/18-20
22. THERMOMETER/
23. THERMOGRAPHY/

24. thermomet\$.tw.
25. thermograph\$.tw.
26. ((chemical\$ or crystal\$ or digital\$ or dispos\$ or electr\$ or forehead\$ or infrared\$ or glass\$ or mercury\$ or tympanic\$) adj5 thermomet\$).tw.
27. (pulmonary adj2 artery adj5 temperature).tw.
28. *TYMPANIC MEMBRANE/
29. (infrared adj (rays or radiation)).tw.
30. or/22-29
31. and/21,30
32. and/17,31
33. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
34. 32 not 33

FEVER_temperature_measurement_tempadot_medline_110506

1. tempa?dot.mp.
2. tempa dot.mp.
3. or/1-2

FEVER_temperature_measurement_tempadot_embase_110506

1. tempa?dot.mp.
2. tempa dot.mp.
3. or/1-2

FEVER_temperature_measurement_tempadot_cinahl_110506

1. tempa?dot.mp.
2. tempa dot.mp.
3. or/1-2

FEVER_temperature_reduction_medline_171005

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. INFANT, LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. INFANT, VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. CHILD, PRESCHOOL/
14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BODY TEMPERATURE/
31. BODY TEMPERATURE REGULATION/
32. ((temperature or thermal or thermo) adj2 (reduc\$ or regulat\$)).tw.
33. thermoregulat\$.tw.
34. cool\$.tw.
35. heat loss.tw.
36. or/30-35
37. ANALGESICS/
38. ANALGESICS, NON-NARCOTIC/
39. (analges\$ or analget\$ or anodyne\$).tw.
40. anti?pyretic\$.tw.
41. (antinociceptive adj (agent\$ or drug\$)).tw.
42. or/37-41
43. ANTI-INFLAMMATORY AGENTS, NON-STEROIDAL/
44. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
45. NSAID\$.tw.
46. or/43-45
47. IBUPROFEN/
48. ibuprofen\$.tw.
49. or/47-48
50. ACETAMINOPHEN/
51. acetaminophen\$.tw.
52. paracetamol\$.tw.
53. or/50-52

-
54. or/42,46,49,53
55. CRYOTHERAPY/
56. cryother\$.tw.
57. cryotreatment\$.tw.
58. cryoanalgesi\$.tw.
59. cyroanalgesi\$.tw.
60. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.
61. or/55-60
62. BATHS/
63. bath\$.tw.
64. spong\$.tw.
65. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.
66. or/62-65
67. WATER/
68. DRINKING/
69. FLUID THERAPY/
70. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.
71. hydrat\$.tw.
72. rehydrat\$.tw.
73. or/67-72
74. CLOTHING/
75. ((light\$ or remov\$) adj2 cloth\$).tw.
76. or/74-75
77. climatotherap\$.tw.
78. (climat\$ adj (therap\$ or treat\$)).tw.
79. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.
80. fan\$.tw.
81. or/77-80
82. HYPOTHERMIA, INDUCED/
83. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.
84. (blanket adj treatment\$).tw.
85. swaddling.tw.
86. or/82-85
87. COMBINED MODALITY THERAPY/
88. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.
89. or/87-88
90. or/54,61,66,73,76,81,86,89
91. and/36,90

92. and/29,91

93. animal/ not (human/ or (human/ and animal/))

94. 92 not 93

FEVER_temperature_reduction_embase_171005

1. PREMATUREITY/

2. POSTMATURITY/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp FEVER/

19. PYREXIA IDIOPATHICA/

20. fever\$.tw.

21. febril\$.tw.

22. hypertherm\$.tw.

23. pyrexia\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGEN/

27. pyrogen\$.tw.

28. or/18-27

29. and/17,28

30. BODY TEMPERATURE/

31. THERMOREGULATION/

32. thermoregulat\$.tw.

33. ((temperature or thermal or thermo) adj2 (reduc\$ or regulat\$)).tw.

34. or/30-33

35. COOLING/

36. cool\$.tw.
37. heat loss.tw.
38. or/35-37
39. or/34,38
40. ANALGESIA/
41. ANALGESIC AGENT/
42. (analges\$ or analget\$ or anodyne\$).tw.
43. (antinociceptive adj (agent\$ or drug\$)).tw.
44. ANTIPYRETIC AGENT/
45. anti?pyretic\$.tw.
46. or/40-45
47. NONSTEROID ANTIINFLAMMATORY AGENT/
48. (non?steroid\$ adj anti?inflammatory adj (agent\$ or drug\$)).tw.
49. NSAID\$.tw.
50. or/47-49
51. IBUPROFEN/
52. ibuprofen\$.tw.
53. or/51-52
54. PARACETAMOL/
55. paracetamol\$.tw.
56. acetaminophen\$.tw.
57. or/54-56
58. or/46,50,53,57
59. CRYOTHERAPY/
60. cryother\$.tw.
61. cryotreatment\$.tw.
62. CRYOANESTHESIA/
63. cryoanalgesi\$.tw.
64. cyroanalgesi\$.tw.
65. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.
66. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.
67. (blanket adj treatment\$).tw.
68. swaddling.tw.
69. or/59-68
70. BATH/
71. bath\$.tw.
72. spong\$.tw.
73. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.
74. or/70-73

75. WATER/

76. FLUID THERAPY/

77. FLUID INTAKE/

78. FLUID BALANCE/

79. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.

80. HYDRATION/

81. REHYDRATION/

82. hydrat\$.tw.

83. rehydrat\$.tw.

84. or/75-83

85. CLOTHING/

86. ((light\$ or remov\$) adj2 cloth\$).tw.

87. or/85-86

88. CLIMATOTHERAPY/

89. climatotherap\$.tw.

90. (climat\$ adj (therap\$ or treat\$)).tw.

91. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.

92. fan\$.tw.

93. or/88-92

94. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.

95. or/58,69,74,84,87,93-94

96. and/39,95

97. and/29,96

98. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

99. 97 not 98

FEVER_temperature_reduction_cinahl_171005

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. BODY TEMPERATURE/
31. BODY TEMPERATURE REGULATION/
32. ((temperature or thermal or thermo) adj2 (reduc\$ or regulat\$)).tw.
33. thermoregulat\$.tw.
34. cool\$.tw.
35. heat loss.tw.
36. or/30-35
37. ANALGESIA/
38. ANALGESICS/
39. ANALGESICS, NONNARCOTIC/
40. (analges\$ or analget\$ or anodyne\$).tw.
41. (antinociceptive adj (agent\$ or drug\$)).tw.
42. (anti-pyretic\$ or antipyretic\$).tw.
43. or/37-42
44. ANTIINFLAMMATORY AGENTS, NON-STEROIDAL/
45. ((non-steroid\$ or nonsteroid\$) adj (anti-inflammatory or antiinflammatory) adj (agent\$ or drug\$)).tw.
46. NSAID\$.tw.
47. or/44-46
48. IBUPROFEN/
49. ibuprofen\$.tw.
50. or/48-49

51. ACETAMINOPHEN/

52. acetaminophen\$.tw.

53. paracetamol\$.tw.

54. or/51-53

55. or/43,47,50,54

56. CRYOTHERAPY/

57. cryother\$.tw.

58. cryotreatment\$.tw.

59. cryoanalgesi\$.tw.

60. cyroanalgesi\$.tw.

61. (cold adj2 (analgesi\$ or an?esthe\$ or therap\$ or treat\$)).tw.

62. or/56-61

63. BATHS/

64. bath\$.tw.

65. spong\$.tw.

66. ((liquid or spray\$ or water) adj2 (cool\$ or immers\$ or submers\$)).tw.

67. or/63-66

68. WATER/

69. DRINKING BEHAVIOR/

70. FLUID THERAPY/

71. ((drink\$ or fluid\$ or liquid\$ or water\$) adj2 (balance\$ or consum\$ or equilibrium\$ or intake\$ or therap\$)).tw.

72. hydrat\$.tw.

73. rehydrat\$.tw.

74. or/68-73

75. CLOTHING/

76. ((light\$ or remov\$) adj2 cloth\$).tw.

77. or/75-76

78. climatotherap\$.tw.

79. (climat\$ adj (therap\$ or treat\$)).tw.

80. ((ambient\$ or environment\$ or room\$) adj5 (chill\$ or cold\$ or cool\$ or lower\$ or reduc\$)).tw.

81. fan\$.tw.

82. or/78-81

83. HYPOTHERMIA, INDUCED/

84. (hypothermi\$ adj2 (blanket\$ or induce\$)).tw.

85. (blanket adj treatment\$).tw.

86. swaddling.tw.

87. or/83-86

88. COMBINED MODALITY THERAPY/

89. ((modal\$ or multimodal\$) adj (combin\$ or therap\$ or treat\$)).tw.

90. or/88-89

91. or/55,62,67,74,77,82,87,90

92. and/36,91

93. and/29,92

FEVER_treatment_iv_fluids_steroids_aciclovir_medline_090506

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. INFANT, LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp MENINGITIS, BACTERIAL/

19. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

20. meningococc\$.tw.

21. or/18-20

22. exp SEPSIS/

23. sepsis.tw.

24. exp SEPTICEMIA/

25. septicemi\$.tw.

26. septicaemia\$.tw.

27. SHOCK, SEPTIC/

28. (septic adj shock).tw.

29. or/22-28

30. ENCEPHALITIS, HERPES SIMPLEX/

31. HERPES SIMPLEX/

32. herpes simplex.tw.

- 33. or/30-32
- 34. or/21,29,33
- 35. INFUSIONS, INTRAVENOUS/
- 36. INFUSIONS, PARENTERAL/
- 37. (infusion\$ adj2 (intravenous or parenteral)).tw.
- 38. bolus.tw.
- 39. or/35-38
- 40. exp ALBUMINS/
- 41. albumin\$.tw.
- 42. or/40-41
- 43. PLASMA SUBSTITUTES/
- 44. plasma substitut\$.tw.
- 45. ((blood or plasma) adj expander\$).tw.
- 46. crystalloid\$.tw.
- 47. or/43-46
- 48. COLLOIDS/
- 49. colloid\$.tw.
- 50. or/48-49
- 51. SODIUM CHLORIDE/
- 52. saline.tw.
- 53. or/51-52
- 54. ELECTROLYTES/
- 55. electrolyte\$.tw.
- 56. or/54-55
- 57. ISOTONIC SOLUTIONS/
- 58. (isotonic adj solution\$).tw.
- 59. or/57-58
- 60. FLUID THERAPY/
- 61. fluid therapy.tw.
- 62. or/60-61
- 63. or/39,42,47,50,53,56,59,62
- 64. exp ADRENAL CORTEX HORMONES/
- 65. adrenal cortex hormone\$.tw.
- 66. corticoid\$.tw.
- 67. corticosteroid\$.tw.
- 68. or/64-67
- 69. exp DEXAMETHASONE/
- 70. dexamethasone\$.tw.
- 71. or/69-70

- 72. or/68,71
- 73. ACYCLOVIR/
- 74. acyclovir.tw.
- 75. aciclovir.tw.
- 76. or/73-75
- 77. or/63,72,76
- 78. and/17,34,77
- 79. exp TREATMENT OUTCOME/
- 80. (treat\$ adj2 (effect\$ or efficac\$ or fail\$ or outcome\$)).tw.
- 81. or/79,80
- 82. and/78,81
- 83. animal/ not (human/ or (human/ and animal/))
- 84. 82 not 83

FEVER_treatment_iv_fluids_steroids_aciclovir_embase_090506

- 1. PREMATUREITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. BACTERIAL MENINGITIS/
- 19. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 20. meningococc\$.tw.
- 21. or/18-20
- 22. SEPSIS/
- 23. sepsis.tw.
- 24. SEPTICEMIA/

- 25. septicemi\$.tw.
- 26. septicaemia\$.tw.
- 27. SEPTIC SHOCK/
- 28. (septic adj shock).tw.
- 29. or/22-28
- 30. HERPES SIMPLEX ENCEPHALITIS/
- 31. HERPES SIMPLEX/
- 32. herpes simplex.tw.
- 33. or/30-32
- 34. or/21,29,33
- 35. BOLUS INJECTION/
- 36. bolus.tw.
- 37. or/35-36
- 38. ALBUMIN/
- 39. albumin\$.tw.
- 40. or/38-39
- 41. exp PLASMA SUBSTITUTE/
- 42. plasma substitut\$.tw.
- 43. ((blood or plasma) adj expander\$).tw.
- 44. crystalloid\$.tw.
- 45. or/41-44
- 46. COLLOID/
- 47. colloid\$.tw.
- 48. or/46-47
- 49. SODIUM CHLORIDE/
- 50. saline.tw.
- 51. or/49-50
- 52. ELECTROLYTE/
- 53. electrolyte\$.tw.
- 54. or/52-53
- 55. ISOTONIC SOLUTION/
- 56. (isotonic adj solution\$).tw.
- 57. or/55-56
- 58. exp FLUID THERAPY/
- 59. fluid therapy.tw.
- 60. or/58-59
- 61. or/37,40,45,48,51,54,57,60
- 62. exp CORTICOSTEROID/
- 63. corticosteroid\$.tw.

64. corticoid\$.tw.
65. adrenal cortex hormone\$.tw.
66. or/62-65
67. DEXAMETHASONE/
68. dexamethasone\$.tw.
69. or/67-68
70. or/66,69
71. ACICLOVIR/
72. aciclovir.tw.
73. acyclovir.tw.
74. or/71-73
75. or/61,70,74
76. and/17,34,75
77. exp TREATMENT OUTCOME/
78. (treat\$ adj2 (effect\$ or efficac\$ or fail\$ or outcome\$)).tw.
79. or/77-78
80. and/76,79
81. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
82. 80 not 81

FEVER_treatment_iv fluids_steroids_aciclovir_cinahl_090506

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp MENINGITIS, BACTERIAL/

19. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
20. meningococc\$.tw.
21. or/18-20
22. exp SEPSIS/
23. septicemi\$.tw.
24. septicaemia\$.tw.
25. SHOCK, SEPTIC/
26. (septic adj shock).tw.
27. or/22-26
28. HERPES SIMPLEX/
29. herpes simplex.tw.
30. or/28-29
31. or/21,27,30
32. INFUSIONS, INTRAVENOUS/
33. INFUSIONS, PARENTERAL/
34. (infusion\$ adj2 (intravenous or parenteral)).tw.
35. bolus.tw.
36. or/32-35
37. exp ALBUMINS/
38. albumin\$.tw.
39. or/37-38
40. PLASMA SUBSTITUTES/
41. plasma substitut\$.tw.
42. ((blood or plasma) adj expander\$).tw.
43. crystalloid\$.tw.
44. or/40-43
45. COLLOIDS/
46. colloid\$.tw.
47. or/45-46
48. SODIUM CHLORIDE/
49. saline.tw.
50. or/48-49
51. ELECTROLYTES/
52. electrolyte\$.tw.
53. or/51-52
54. ISOTONIC SOLUTIONS/
55. (isotonic adj solution\$).tw.
56. or/54-55

57. FLUID THERAPY/

58. fluid therapy.tw.

59. or/57-58

60. or/36,39,44,47,50,53,56,59

61. exp ADRENAL CORTEX HORMONES/

62. adrenal cortex hormone\$.tw.

63. corticoid\$.tw.

64. corticosteroid\$.tw.

65. or/61-64

66. exp DEXAMETHASONE/

67. dexamethasone\$.tw.

68. or/66-67

69. or/65,68

70. ACYCLOVIR/

71. acyclovir.tw.

72. aciclovir.tw.

73. or/70-72

74. or/60,69,73

75. and/17,31,74

76. exp TREATMENT OUTCOMES/

77. (treat\$ adj2 (effect\$ or efficac\$ or fail\$ or outcome\$)).tw.

78. or/76-77

79. and/75,78

FEVER_treatment_iv_fluids_steroids_aciclovir_health_economics_medline_110506

1. INFANT, PREMATURE/

2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.

3. INFANT, POSTMATURE/

4. ((postmature\$ or postterm\$ or post?term\$) adj (baby or babies or child\$ or infan\$)).tw.

5. INFANT, NEWBORN/

6. neonat\$.tw.

7. newborn\$.tw.

8. exp INFANT/

9. infan\$.tw.

10. INFANT, SMALL FOR GESTATIONAL AGE/

11. (small adj2 gestational age).tw.

12. INFANT, LOW BIRTH WEIGHT/

13. INFANT, VERY LOW BIRTH WEIGHT/

14. (low adj birth adj weight).tw.

15. (low adj birth?weight).tw.
16. lbw.tw.
17. vlbw.tw.
18. (baby or babies).tw.
19. CHILD, PRESCHOOL/
20. toddler\$.tw.
21. exp CHILD/
22. child\$.tw.
23. ADOLESCENT/
24. adolescen\$.tw.
25. juvenile\$.tw.
26. youth\$.tw.
27. teen\$.tw.
28. PUBERTY/
29. pubert\$.tw.
30. pubesc\$.tw.
31. MINORS/
32. minors.tw.
33. or/1-32
34. exp MENINGITIS, BACTERIAL/
35. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
36. meningococc\$.tw.
37. or/34-36
38. exp SEPSIS/
39. sepsis.tw.
40. exp SEPTICEMIA/
41. septicemi\$.tw.
42. septicaemia\$.tw.
43. SHOCK, SEPTIC/
44. (septic adj shock).tw.
45. or/38-44
46. ENCEPHALITIS, HERPES SIMPLEX/
47. HERPES SIMPLEX/
48. herpes simplex.tw.
49. or/46-48
50. or/37,45,49
51. INFUSIONS, INTRAVENOUS/
52. INFUSIONS, PARENTERAL/

- 53. (infusion\$ adj2 (intravenous or parenteral)).tw.
- 54. bolus.tw.
- 55. or/51-54
- 56. exp ALBUMINS/
- 57. albumin\$.tw.
- 58. or/56-57
- 59. PLASMA SUBSTITUTES/
- 60. plasma substitut\$.tw.
- 61. ((blood or plasma) adj expander\$).tw.
- 62. crystalloid\$.tw.
- 63. or/59-62
- 64. COLLOIDS/
- 65. colloid\$.tw.
- 66. or/64-65
- 67. SODIUM CHLORIDE/
- 68. saline.tw.
- 69. or/67-68
- 70. ELECTROLYTES/
- 71. electrolyte\$.tw.
- 72. or/70-71
- 73. ISOTONIC SOLUTIONS/
- 74. (isotonic adj solution\$).tw.
- 75. or/73-74
- 76. FLUID THERAPY/
- 77. fluid therapy.tw.
- 78. or/76-77
- 79. or/55,58,63,66,69,72,75,78
- 80. exp ADRENAL CORTEX HORMONES/
- 81. adrenal cortex hormone\$.tw.
- 82. corticoid\$.tw.
- 83. corticosteroid\$.tw.
- 84. or/80-83
- 85. exp DEXAMETHASONE/
- 86. dexamethasone\$.tw.
- 87. or/85-86
- 88. or/84,87
- 89. ACYCLOVIR/
- 90. acyclovir.tw.
- 91. aciclovir.tw.

- 92. or/89-91
- 93. or/79,88,92
- 94. ECONOMICS/
- 95. "COSTS AND COST ANALYSIS"/
- 96. COST ALLOCATION/
- 97. COST-BENEFIT ANALYSIS/
- 98. COST CONTROL/
- 99. COST SAVINGS/
- 100. COST OF ILLNESS/
- 101. COST SHARING/
- 102. HEALTH CARE COSTS/
- 103. DIRECT SERVICE COSTS/
- 104. DRUG COSTS/
- 105. EMPLOYER HEALTH COSTS/
- 106. HOSPITAL COSTS/
- 107. HEALTH RESOURCES/
- 108. "HEALTH SERVICES NEEDS AND DEMAND"/
- 109. HEALTH PRIORITIES/
- 110. HEALTH EXPENDITURES/
- 111. CAPITAL EXPENDITURES/
- 112. FINANCIAL MANAGEMENT/
- 113. FINANCIAL MANAGEMENT, HOSPITAL/
- 114. QUALITY-ADJUSTED LIFE YEARS/
- 115. "DEDUCTIBLES AND COINSURANCE"/
- 116. MEDICAL SAVINGS ACCOUNTS/
- 117. ECONOMICS, HOSPITAL/
- 118. ECONOMICS, MEDICAL/
- 119. ECONOMICS, NURSING/
- 120. ECONOMICS, PHARMACEUTICAL/
- 121. MODELS, ECONOMIC/
- 122. MODELS, ECONOMETRIC/
- 123. RESOURCE ALLOCATION/
- 124. HEALTH CARE RATIONING/
- 125. "FEES AND CHARGES"/
- 126. BUDGETS/
- 127. VALUE OF LIFE/
- 128. (financ\$ or fiscal\$ or funding).tw.
- 129. (QALY\$ or life?year\$).tw.
- 130. (econom\$ or cost\$).tw.

131. pharmacoeconomic\$.tw.

132. ec.fs.

133. or/94-132

134. and/33,50,93,133

FEVER_treatment_iv_fluids_steroids_aciclovir_health_economics_embase_110506

1. PREMATURETY/

2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.

3. exp NEWBORN/

4. neonat\$.tw.

5. newborn\$.tw.

6. NEWBORN PERIOD/

7. PERINATAL PERIOD/

8. perinatal\$.tw.

9. postnatal\$.tw.

10. exp INFANT/

11. INFANCY/

12. BABY/

13. infan\$.tw.

14. (baby or babies).tw.

15. SMALL FOR DATE INFANT/

16. (small adj2 (date or "gestational age")).tw.

17. lbw.tw.

18. vlbw.tw.

19. CHILD/

20. CHILDHOOD/

21. PRESCHOOL CHILD/

22. SCHOOL CHILD/

23. child\$.tw.

24. PREPUBERTY/

25. PUBERTY/

26. prepube\$.tw.

27. pubert\$.tw.

28. pubesc\$.tw.

29. ADOLESCENCE/

30. adolescen\$.tw.

31. JUVENILE/

32. ADOLESCENT/

33. juvenile\$.tw.

- 34. minors.tw.
- 35. youth\$.tw.
- 36. teen\$.tw.
- 37. or/1-36
- 38. BACTERIAL MENINGITIS/
- 39. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 40. meningococc\$.tw.
- 41. or/38-40
- 42. SEPSIS/
- 43. sepsis.tw.
- 44. SEPTICEMIA/
- 45. septicemi\$.tw.
- 46. septicemia\$.tw.
- 47. SEPTIC SHOCK/
- 48. (septic adj shock).tw.
- 49. or/42-48
- 50. HERPES SIMPLEX ENCEPHALITIS/
- 51. HERPES SIMPLEX/
- 52. herpes simplex.tw.
- 53. or/50-52
- 54. or/41,49,53
- 55. BOLUS INJECTION/
- 56. bolus.tw.
- 57. or/55-56
- 58. ALBUMIN/
- 59. albumin\$.tw.
- 60. or/58-59
- 61. exp PLASMA SUBSTITUTE/
- 62. plasma substitut\$.tw.
- 63. ((blood or plasma) adj expander\$).tw.
- 64. crystalloid\$.tw.
- 65. or/61-64
- 66. COLLOID/
- 67. colloid\$.tw.
- 68. or/66-67
- 69. SODIUM CHLORIDE/
- 70. saline.tw.
- 71. or/69-70

- 72. ELECTROLYTE/
- 73. electrolyte\$.tw.
- 74. or/72-73
- 75. ISOTONIC SOLUTION/
- 76. (isotonic adj solution\$).tw.
- 77. or/75-76
- 78. exp FLUID THERAPY/
- 79. fluid therapy.tw.
- 80. or/78-79
- 81. or/57,60,65,68,71,74,77,80
- 82. exp CORTICOSTEROID/
- 83. corticosteroid\$.tw.
- 84. corticoid\$.tw.
- 85. adrenal cortex hormone\$.tw.
- 86. or/82-85
- 87. DEXAMETHASONE/
- 88. dexamethasone\$.tw.
- 89. or/87-88
- 90. or/86,89
- 91. ACICLOVIR/
- 92. aciclovir.tw.
- 93. acyclovir.tw.
- 94. or/91-93
- 95. or/81,90,94
- 96. ECONOMICS/
- 97. HEALTH ECONOMICS/
- 98. ECONOMIC EVALUATION/
- 99. COST BENEFIT ANALYSIS/
- 100. COST CONTROL/
- 101. COST EFFECTIVENESS ANALYSIS/
- 102. COST MINIMIZATION ANALYSIS/
- 103. COST OF ILLNESS/
- 104. COST UTILITY ANALYSIS/
- 105. COST/
- 106. HEALTH CARE COST/
- 107. DRUG COST/
- 108. HEALTH CARE FINANCING/
- 109. HOSPITAL COST/
- 110. SOCIOECONOMICS/

- 111. ECONOMIC ASPECT/
- 112. QUALITY-ADJUSTED LIFE YEARS/
- 113. FINANCIAL MANAGEMENT/
- 114. PHARMACOECONOMICS/
- 115. RESOURCE ALLOCATION/
- 116. (financ\$ or fiscal\$ or funding).tw.
- 117. (QALY\$ or life?year\$).tw.
- 118. (econom\$ or cost\$).tw.
- 119. pharmacoeconomic\$.tw.
- 120. or/96-119
- 121. and/37,54,95,120

FEVER_treatment_iv fluids_steroids_aciclovir_health_economics_cinahl_110506

- 1. INFANT, PREMATURE/
- 2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.
- 3. INFANT, NEWBORN/
- 4. neonat\$.tw.
- 5. newborn\$.tw.
- 6. perinatal\$.tw.
- 7. postnatal\$.tw.
- 8. exp INFANT/
- 9. infan\$.tw.
- 10. (baby or babies).tw.
- 11. INFANT, LOW BIRTH WEIGHT/
- 12. INFANT, VERY LOW BIRTH WEIGHT/
- 13. INFANT, SMALL FOR GESTATIONAL AGE/
- 14. (small adj2 (date or "gestational age")).tw.
- 15. lbw.tw.
- 16. vlbw.tw.
- 17. CHILD/
- 18. CHILD, PRESCHOOL/
- 19. SCHOOL CHILD/
- 20. child\$.tw.
- 21. PREPUBERTY/
- 22. PUBERTY/
- 23. prepube\$.tw.
- 24. pubert\$.tw.
- 25. pubesc\$.tw.
- 26. ADOLESCENCE/
- 27. adolescen\$.tw.

28. "MINORS (LEGAL)"/
29. juvenile\$.tw.
30. minors.tw.
31. youth\$.tw.
32. teen\$.tw.
33. or/1-32
34. exp MENINGITIS, BACTERIAL/
35. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
36. meningococc\$.tw.
37. or/34-36
38. exp SEPSIS/
39. septicemi\$.tw.
40. septicemia\$.tw.
41. SHOCK, SEPTIC/
42. (septic adj shock).tw.
43. or/38-42
44. HERPES SIMPLEX/
45. herpes simplex.tw.
46. or/44-45
47. or/37,43,46
48. INFUSIONS, INTRAVENOUS/
49. INFUSIONS, PARENTERAL/
50. (infusion\$ adj2 (intravenous or parenteral)).tw.
51. bolus.tw.
52. or/48-51
53. exp ALBUMINS/
54. albumin\$.tw.
55. or/53-54
56. PLASMA SUBSTITUTES/
57. plasma substitut\$.tw.
58. ((blood or plasma) adj expander\$).tw.
59. crystalloid\$.tw.
60. or/56-59
61. COLLOIDS/
62. colloid\$.tw.
63. or/61-62
64. SODIUM CHLORIDE/
65. saline.tw.

- 66. or/64-65
- 67. ELECTROLYTES/
- 68. electrolyte\$.tw.
- 69. or/67-68
- 70. ISOTONIC SOLUTIONS/
- 71. (isotonic adj solution\$).tw.
- 72. or/70-71
- 73. FLUID THERAPY/
- 74. fluid therapy.tw.
- 75. or/73-74
- 76. or/52,55,60,63,66,69,72,75
- 77. exp ADRENAL CORTEX HORMONES/
- 78. adrenal cortex hormone\$.tw.
- 79. corticoid\$.tw.
- 80. corticosteroid\$.tw.
- 81. or/77-80
- 82. exp DEXAMETHASONE/
- 83. dexamethasone\$.tw.
- 84. or/82-83
- 85. or/81,84
- 86. ACYCLOVIR/
- 87. acyclovir.tw.
- 88. aciclovir.tw.
- 89. or/86-88
- 90. or/76,85,89
- 91. ECONOMICS/
- 92. "COSTS AND COST ANALYSIS"/
- 93. COST BENEFIT ANALYSIS/
- 94. COST CONTROL/
- 95. COST SAVINGS/
- 96. COST OF ILLNESS/
- 97. HEALTH CARE COSTS/
- 98. ECONOMIC ASPECTS OF ILLNESS/
- 99. ECONOMICS, PHARMACEUTICAL/
- 100. HEALTH CARE FINANCING/
- 101. FINANCIAL MANAGEMENT/
- 102. HOSPITAL COST/
- 103. SOCIOECONOMIC FACTORS/
- 104. HEALTH RESOURCE ALLOCATION/

105. (financ\$ or fiscal\$ or funding).tw.

106. (QALY\$ or life?year\$).tw.

107. (econom\$ or cost\$).tw.

108. pharmacoeconomic\$.tw.

109. or/91-108

110. and/33,47,90,109

FEVER_treatment_oral_pharmaceutical_empirical_medline_270406

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. INFANT, LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. exp FEVER/

19. "FEVER OF UNKNOWN ORIGIN"/

20. fever\$.tw.

21. febril\$.tw.

22. hypertherm\$.tw.

23. pyrexia\$.tw.

24. MALIGNANT HYPERTHERMIA/

25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.

26. exp PYROGENS/

27. pyrogen\$.tw.

28. or/18-27

29. ANTI-INFECTIVE AGENTS/

30. antibiotic\$.tw.

31. bactericide\$.tw.

32. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.

- 33. or/29-32
- 34. PENICILLINS/
- 35. penicillin\$.tw.
- 36. or/33-34
- 37. PENICILLIN G/
- 38. benzylpenicillin\$.tw.
- 39. or/37-38
- 40. AMOXICILLIN/
- 41. amoxicil\$.tw.
- 42. amoxycil\$.tw.
- 43. amoxil\$.tw.
- 44. or/40-43
- 45. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 46. augmentin\$.tw.
- 47. or/45-46
- 48. AMPICILLIN/
- 49. ampicillin\$.tw.
- 50. penbritin\$.tw.
- 51. or/48-50
- 52. CEFADROXIL/
- 53. cefadroxil\$.tw.
- 54. cephadrox\$.tw.
- 55. or/52-54
- 56. CEPHALEXIN/
- 57. cephalixin\$.tw.
- 58. cefalexin\$.tw.
- 59. cefaclor\$.tw.
- 60. ceporex\$.tw.
- 61. keflex\$.tw.
- 62. or/56-61
- 63. CEFIXIME/
- 64. cefixim\$.tw.
- 65. suprax\$.tw.
- 66. or/63-65
- 67. CEFOTAXIME/
- 68. cefotaxim\$.tw.
- 69. cephotaxim\$.tw.
- 70. claforan\$.tw.
- 71. klaforan\$.tw.

- 72. or/67-71
- 73. CEPHALOSPORINS/
- 74. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 75. cefpirome\$.tw.
- 76. or/73-75
- 77. CEFTIZOXIME/
- 78. cefpodoxim\$.tw.
- 79. ceftizoxim\$.tw.
- 80. orelox\$.tw.
- 81. or/77-80
- 82. CEPHRADINE/
- 83. cefradin\$.tw.
- 84. velosef\$.tw.
- 85. or/82-84
- 86. CEFTAZIDIME/
- 87. ceftazidim\$.tw.
- 88. fortum\$.tw.
- 89. or/86-88
- 90. CEFTRIAXONE/
- 91. ceftriaxon\$.tw.
- 92. rocephin\$.tw.
- 93. or/90-92
- 94. CEFUROXIME/
- 95. cefuroxim\$.tw.
- 96. zinacef\$.tw.
- 97. zinnat\$.tw.
- 98. or/94-97
- 99. GENTAMICINS/
- 100. gentamicin\$.tw.
- 101. cidomycin\$.tw.
- 102. genticin\$.tw.
- 103. or/99-102
- 104. AMIKACIN/
- 105. amikacin\$.tw.
- 106. or/104-105
- 107. AMINOGLYCOSIDES/
- 108. aminoglycoside\$.tw.
- 109. aminoglucoside\$.tw.
- 110. or/107-109

- 111. TOBRAMYCIN/
- 112. tobramycin\$.tw.
- 113. nebcin\$.tw.
- 114. tobi.tw.
- 115. or/111-114
- 116. NETILMICIN/
- 117. netilmicin\$.tw.
- 118. netillin\$.tw.
- 119. or/116-118
- 120. or/33,36,39,44,47,51,55,62,66,72,76,81,85,89,93,98,103,106,110,115,119
- 121. exp ADMINISTRATION, ORAL/
- 122. (administ\$ adj2 (mouth or oral\$)).tw.
- 123. or/121-122
- 124. empiric\$.tw.
- 125. ((blind\$ or early) adj5 treat\$).tw.
- 126. or/124-125
- 127. and/17,28,120,123,126
- 128. animal/ not (human/ or (human/ and animal/))
- 129. 127 not 128

FEVER_treatment_oral_pharmaceutical_empirical_embase_270406

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. PYREXIA IDIOPATHICA/

20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. ANTIINFECTIVE AGENT/
30. ANTIBIOTIC AGENT/
31. antibiotic\$.tw.
32. bacteriocide\$.tw.
33. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
34. penicillin\$.tw.
35. PENICILLIN G/
36. benzylpenicillin\$.tw.
37. or/29-36
38. AMOXICILLIN/
39. amoxicil\$.tw.
40. amoxycil\$.tw.
41. amoxil\$.tw.
42. or/38-41
43. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
44. augmentin\$.tw.
45. or/43-44
46. AMPICILLIN/
47. ampicillin\$.tw.
48. penbritin\$.tw.
49. or/46-48
50. CEFADROXIL/
51. cefadroxil\$.tw.
52. cephadrox\$.tw.
53. or/50-52
54. CEPHALEXIN/
55. cephalixin\$.tw.
56. cefalexin\$.tw.
57. cefaclor\$.tw.
58. ceporex\$.tw.

- 59. keflex\$.tw.
- 60. or/54-59
- 61. CEFIXIME/
- 62. cefixim\$.tw.
- 63. suprax\$.tw.
- 64. or/61-63
- 65. CEFOTAXIME/
- 66. cefotaxim\$.tw.
- 67. cephotaxim\$.tw.
- 68. claforan\$.tw.
- 69. klaforan\$.tw.
- 70. or/65-69
- 71. CEPHALOSPORINS/
- 72. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 73. cefpirome\$.tw.
- 74. cefrom\$.tw.
- 75. or/71-74
- 76. CEFTIZOXIME/
- 77. cefpodoxim\$.tw.
- 78. ceftizoxim\$.tw.
- 79. orelox\$.tw.
- 80. or/76-79
- 81. CEPHRADINE/
- 82. cefradin\$.tw.
- 83. velosef\$.tw.
- 84. or/81-83
- 85. CEFTAZIDIME/
- 86. ceftazidim\$.tw.
- 87. fortum\$.tw.
- 88. kefadim\$.tw.
- 89. or/85-88
- 90. CEFTRIAXONE/
- 91. ceftriaxon\$.tw.
- 92. rocephin\$.tw.
- 93. or/90-92
- 94. CEFUROXIME/
- 95. cefuroxim\$.tw.
- 96. zinacef\$.tw.
- 97. zinnat\$.tw.

98. or/94-97
99. GENTAMICINS/
100. gentamicin\$.tw.
101. cidomycin\$.tw.
102. genticin\$.tw.
103. or/99-102
104. AMIKACIN/
105. amikacin\$.tw.
106. AMINOGLYCOSIDE/
107. (aminoglycoside\$ or aminoglucoside\$).tw.
108. TOBRAMYCIN/
109. tobramycin\$.tw.
110. TOBRAMYCIN SULPHATE/
111. nebcin\$.tw.
112. tobi.tw.
113. NETILMICIN/
114. netilmicin\$.tw.
115. netillin\$.tw.
116. or/104-115
117. or/37,42,45,49,53,60,64,70,75,80,84,89,93,98,103,116
118. ORAL DRUG ADMINISTRATION/
119. (administ\$ adj2 (mouth or oral\$)).tw.
120. or/118-119
121. empiric\$.tw.
122. ((blind\$ or early) adj5 treat\$).tw.
123. or/121-122
124. and/17,28,117,120,123
125. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))
126. 124 not 125

FEVER_treatment_oral_pharmaceutical_empirical_cinahl_270406

1. INFANT, PREMATURE/
2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.

10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. ANTIINFECTIVE AGENT/
30. ANTIBIOTIC AGENT/
31. PENICILLINS/
32. penicillin\$.tw.
33. antibiotic\$.tw.
34. bacteriocide\$.tw.
35. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
36. or/29-35
37. AMOXICILLIN/
38. amoxicil\$.tw.
39. amoxycil\$.tw.
40. amoxil\$.tw.
41. or/37-40
42. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
43. augmentin\$.tw.
44. or/42-43
45. AMPICILLIN/
46. ampicillin\$.tw.
47. penbritin\$.tw.
48. or/45-47

- 49. CEFADROXIL/
- 50. cefadroxil\$.tw.
- 51. cephadrox\$.tw.
- 52. or/49-51
- 53. CEPHALEXIN/
- 54. cephalixin\$.tw.
- 55. cefalexin\$.tw.
- 56. cefaclor\$.tw.
- 57. ceporex\$.tw.
- 58. keflex\$.tw.
- 59. or/53-58
- 60. CEFIXIME/
- 61. cefixim\$.tw.
- 62. suprax\$.tw.
- 63. or/60-62
- 64. CEFOTAXIME/
- 65. cefotaxim\$.tw.
- 66. cephotaxim\$.tw.
- 67. claforan\$.tw.
- 68. klaforan\$.tw.
- 69. or/64-68
- 70. CEPHALOSPORINS/
- 71. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 72. cefpirome\$.tw.
- 73. cefrom\$.tw.
- 74. or/70-73
- 75. CEFTIZOXIME/
- 76. cefpodoxim\$.tw.
- 77. ceftizoxim\$.tw.
- 78. orelox\$.tw.
- 79. or/75-78
- 80. CEPHRADINE/
- 81. ceftazidim\$.tw.
- 82. velosef\$.tw.
- 83. or/80-82
- 84. CEFTAZIDIME/
- 85. ceftazidim\$.tw.
- 86. fortum\$.tw.
- 87. kefadim\$.tw.

- 88. or/84-87
- 89. CEFTRIAXONE/
- 90. ceftriaxon\$.tw.
- 91. rocephin\$.tw.
- 92. or/89-91
- 93. CEFUROXIME/
- 94. cefuroxim\$.tw.
- 95. zinacef\$.tw.
- 96. zinnat\$.tw.
- 97. or/93-96
- 98. GENTAMICINS/
- 99. gentamicin\$.tw.
- 100. cidomycin\$.tw.
- 101. genticin\$.tw.
- 102. or/98-101
- 103. AMIKACIN/
- 104. amikacin\$.tw.
- 105. AMINOGLYCOSIDES/
- 106. (aminoglycoside\$ or aminoglucoside\$).tw.
- 107. TOBRAMYCIN/
- 108. tobramycin\$.tw.
- 109. nebcin\$.tw.
- 110. tobi.tw.
- 111. netilmicin\$.tw.
- 112. or/103-111
- 113. or/36,41,44,48,52,59,63,69,74,79,83,88,92,97,102,112
- 114. exp ADMINISTRATION, ORAL/
- 115. (administ\$ adj2 (mouth or oral\$)).tw.
- 116. or/114-115
- 117. empiric\$.tw.
- 118. ((blind\$ or early) adj5 treat\$).tw.
- 119. or/117-118
- 120. and/17,28,113,116,119

FEVER_treatment_pharmaceutical_empirical_IV_versus_IM_medline_230406

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.

6. INFANT, VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. CHILD, PRESCHOOL/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. SEPTICEMIA/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34

36. HERPES SIMPLEX/

37. herpes simplex.tw.

38. or/36-37

39. exp ARTHRITIS, INFECTIOUS/

40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

41. pyarthrosis.tw.

42. pyoarthritis.tw.

43. or/39-42

44. STAPHYLOCOCCAL INFECTIONS/

45. STREPTOCOCCAL INFECTIONS/

46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.

47. or/44-46

48. OSTEOMYELITIS/

49. osteomyeliti\$.tw.

50. or/48-49

51. exp URINARY TRACT INFECTIONS/

52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

53. UTI.tw.

54. ((upper or lower) adj5 urin\$).tw.

55. exp CYSTITIS/

56. cystitis\$.tw.

57. PYELONEPHRITIS/

58. pyelonephriti\$.tw.

59. pyonephrosi\$.tw.

60. pyelocystiti\$.tw.

61. or/51-60

62. MUCOCUTANEOUS LYMPH NODE SYNDROME/

63. (mucocutaneous adj2 lymph\$).tw.

64. mcls.tw.

65. (kawasaki adj (disease or syndrome)).tw.

66. or/62-65

67. or/20,24,28,32,35,38,43,47,50,61,66

68. ANTI-INFECTIVE AGENTS/

69. antibiotic\$.tw.

70. bacteriocide\$.tw.

71. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.

72. or/68-71

73. PENICILLINS/

74. penicillin\$.tw.

75. or/72-73

76. PENICILLIN G/

77. benzylpenicillin\$.tw.

78. or/76-77

79. AMOXICILLIN/

80. amoxicil\$.tw.

81. amoxycil\$.tw.

- 82. amoxil\$.tw.
- 83. or/79-82
- 84. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 85. augmentin\$.tw.
- 86. or/84-85
- 87. AMPICILLIN/
- 88. ampicillin\$.tw.
- 89. penbritin\$.tw.
- 90. or/87-89
- 91. CEFADROXIL/
- 92. cefadroxil\$.tw.
- 93. cephadrox\$.tw.
- 94. or/91-93
- 95. CEPHALEXIN/
- 96. cephalixin\$.tw.
- 97. cefalexin\$.tw.
- 98. cefaclor\$.tw.
- 99. ceporex\$.tw.
- 100. keflex\$.tw.
- 101. or/95-100
- 102. CEFIXIME/
- 103. cefixim\$.tw.
- 104. suprax\$.tw.
- 105. or/102-104
- 106. CEFOTAXIME/
- 107. cefotaxim\$.tw.
- 108. cephotaxim\$.tw.
- 109. claforan\$.tw.
- 110. klaforan\$.tw.
- 111. or/106-110
- 112. CEPHALOSPORINS/
- 113. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 114. cefpirome\$.tw.
- 115. or/112-114
- 116. CEFTIZOXIME/
- 117. cefpodoxim\$.tw.
- 118. ceftizoxim\$.tw.
- 119. orelox\$.tw.
- 120. or/116-119

- 121. CEPHRADINE/
- 122. cefradin\$.tw.
- 123. velosef\$.tw.
- 124. or/121-123
- 125. CEFTAZIDIME/
- 126. ceftazidim\$.tw.
- 127. fortum\$.tw.
- 128. or/125-127
- 129. CEFTRIAXONE/
- 130. ceftriaxon\$.tw.
- 131. rocephin\$.tw.
- 132. or/129-131
- 133. CEFUROXIME/
- 134. cefuroxim\$.tw.
- 135. zinacef\$.tw.
- 136. zinnat\$.tw.
- 137. or/133-136
- 138. GENTAMICINS/
- 139. gentamicin\$.tw.
- 140. cidomycin\$.tw.
- 141. genticin\$.tw.
- 142. or/138-141
- 143. AMIKACIN/
- 144. amikacin\$.tw.
- 145. or/143-144
- 146. AMINOGLYCOSIDES/
- 147. aminoglycoside\$.tw.
- 148. aminoglucoside\$.tw.
- 149. or/146-148
- 150. TOBRAMYCIN/
- 151. tobramycin\$.tw.
- 152. nebcin\$.tw.
- 153. tobi.tw.
- 154. or/150-153
- 155. NETILMICIN/
- 156. netilmicin\$.tw.
- 157. netillin\$.tw.
- 158. or/155-157
- 159. or/72,75,78,83,86,90,94,101,105,111,115,120,124,128,132,137,142,145,149,154,158

- 160. INJECTIONS, INTRAVENOUS/
- 161. INFUSIONS, INTRAVENOUS/
- 162. ((intravenous\$ or iv) adj (administ\$ or deliver\$ or infus\$ or inject\$)).tw.
- 163. ((infusion or intravenous or iv) adj drip\$).tw.
- 164. or/160-163
- 165. INJECTIONS, INTRAMUSCULAR/
- 166. ((im or intramuscular\$) adj (administ\$ or deliver\$ or inject\$)).tw.
- 167. or/165-166
- 168. parenteral\$.tw.
- 169. or/164,167-168
- 170. and/159,169
- 171. and/17,67,170
- 172. empiric\$.tw.
- 173. ((blind\$ or early) adj5 treat\$).tw.
- 174. ((before or prior) adj5 (admission or admit\$)).tw.
- 175. or/172-174
- 176. and/171,175
- 177. animal/ not (human/ or (human/ and animal/))
- 178. 176 not 177

FEVER_treatment_pharmaceutical_empirical_IV_versus_IM_embase_230406

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. PRESCHOOL CHILD/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. BACTERIAL INFECTION/
- 19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. BACTERIAL MENINGITIS/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. SEPTICEMIA/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34

36. HERPES SIMPLEX/

37. herpes simplex.tw.

38. or/36-37

39. BACTERIAL ARTHRITIS/

40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

41. pyarthrosis.tw.

42. pyoarthritis.tw.

43. or/39-42

44. STAPHYLOCOCCAL INFECTION/

45. STREPTOCOCCAL INFECTION/

46. straphylococc\$.tw.

47. streptococc\$.tw.

48. or/44-47

49. OSTEOMYELITIS/

50. osteomyeliti\$.tw.

51. or/49-50

52. exp URINARY TRACT INFECTION/

53. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

54. UTI.tw.

55. ((upper or lower) adj5 urin\$).tw.

56. exp CYSTITIS/

- 57. cystitis\$.tw.
- 58. or/52-57
- 59. PYELONEPHRITIS/
- 60. pyelonephriti\$.tw.
- 61. pyonephrosi\$.tw.
- 62. pyelocystiti\$.tw.
- 63. or/59-62
- 64. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 65. (mucocutaneous adj2 lymph\$).tw.
- 66. mcls.tw.
- 67. (kawasaki adj (disease or syndrome)).tw.
- 68. or/64-67
- 69. or/20,24,28,32,35,38,43,48,51,58,63,68
- 70. ANTIINFECTIVE AGENT/
- 71. ANTIBIOTIC AGENT/
- 72. antibiotic\$.tw.
- 73. bacteriocide\$.tw.
- 74. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
- 75. penicillin\$.tw.
- 76. PENICILLIN G/
- 77. benzylpenicillin\$.tw.
- 78. or/70-77
- 79. AMOXICILLIN/
- 80. amoxicil\$.tw.
- 81. amoxycil\$.tw.
- 82. amoxil\$.tw.
- 83. or/79-82
- 84. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 85. augmentin\$.tw.
- 86. or/84-85
- 87. AMPICILLIN/
- 88. ampicillin\$.tw.
- 89. penbritin\$.tw.
- 90. or/87-89
- 91. CEFADROXIL/
- 92. cefadroxil\$.tw.
- 93. cephadrox\$.tw.
- 94. or/91-93
- 95. CEPHALEXIN/

- 96. cephalixin\$.tw.
- 97. cefalexin\$.tw.
- 98. cefaclor\$.tw.
- 99. ceporex\$.tw.
- 100. keflex\$.tw.
- 101. or/95-100
- 102. CEFIXIME/
- 103. cefixim\$.tw.
- 104. suprax\$.tw.
- 105. or/102-104
- 106. CEFOTAXIME/
- 107. cefotaxim\$.tw.
- 108. cephotaxim\$.tw.
- 109. claforan\$.tw.
- 110. klaforan\$.tw.
- 111. or/106-110
- 112. CEPHALOSPORINS/
- 113. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 114. cefpirome\$.tw.
- 115. cefrom\$.tw.
- 116. or/112-115
- 117. CEFTIZOXIME/
- 118. cefpodoxim\$.tw.
- 119. ceftizoxim\$.tw.
- 120. orelox\$.tw.
- 121. or/117-120
- 122. CEPHRADINE/
- 123. cefradin\$.tw.
- 124. velosef\$.tw.
- 125. or/122-124
- 126. CEFTAZIDIME/
- 127. ceftazidim\$.tw.
- 128. fortum\$.tw.
- 129. kefadim\$.tw.
- 130. or/126-129
- 131. CEFTRIAXONE/
- 132. ceftriaxon\$.tw.
- 133. rocephin\$.tw.
- 134. or/131-133

135. CEFUROXIME/
136. cefuroxim\$.tw.
137. zinacef\$.tw.
138. zinnat\$.tw.
139. or/135-138
140. GENTAMICINS/
141. gentamicin\$.tw.
142. cidomycin\$.tw.
143. genticin\$.tw.
144. or/140-143
145. AMIKACIN/
146. amikacin\$.tw.
147. AMINOGLYCOSIDE/
148. (aminoglycoside\$ or aminoglucoside\$).tw.
149. TOBRAMYCIN/
150. tobramycin\$.tw.
151. TOBRAMYCIN SULPHATE/
152. nebcin\$.tw.
153. tobi.tw.
154. NETILMICIN/
155. netilmicin\$.tw.
156. netillin\$.tw.
157. or/145-156
158. or/78,83,86,90,94,101,105,111,116,121,125,130,134,139,144,157
159. INTRAVENOUS DRUG ADMINISTRATION/
160. ((intravenous\$ or iv) adj (administ\$ or deliver\$ or infus\$ or inject\$)).tw.
161. ((infusion or intravenous or iv) adj drip\$).tw.
162. or/159-161
163. INTRAMUSCULAR DRUG ADMINISTRATION/
164. ((im or intramuscular\$) adj (administ\$ or deliver\$ or inject\$)).tw.
165. or/163-164
166. parenteral\$.tw.
167. or/162,165-166
168. and/158,167
169. and/17,69,168
170. empiric\$.tw.
171. ((blind\$ or early) adj5 treat\$).tw.
172. ((before or prior) adj5 (admission or admit\$)).tw.
173. or/170-172

174. and/169,173

175. (animal/ or nonhuman/) not (human/ or ((animal/ or nonhuman/) and human/))

176. 174 not 175

FEVER_treatment_pharmaceutical_empirical_IV_versus_IM_cinahl_230406

1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/

3. LOW BIRTH WEIGHT/

4. (low adj birth adj weight).tw.

5. lbw.tw.

6. VERY LOW BIRTH WEIGHT/

7. vlbw.tw.

8. INFANT, NEWBORN/

9. neonat\$.tw.

10. newborn\$.tw.

11. exp INFANT/

12. infan\$.tw.

13. PRESCHOOL CHILD/

14. (baby or babies).tw.

15. (child\$ adj5 pre?school).tw.

16. toddler\$.tw.

17. or/1-16

18. BACTERIAL INFECTIONS/

19. (bacteri\$ adj infect\$).tw.

20. or/18-19

21. exp MENINGITIS, BACTERIAL/

22. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

23. meningococc\$.tw.

24. or/21-23

25. exp SEPSIS/

26. septicemi\$.tw.

27. septicaemia\$.tw.

28. or/25-27

29. BACTEREMIA/

30. bacteremi\$.tw.

31. bacteraemia\$.tw.

32. or/29-31

33. exp PNEUMONIA/

34. pneumoni\$.tw.

35. or/33-34
36. HERPES SIMPLEX/
37. herpes simplex.tw.
38. or/36-37
39. exp ARTHRITIS, INFECTIOUS/
40. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
41. pyarthrosis.tw.
42. pyoarthritis.tw.
43. or/39-42
44. STAPHYLOCOCCAL INFECTIONS/
45. STREPTOCOCCAL INFECTIONS/
46. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
47. or/44-46
48. OSTEOMYELITIS/
49. osteomyeliti\$.tw.
50. or/48-49
51. exp URINARY TRACT INFECTION/
52. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
53. UTI.tw.
54. ((upper or lower) adj5 urin\$).tw.
55. CYSTITIS/
56. cystitis\$.tw.
57. PYELONEPHRITIS/
58. pyelonephriti\$.tw.
59. pyonephrosi\$.tw.
60. pyelocystiti\$.tw.
61. or/51-60
62. MUCOCUTANEOUS LYMPH NODE SYNDROME/
63. (mucocutaneous adj2 lymph\$).tw.
64. mcls.tw.
65. (kawasaki adj (disease or syndrome)).tw.
66. or/62-65
67. or/20,24,28,32,35,38,43,47,50,61,66
68. ANTIINFECTIVE AGENT/
69. ANTIBIOTIC AGENT/
70. PENICILLINS/
71. penicillin\$.tw.
72. antibiotic\$.tw.

- 73. bacteriocide\$.tw.
- 74. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$.tw.
- 75. or/68-74
- 76. AMOXICILLIN/
- 77. amoxicil\$.tw.
- 78. amoxycil\$.tw.
- 79. amoxil\$.tw.
- 80. or/76-79
- 81. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 82. augmentin\$.tw.
- 83. or/81-82
- 84. AMPICILLIN/
- 85. ampicillin\$.tw.
- 86. penbritin\$.tw.
- 87. or/84-86
- 88. CEFADROXIL/
- 89. cefadroxil\$.tw.
- 90. cephadrox\$.tw.
- 91. or/88-90
- 92. CEPHALEXIN/
- 93. cephalixin\$.tw.
- 94. cefalexin\$.tw.
- 95. cefaclor\$.tw.
- 96. ceporex\$.tw.
- 97. keflex\$.tw.
- 98. or/92-97
- 99. CEFIXIME/
- 100. cefixim\$.tw.
- 101. suprax\$.tw.
- 102. or/99-101
- 103. CEFOTAXIME/
- 104. cefotaxim\$.tw.
- 105. cephotaxim\$.tw.
- 106. claforan\$.tw.
- 107. klaforan\$.tw.
- 108. or/103-107
- 109. CEPHALOSPORINS/
- 110. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 111. cefpirome\$.tw.

- 112. cefrom\$.tw.
- 113. or/109-112
- 114. CEFTIZOXIME/
- 115. cefpodoxim\$.tw.
- 116. ceftizoxim\$.tw.
- 117. orelox\$.tw.
- 118. or/114-117
- 119. CEPHRADINE/
- 120. cefradin\$.tw.
- 121. velosef\$.tw.
- 122. or/119-121
- 123. CEFTAZIDIME/
- 124. ceftazidim\$.tw.
- 125. fortum\$.tw.
- 126. kefadim\$.tw.
- 127. or/123-126
- 128. CEFTRIAXONE/
- 129. ceftriaxon\$.tw.
- 130. rocephin\$.tw.
- 131. or/128-130
- 132. CEFUROXIME/
- 133. cefuroxim\$.tw.
- 134. zinacef\$.tw.
- 135. zinnat\$.tw.
- 136. or/132-135
- 137. GENTAMICINS/
- 138. gentamicin\$.tw.
- 139. cidomycin\$.tw.
- 140. genticin\$.tw.
- 141. or/137-140
- 142. AMIKACIN/
- 143. amikacin\$.tw.
- 144. AMINOGLYCOSIDES/
- 145. (aminoglycoside\$ or aminoglucoside\$).tw.
- 146. TOBRAMYCIN/
- 147. tobramycin\$.tw.
- 148. nebcin\$.tw.
- 149. tobi.tw.
- 150. netilmicin\$.tw.

- 151. or/142-150
- 152. or/75,80,83,87,91,98,102,108,113,118,122,127,131,136,141,151
- 153. INJECTIONS, INTRAVENOUS/
- 154. INFUSIONS, INTRAVENOUS/
- 155. ((intravenous\$ or iv) adj (administ\$ or deliver\$ or infus\$ or inject\$)).tw.
- 156. ((infusion or intravenous or iv) adj drip\$).tw.
- 157. or/153-156
- 158. INJECTIONS, INTRAMUSCULAR/
- 159. ((im or intramuscular\$) adj (administ\$ or deliver\$ or inject\$)).tw.
- 160. or/158-159
- 161. parenteral\$.tw.
- 162. or/157,160-161
- 163. and/152,162
- 164. and/17,67,163
- 165. empiric\$.tw.
- 166. ((blind\$ or early) adj5 treat\$).tw.
- 167. ((before or prior) adj5 (admission or admit\$)).tw.
- 168. or/165-167
- 169. and/164,168

FEVER_treatment_pharmaceuticals_RCT_SR_medline_300306

- 1. INFANT, PREMATURE/
- 2. INFANT, POSTMATURE/
- 3. INFANT, LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. INFANT, VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. INFANT, NEWBORN/
- 9. neonat\$.tw.
- 10. newborn\$.tw.
- 11. exp INFANT/
- 12. infan\$.tw.
- 13. CHILD, PRESCHOOL/
- 14. (baby or babies).tw.
- 15. (child\$ adj5 pre?school).tw.
- 16. toddler\$.tw.
- 17. or/1-16
- 18. exp FEVER/
- 19. "FEVER OF UNKNOWN ORIGIN"/

20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANTI-INFECTIVE AGENTS/
31. antibiotic\$.tw.
32. bacteriocide\$.tw.
33. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
34. or/30-33
35. PENICILLINS/
36. penicillin\$.tw.
37. or/34-35
38. PENICILLIN G/
39. benzylpenicillin\$.tw.
40. or/38-39
41. AMOXICILLIN/
42. amoxicil\$.tw.
43. amoxycil\$.tw.
44. amoxil\$.tw.
45. or/41-44
46. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
47. augmentin\$.tw.
48. or/46-47
49. AMPICILLIN/
50. ampicillin\$.tw.
51. penbritin\$.tw.
52. or/49-51
53. CEFADROXIL/
54. cefadroxil\$.tw.
55. cephadrox\$.tw.
56. or/53-55
57. CEPHALEXIN/
58. cephalixin\$.tw.

- 59. cefalexin\$.tw.
- 60. cefaclor\$.tw.
- 61. ceporex\$.tw.
- 62. keflex\$.tw.
- 63. or/57-62
- 64. CEFIXIME/
- 65. cefixim\$.tw.
- 66. suprax\$.tw.
- 67. or/64-66
- 68. CEFOTAXIME/
- 69. cefotaxim\$.tw.
- 70. cephotaxim\$.tw.
- 71. claforan\$.tw.
- 72. klaforan\$.tw.
- 73. or/68-72
- 74. CEPHALOSPORINS/
- 75. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 76. cefpirome\$.tw.
- 77. or/74-76
- 78. CEFTIZOXIME/
- 79. cefpodoxim\$.tw.
- 80. ceftizoxim\$.tw.
- 81. orelox\$.tw.
- 82. or/78-81
- 83. CEPHRADINE/
- 84. cefradin\$.tw.
- 85. velosef\$.tw.
- 86. or/83-85
- 87. CEFTAZIDIME/
- 88. ceftazidim\$.tw.
- 89. fortum\$.tw.
- 90. or/87-89
- 91. CEFTRIAXONE/
- 92. ceftriaxon\$.tw.
- 93. rocephin\$.tw.
- 94. or/91-93
- 95. CEFUROXIME/
- 96. cefuroxim\$.tw.
- 97. zinacef\$.tw.

98. zinnat\$.tw.
99. or/95-98
100. GENTAMICINS/
101. gentamicin\$.tw.
102. cidomycin\$.tw.
103. genticin\$.tw.
104. or/100-103
105. AMIKACIN/
106. amikacin\$.tw.
107. or/105-106
108. AMINOGLYCOSIDES/
109. aminoglycoside\$.tw.
110. aminoglucoside\$.tw.
111. or/108-110
112. TOBRAMYCIN/
113. tobramycin\$.tw.
114. nebcin\$.tw.
115. tobi.tw.
116. or/112-115
117. NETILMICIN/
118. netilmicin\$.tw.
119. netillin\$.tw.
120. or/117-119
121. or/34,37,40,45,48,52,56,63,67,73,77,82,86,90,94,99,104,107,111,116,120
122. and/29,121
123. randomized controlled trial.pt.
124. controlled clinical trial.pt.
125. DOUBLE BLIND METHOD/
126. SINGLE BLIND METHOD/
127. RANDOM ALLOCATION/
128. RANDOMIZED CONTROLLED TRIALS/
129. or/123-128
130. ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
131. clinical trial.pt.
132. exp CLINICAL TRIALS/
133. (clinic\$ adj5 trial\$).tw,sh.
134. PLACEBOS/
135. placebo\$.tw,sh.
136. random\$.tw,sh.

- 137. or/130-136
- 138. or/129,137
- 139. META ANALYSIS/
- 140. meta analysis.pt.
- 141. (metaanaly\$ or meta-analy\$ or (meta adj analy\$)).tw,sh.
- 142. (systematic\$ adj5 (review\$ or overview\$)).tw,sh.
- 143. (methodologic\$ adj5 (review\$ or overview\$)).tw,sh.
- 144. or/139-143
- 145. review\$.pt.
- 146. (medline or medlars or embase or cinahl or cochrane or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation" or scisearch).tw.
- 147. ((hand or manual\$) adj2 search\$).tw.
- 148. (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw,sh.
- 149. (pooling or pooled or mantel haenszel).tw,sh.
- 150. (peto or dersimonian or der simonian or fixed effect).tw,sh.
- 151. or/146-150
- 152. 145 and 151
- 153. or/144,152
- 154. letter.pt.
- 155. case report.tw.
- 156. comment.pt.
- 157. editorial.pt.
- 158. historical article.pt.
- 159. ANIMAL/ not (HUMAN/ and ANIMAL/)
- 160. or/154-159
- 161. 138 not 160
- 162. 153 not 160
- 163. or/161-162
- 164. and/122,163

FEVER_treatment_pharmaceuticals_RCT_SR_embase_300306

- 1. PREMATURITY/
- 2. POSTMATURITY/
- 3. LOW BIRTH WEIGHT/
- 4. (low adj birth adj weight).tw.
- 5. lbw.tw.
- 6. VERY LOW BIRTH WEIGHT/
- 7. vlbw.tw.
- 8. NEWBORN/

9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. PYREXIA IDIOPATHICA/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGEN/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANTIINFECTIVE AGENT/
31. ANTIBIOTIC AGENT/
32. antibiotic\$.tw.
33. bacteriocide\$.tw.
34. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
35. penicillin\$.tw.
36. PENICILLIN G/
37. benzylpenicillin\$.tw.
38. or/30-37
39. AMOXICILLIN/
40. amoxicil\$.tw.
41. amoxycil\$.tw.
42. amoxil\$.tw.
43. or/39-42
44. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
45. augmentin\$.tw.
46. or/44-45
47. AMPICILLIN/

- 48. ampicillin\$.tw.
- 49. penbritin\$.tw.
- 50. or/47-49
- 51. CEFADROXIL/
- 52. cefadroxil\$.tw.
- 53. cephadrox\$.tw.
- 54. or/51-53
- 55. CEPHALEXIN/
- 56. cephalixin\$.tw.
- 57. cefalexin\$.tw.
- 58. cefaclor\$.tw.
- 59. ceporex\$.tw.
- 60. keflex\$.tw.
- 61. or/55-60
- 62. CEFIXIME/
- 63. cefixim\$.tw.
- 64. suprax\$.tw.
- 65. or/62-64
- 66. CEFOTAXIME/
- 67. cefotaxim\$.tw.
- 68. cephotaxim\$.tw.
- 69. claforan\$.tw.
- 70. klaforan\$.tw.
- 71. or/66-70
- 72. CEPHALOSPORINS/
- 73. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 74. cefpirome\$.tw.
- 75. cefrom\$.tw.
- 76. or/72-75
- 77. CEFTIZOXIME/
- 78. cefpodoxim\$.tw.
- 79. ceftizoxim\$.tw.
- 80. orelox\$.tw.
- 81. or/77-80
- 82. CEPHRADINE/
- 83. ceftin\$.tw.
- 84. velosef\$.tw.
- 85. or/82-84
- 86. CEFTAZIDIME/

87. ceftazidim\$.tw.
88. fortum\$.tw.
89. kefadim\$.tw.
90. or/86-89
91. CEFTRIAXONE/
92. ceftriaxon\$.tw.
93. rocephin\$.tw.
94. or/91-93
95. CEFUROXIME/
96. cefuroxim\$.tw.
97. zinacef\$.tw.
98. zinnat\$.tw.
99. or/95-98
100. GENTAMICINS/
101. gentamicin\$.tw.
102. cidomycin\$.tw.
103. genticin\$.tw.
104. or/100-103
105. AMIKACIN/
106. amikacin\$.tw.
107. AMINOGLYCOSIDE/
108. (aminoglycoside\$ or aminoglucoside\$).tw.
109. TOBRAMYCIN/
110. tobramycin\$.tw.
111. TOBRAMYCIN SULPHATE/
112. nebcin\$.tw.
113. tobi.tw.
114. NETILMICIN/
115. netilmicin\$.tw.
116. netillin\$.tw.
117. or/105-116
118. or/38,43,46,50,54,61,65,71,76,81,85,90,94,99,104,117
119. and/29,118
120. CLINICAL TRIALS/
121. (clinic\$ adj5 trial\$).ti,ab,sh.
122. SINGLE BLIND PROCEDURE/
123. DOUBLE BLIND PROCEDURE/
124. RANDOM ALLOCATION/
125. CROSSOVER PROCEDURE/

- 126. PLACEBO/
- 127. placebo\$.ti,ab,sh.
- 128. random\$.ti,ab,sh.
- 129. RANDOMIZED CONTROLLED TRIALS/
- 130. ((single or double or triple or treble) adj (blind\$ or mask\$)).ti,ab,sh.
- 131. randomi?ed control\$ trial\$.tw.
- 132. or/120-131
- 133. META ANALYSIS/
- 134. ((meta adj analy\$) or metaanalys\$ or meta-analy\$).ti,ab,sh.
- 135. (systematic\$ adj5 (review\$ or overview\$)).ti,sh,ab.
- 136. (methodologic\$ adj5 (review\$ or overview\$)).ti,ab,sh.
- 137. or/133-136
- 138. review.pt.
- 139. (medline or medlars or embase).ab.
- 140. (scisearch or science citation index).ab.
- 141. (psychlit or psyclit or psychinfo or psycinfo or cinahl or cochrane).ab.
- 142. ((hand or manual\$) adj2 search\$).tw.
- 143. (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
- 144. (pooling or pooled or mantel haenszel).tw.
- 145. (peto or dersimonian or "der simonian" or fixed effect).tw.
- 146. or/139-145
- 147. 138 and 146
- 148. or/137,147
- 149. case study.tw,sh.
- 150. abstract report.tw,sh.
- 151. note.tw,sh.
- 152. short survey.tw,sh.
- 153. letter.tw,sh.
- 154. case report.tw,sh.
- 155. editorial.tw,sh.
- 156. (ANIMAL/ or NONHUMAN/) not (HUMAN/ or ((ANIMAL/ or NONHUMAN/) and HUMAN/))
- 157. or/149-156
- 158. 132 not 157
- 159. 148 not 157
- 160. or/158-159
- 161. and/119,160

FEVER_treatment_pharmaceuticals_RCT_SR_cinahl_300306

- 1. INFANT, PREMATURE/

2. INFANT, POSTMATURE/
3. LOW BIRTH WEIGHT/
4. (low adj birth adj weight).tw.
5. lbw.tw.
6. VERY LOW BIRTH WEIGHT/
7. vlbw.tw.
8. INFANT, NEWBORN/
9. neonat\$.tw.
10. newborn\$.tw.
11. exp INFANT/
12. infan\$.tw.
13. PRESCHOOL CHILD/
14. (baby or babies).tw.
15. (child\$ adj5 pre?school).tw.
16. toddler\$.tw.
17. or/1-16
18. exp FEVER/
19. "FEVER OF UNKNOWN ORIGIN"/
20. fever\$.tw.
21. febril\$.tw.
22. hypertherm\$.tw.
23. pyrexia\$.tw.
24. MALIGNANT HYPERTHERMIA/
25. (malignan\$ adj3 (hypertherm\$ or hyperpyrex\$)).tw.
26. exp PYROGENS/
27. pyrogen\$.tw.
28. or/18-27
29. and/17,28
30. ANTIINFECTIVE AGENT/
31. ANTIBIOTIC AGENT/
32. PENICILLINS/
33. penicillin\$.tw.
34. antibiotic\$.tw.
35. bacteriocide\$.tw.
36. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
37. or/30-36
38. AMOXICILLIN/
39. amoxicil\$.tw.
40. amoxycil\$.tw.

- 41. amoxil\$.tw.
- 42. or/38-41
- 43. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 44. augmentin\$.tw.
- 45. or/43-44
- 46. AMPICILLIN/
- 47. ampicillin\$.tw.
- 48. penbritin\$.tw.
- 49. or/46-48
- 50. CEFADROXIL/
- 51. cefadroxil\$.tw.
- 52. cephadrox\$.tw.
- 53. or/50-52
- 54. CEPHALEXIN/
- 55. cephalixin\$.tw.
- 56. cefalexin\$.tw.
- 57. cefaclor\$.tw.
- 58. ceporex\$.tw.
- 59. keflex\$.tw.
- 60. or/54-59
- 61. CEFIXIME/
- 62. cefixim\$.tw.
- 63. suprax\$.tw.
- 64. or/61-63
- 65. CEFOTAXIME/
- 66. cefotaxim\$.tw.
- 67. cephotaxim\$.tw.
- 68. claforan\$.tw.
- 69. klaforan\$.tw.
- 70. or/65-69
- 71. CEPHALOSPORINS/
- 72. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 73. cefpirome\$.tw.
- 74. cefrom\$.tw.
- 75. or/71-74
- 76. CEFTIZOXIME/
- 77. cefpodoxim\$.tw.
- 78. ceftizoxim\$.tw.
- 79. orelox\$.tw.

- 80. or/76-79
- 81. CEPHRADINE/
- 82. cefradin\$.tw.
- 83. velosef\$.tw.
- 84. or/81-83
- 85. CEFTAZIDIME/
- 86. ceftazidim\$.tw.
- 87. fortum\$.tw.
- 88. kefadim\$.tw.
- 89. or/85-88
- 90. CEFTRIAXONE/
- 91. ceftriaxon\$.tw.
- 92. rocephin\$.tw.
- 93. or/90-92
- 94. CEFUROXIME/
- 95. cefuroxim\$.tw.
- 96. zinacef\$.tw.
- 97. zinnat\$.tw.
- 98. or/94-97
- 99. GENTAMICINS/
- 100. gentamicin\$.tw.
- 101. cidomycin\$.tw.
- 102. genticin\$.tw.
- 103. or/99-102
- 104. AMIKACIN/
- 105. amikacin\$.tw.
- 106. AMINOGLYCOSIDES/
- 107. (aminoglycoside\$ or aminoglucoside\$).tw.
- 108. TOBRAMYCIN/
- 109. tobramycin\$.tw.
- 110. nebcin\$.tw.
- 111. tobi.tw.
- 112. netilmicin\$.tw.
- 113. or/104-112
- 114. or/37,42,45,49,53,60,64,70,75,80,84,89,93,98,103,113
- 115. and/29,114
- 116. exp CLINICAL TRIALS/
- 117. (clinic\$ adj5 trial\$).tw,sh.
- 118. clinical trial.pt.

- 119. SINGLE-BLIND STUDIES/
- 120. DOUBLE-BLIND STUDIES/
- 121. TRIPLE-BLIND STUDIES/
- 122. ((single or double or triple or treble) adj5 (blind\$ or mask\$)).tw,sh.
- 123. RANDOM ASSIGNMENT/
- 124. random\$.tw.
- 125. RANDOMIZED CONTROLLED TRIALS/
- 126. randomi?ed control\$ trial\$.tw.
- 127. PLACEBOS/
- 128. placebo\$.tw.
- 129. or/116-128
- 130. META ANALYSIS/
- 131. ((meta adj analy\$) or metaanalys\$ or meta-analy\$).tw.
- 132. SYSTEMATIC REVIEW/
- 133. systematic review\$.pt.
- 134. (systematic\$ adj5 (review\$ or overview\$)).tw.
- 135. LITERATURE REVIEW/
- 136. or/130-135
- 137. ("review" or "review studies" or "review academic" or "review tutorial").ti,ab,sh,pt.
- 138. (medline or medlars or embase or cochrane or scisearch or psycinfo or psychinfo or psychlit or psyclit or "web of science" or "science citation").tw.
- 139. ((hand or manual\$) adj2 search\$).tw.
- 140. (electronic database\$ or bibliographic database\$ or computeri?ed database\$ or online database\$).tw.
- 141. (pooling or pooled or mantel haenszel).tw.
- 142. (peto or dersimonian or "der simonian" or fixed effect).tw.
- 143. or/138-142
- 144. 137 and 143
- 145. or/136,144
- 146. letter.pt,sh.
- 147. commentary.pt,sh.
- 148. editorial.pt,sh.
- 149. manuscripts.pt,sh.
- 150. pamphlets.pt,sh.
- 151. reports.pt,sh.
- 152. newsletters.pt,sh.
- 153. newspapers.pt,sh.
- 154. ANIMALS/ or ANIMAL STUDIES/
- 155. or/146-154

156. 129 not 155

157. 145 not 155

158. or/156-157

159. and/115,158

FEVER_treatment_pharmaceuticals_health_economics_medline_150506

1. INFANT, PREMATURE/

2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.

3. INFANT, POSTMATURE/

4. ((postmature\$ or postterm\$ or post?term\$) adj (baby or babies or child\$ or infan\$)).tw.

5. INFANT, NEWBORN/

6. neonat\$.tw.

7. newborn\$.tw.

8. exp INFANT/

9. infan\$.tw.

10. INFANT, SMALL FOR GESTATIONAL AGE/

11. (small adj2 gestational age).tw.

12. INFANT, LOW BIRTH WEIGHT/

13. INFANT, VERY LOW BIRTH WEIGHT/

14. (low adj birth adj weight).tw.

15. (low adj birth?weight).tw.

16. lbw.tw.

17. vlbw.tw.

18. (baby or babies).tw.

19. CHILD, PRESCHOOL/

20. toddler\$.tw.

21. exp CHILD/

22. child\$.tw.

23. ADOLESCENT/

24. adolescen\$.tw.

25. juvenile\$.tw.

26. youth\$.tw.

27. teen\$.tw.

28. PUBERTY/

29. pubert\$.tw.

30. pubesc\$.tw.

31. MINORS/

32. minors.tw.

33. or/1-32

34. BACTERIAL INFECTIONS/

- 35. (bacteri\$ adj infect\$).tw.
- 36. or/34-35
- 37. exp MENINGITIS, BACTERIAL/
- 38. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
- 39. meningococc\$.tw.
- 40. or/37-39
- 41. SEPTICEMIA/
- 42. septicemi\$.tw.
- 43. septicaemia\$.tw.
- 44. or/41-43
- 45. BACTEREMIA/
- 46. bacteremi\$.tw.
- 47. bacteraemia\$.tw.
- 48. or/45-47
- 49. exp PNEUMONIA/
- 50. pneumoni\$.tw.
- 51. or/49-50
- 52. HERPES SIMPLEX/
- 53. herpes simplex.tw.
- 54. or/52-53
- 55. exp ARTHRITIS, INFECTIOUS/
- 56. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 57. pyarthrosis.tw.
- 58. pyoarthritis.tw.
- 59. or/55-58
- 60. STAPHYLOCOCCAL INFECTIONS/
- 61. STREPTOCOCCAL INFECTIONS/
- 62. ((staphylococc\$ or streptococc\$) adj infect\$).tw.
- 63. or/60-62
- 64. OSTEOMYELITIS/
- 65. osteomyeliti\$.tw.
- 66. or/64-65
- 67. exp URINARY TRACT INFECTIONS/
- 68. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 69. UTI.tw.
- 70. ((upper or lower) adj5 urin\$).tw.
- 71. exp CYSTITIS/

72. cystitis\$.tw.
73. PYELONEPHRITIS/
74. pyelonephriti\$.tw.
75. pyonephrosi\$.tw.
76. pyelocystiti\$.tw.
77. or/67-76
78. MUCOCUTANEOUS LYMPH NODE SYNDROME/
79. (mucocutaneous adj2 lymph\$).tw.
80. mcls.tw.
81. (kawasaki adj (disease or syndrome)).tw.
82. or/78-81
83. or/36,40,44,48,51,54,59,63,66,77,82
84. ANTI-INFECTIVE AGENTS/
85. antibiotic\$.tw.
86. bacteriocide\$.tw.
87. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
88. or/84-87
89. PENICILLINS/
90. penicillin\$.tw.
91. or/88-89
92. PENICILLIN G/
93. benzylpenicillin\$.tw.
94. or/92-93
95. AMOXICILLIN/
96. amoxicil\$.tw.
97. amoxycil\$.tw.
98. amoxil\$.tw.
99. or/95-98
100. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
101. augmentin\$.tw.
102. or/100-101
103. AMPICILLIN/
104. ampicillin\$.tw.
105. penbritin\$.tw.
106. or/103-105
107. CEFADROXIL/
108. cefadroxil\$.tw.
109. cephadrox\$.tw.
110. or/107-109

- 111. CEPHALEXIN/
- 112. cephalixin\$.tw.
- 113. cefalexin\$.tw.
- 114. cefaclor\$.tw.
- 115. ceporex\$.tw.
- 116. keflex\$.tw.
- 117. or/111-116
- 118. CEFIXIME/
- 119. cefixim\$.tw.
- 120. suprax\$.tw.
- 121. or/118-120
- 122. CEFOTAXIME/
- 123. cefotaxim\$.tw.
- 124. cephotaxim\$.tw.
- 125. claforan\$.tw.
- 126. klaforan\$.tw.
- 127. or/122-126
- 128. CEPHALOSPORINS/
- 129. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 130. cefpirome\$.tw.
- 131. or/128-130
- 132. CEFTIZOXIME/
- 133. cefpodoxim\$.tw.
- 134. ceftizoxim\$.tw.
- 135. orelox\$.tw.
- 136. or/132-135
- 137. CEPHRADINE/
- 138. cefradin\$.tw.
- 139. velosef\$.tw.
- 140. or/137-139
- 141. CEFTAZIDIME/
- 142. ceftazidim\$.tw.
- 143. fortum\$.tw.
- 144. or/141-143
- 145. CEFTRIAXONE/
- 146. ceftriaxon\$.tw.
- 147. rocephin\$.tw.
- 148. or/145-147
- 149. CEFUROXIME/

-
150. cefuroxim\$.tw.
 151. zinacef\$.tw.
 152. zinnat\$.tw.
 153. or/149-152
 154. GENTAMICINS/
 155. gentamicin\$.tw.
 156. cidomycin\$.tw.
 157. genticin\$.tw.
 158. or/154-157
 159. AMIKACIN/
 160. amikacin\$.tw.
 161. or/159-160
 162. AMINOGLYCOSIDES/
 163. aminoglycoside\$.tw.
 164. aminoglucoside\$.tw.
 165. or/162-164
 166. TOBRAMYCIN/
 167. tobramycin\$.tw.
 168. nebcin\$.tw.
 169. tobi.tw.
 170. or/166-169
 171. NETILMICIN/
 172. netilmicin\$.tw.
 173. netillin\$.tw.
 174. or/171-173
 175. or/88,91,94,99,102,106,110,117,121,127,131,136,140,144,148,153,158,161,165,170,174
 176. ECONOMICS/
 177. "COSTS AND COST ANALYSIS"/
 178. COST ALLOCATION/
 179. COST-BENEFIT ANALYSIS/
 180. COST CONTROL/
 181. COST SAVINGS/
 182. COST OF ILLNESS/
 183. COST SHARING/
 184. HEALTH CARE COSTS/
 185. DIRECT SERVICE COSTS/
 186. DRUG COSTS/
 187. EMPLOYER HEALTH COSTS/
 188. HOSPITAL COSTS/

- 189. HEALTH RESOURCES/
- 190. "HEALTH SERVICES NEEDS AND DEMAND"/
- 191. HEALTH PRIORITIES/
- 192. HEALTH EXPENDITURES/
- 193. CAPITAL EXPENDITURES/
- 194. FINANCIAL MANAGEMENT/
- 195. FINANCIAL MANAGEMENT, HOSPITAL/
- 196. QUALITY-ADJUSTED LIFE YEARS/
- 197. "DEDUCTIBLES AND COINSURANCE"/
- 198. MEDICAL SAVINGS ACCOUNTS/
- 199. ECONOMICS, HOSPITAL/
- 200. ECONOMICS, MEDICAL/
- 201. ECONOMICS, NURSING/
- 202. ECONOMICS, PHARMACEUTICAL/
- 203. MODELS, ECONOMIC/
- 204. MODELS, ECONOMETRIC/
- 205. RESOURCE ALLOCATION/
- 206. HEALTH CARE RATIONING/
- 207. "FEES AND CHARGES"/
- 208. BUDGETS/
- 209. VALUE OF LIFE/
- 210. (financ\$ or fiscal\$ or funding).tw.
- 211. (QALY\$ or life?year\$).tw.
- 212. (econom\$ or cost\$).tw.
- 213. pharmacoeconomic\$.tw.
- 214. ec.fs.
- 215. or/176-214
- 216. and/33,83,175,215
- 217. animal/ not (human/ or (human/ and animal/))
- 218. 216 not 217

FEVER_treatment_pharmaceuticals_health_economics_embase_150506

- 1. PREMATURITY/
- 2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.
- 3. exp NEWBORN/
- 4. neonat\$.tw.
- 5. newborn\$.tw.
- 6. NEWBORN PERIOD/
- 7. PERINATAL PERIOD/
- 8. perinatal\$.tw.

9. postnatal\$.tw.
10. exp INFANT/
11. INFANCY/
12. BABY/
13. infan\$.tw.
14. (baby or babies).tw.
15. SMALL FOR DATE INFANT/
16. (small adj2 (date or "gestational age")).tw.
17. lbw.tw.
18. vlbw.tw.
19. CHILD/
20. CHILDHOOD/
21. PRESCHOOL CHILD/
22. SCHOOL CHILD/
23. child\$.tw.
24. PREPUBERTY/
25. PUBERTY/
26. prepube\$.tw.
27. pubert\$.tw.
28. pubesc\$.tw.
29. ADOLESCENCE/
30. adolescen\$.tw.
31. JUVENILE/
32. ADOLESCENT/
33. juvenile\$.tw.
34. minors.tw.
35. youth\$.tw.
36. teen\$.tw.
37. or/1-36
38. BACTERIAL INFECTION/
39. (bacteri\$ adj infect\$).tw.
40. or/38-39
41. BACTERIAL MENINGITIS/
42. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.
43. meningococc\$.tw.
44. or/41-43
45. SEPTICEMIA/
46. septicemi\$.tw.

- 47. septicaemia\$.tw.
- 48. or/45-47
- 49. BACTEREMIA/
- 50. bacteremi\$.tw.
- 51. bacteraemia\$.tw.
- 52. or/49-51
- 53. exp PNEUMONIA/
- 54. pneumoni\$.tw.
- 55. or/53-54
- 56. HERPES SIMPLEX/
- 57. herpes simplex.tw.
- 58. or/56-57
- 59. BACTERIAL ARTHRITIS/
- 60. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.
- 61. pyarthrosis.tw.
- 62. pyoarthritis.tw.
- 63. or/59-62
- 64. STAPHYLOCOCCAL INFECTION/
- 65. STREPTOCOCCAL INFECTION/
- 66. straphylococc\$.tw.
- 67. streptococc\$.tw.
- 68. or/64-67
- 69. OSTEOMYELITIS/
- 70. osteomyeliti\$.tw.
- 71. or/69-70
- 72. exp URINARY TRACT INFECTION/
- 73. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.
- 74. UTI.tw.
- 75. ((upper or lower) adj5 urin\$).tw.
- 76. exp CYSTITIS/
- 77. cystitis\$.tw.
- 78. or/72-77
- 79. PYELONEPHRITIS/
- 80. pyelonephriti\$.tw.
- 81. pyonephrosi\$.tw.
- 82. pyelocystiti\$.tw.
- 83. or/79-82
- 84. MUCOCUTANEOUS LYMPH NODE SYNDROME/

- 85. (mucocutaneous adj2 lymph\$.tw.
- 86. mcls.tw.
- 87. (kawasaki adj (disease or syndrome)).tw.
- 88. or/84-87
- 89. or/40,44,48,52,55,58,63,68,71,78,83,88
- 90. ANTIINFECTIVE AGENT/
- 91. ANTIBIOTIC AGENT/
- 92. antibiotic\$.tw.
- 93. bacteriocide\$.tw.
- 94. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
- 95. penicillin\$.tw.
- 96. PENICILLIN G/
- 97. benzylpenicillin\$.tw.
- 98. or/90-97
- 99. AMOXICILLIN/
- 100. amoxicil\$.tw.
- 101. amoxycil\$.tw.
- 102. amoxil\$.tw.
- 103. or/99-102
- 104. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 105. augmentin\$.tw.
- 106. or/104-105
- 107. AMPICILLIN/
- 108. ampicillin\$.tw.
- 109. penbritin\$.tw.
- 110. or/107-109
- 111. CEFADROXIL/
- 112. cefadroxil\$.tw.
- 113. cephadrox\$.tw.
- 114. or/111-113
- 115. CEPHALEXIN/
- 116. cephalixin\$.tw.
- 117. cefalexin\$.tw.
- 118. cefaclor\$.tw.
- 119. ceporex\$.tw.
- 120. keflex\$.tw.
- 121. or/115-120
- 122. CEFIXIME/
- 123. cefixim\$.tw.

- 124. suprax\$.tw.
- 125. or/122-124
- 126. CEFOTAXIME/
- 127. cefotaxim\$.tw.
- 128. cephotaxim\$.tw.
- 129. claforan\$.tw.
- 130. klaforan\$.tw.
- 131. or/126-130
- 132. CEPHALOSPORINS/
- 133. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 134. cefpirome\$.tw.
- 135. cefrom\$.tw.
- 136. or/132-135
- 137. CEFTIZOXIME/
- 138. cefpodoxim\$.tw.
- 139. ceftizoxim\$.tw.
- 140. orelox\$.tw.
- 141. or/137-140
- 142. CEPHRADINE/
- 143. cefradin\$.tw.
- 144. velosef\$.tw.
- 145. or/142-144
- 146. CEFTAZIDIME/
- 147. ceftazidim\$.tw.
- 148. fortum\$.tw.
- 149. kefadim\$.tw.
- 150. or/146-149
- 151. CEFTRIAXONE/
- 152. ceftriaxon\$.tw.
- 153. rocephin\$.tw.
- 154. or/151-153
- 155. CEFUROXIME/
- 156. cefuroxim\$.tw.
- 157. zinacef\$.tw.
- 158. zinnat\$.tw.
- 159. or/155-158
- 160. GENTAMICINS/
- 161. gentamicin\$.tw.
- 162. cidomycin\$.tw.

163. genticin\$.tw.
164. or/160-163
165. AMIKACIN/
166. amikacin\$.tw.
167. AMINOGLYCOSIDE/
168. (aminoglycoside\$ or aminoglucoside\$).tw.
169. TOBRAMYCIN/
170. tobramycin\$.tw.
171. TOBRAMYCIN SULPHATE/
172. nebcin\$.tw.
173. tobi.tw.
174. NETILMICIN/
175. netilmicin\$.tw.
176. netillin\$.tw.
177. or/165-176
178. or/98,103,106,110,114,121,125,131,136,141,145,150,154,159,164,177
179. ECONOMICS/
180. HEALTH ECONOMICS/
181. ECONOMIC EVALUATION/
182. COST BENEFIT ANALYSIS/
183. COST CONTROL/
184. COST EFFECTIVENESS ANALYSIS/
185. COST MINIMIZATION ANALYSIS/
186. COST OF ILLNESS/
187. COST UTILITY ANALYSIS/
188. COST/
189. HEALTH CARE COST/
190. DRUG COST/
191. HEALTH CARE FINANCING/
192. HOSPITAL COST/
193. SOCIOECONOMICS/
194. ECONOMIC ASPECT/
195. QUALITY-ADJUSTED LIFE YEARS/
196. FINANCIAL MANAGEMENT/
197. PHARMACOECONOMICS/
198. RESOURCE ALLOCATION/
199. (financ\$ or fiscal\$ or funding).tw.
200. (QALY\$ or life?year\$).tw.
201. (econom\$ or cost\$).tw.

202. pharmaco-economic\$.tw.

203. or/179-202

204. and/37,89,178,203

205. (ANIMAL/ or NONHUMAN/) not (HUMAN/ or ((ANIMAL/ or NONHUMAN/) and HUMAN/))

206. 204 not 205

FEVER_treatment_pharmaceuticals_health_economics_cinahl_150506

1. INFANT, PREMATURE/

2. ((premature\$ or preterm\$ or pre?term\$) adj (baby or babies or child\$ or infan\$)).tw.

3. INFANT, NEWBORN/

4. neonat\$.tw.

5. newborn\$.tw.

6. perinatal\$.tw.

7. postnatal\$.tw.

8. exp INFANT/

9. infan\$.tw.

10. (baby or babies).tw.

11. INFANT, LOW BIRTH WEIGHT/

12. INFANT, VERY LOW BIRTH WEIGHT/

13. INFANT, SMALL FOR GESTATIONAL AGE/

14. (small adj2 (date or "gestational age")).tw.

15. lbw.tw.

16. vlbw.tw.

17. CHILD/

18. CHILD, PRESCHOOL/

19. SCHOOL CHILD/

20. child\$.tw.

21. PREPUBERTY/

22. PUBERTY/

23. prepube\$.tw.

24. pubert\$.tw.

25. pubesc\$.tw.

26. ADOLESCENCE/

27. adolescen\$.tw.

28. "MINORS (LEGAL)"/

29. juvenile\$.tw.

30. minors.tw.

31. youth\$.tw.

32. teen\$.tw.

33. or/1-32

34. BACTERIAL INFECTIONS/

35. (bacteri\$ adj infect\$).tw.

36. or/34-35

37. exp MENINGITIS, BACTERIAL/

38. (meningitis\$ adj2 (bacteri\$ or coli or escheichia or listeria or pneumococc\$ or purulent\$ or pyrogen\$)).tw.

39. meningococc\$.tw.

40. or/37-39

41. exp SEPSIS/

42. septicemi\$.tw.

43. septicaemia\$.tw.

44. or/41-43

45. BACTEREMIA/

46. bacteremi\$.tw.

47. bacteraemia\$.tw.

48. or/45-47

49. exp PNEUMONIA/

50. pneumoni\$.tw.

51. or/49-50

52. HERPES SIMPLEX/

53. herpes simplex.tw.

54. or/52-53

55. exp ARTHRITIS, INFECTIOUS/

56. (arthriti\$ adj2 (bacteri\$ or infect\$ or purulen\$ or pyogenic\$ or septic\$ or suppurative\$)).tw.

57. pyarthrosis.tw.

58. pyoarthritis.tw.

59. or/55-58

60. STAPHYLOCOCCAL INFECTIONS/

61. STREPTOCOCCAL INFECTIONS/

62. ((staphylococc\$ or streptococc\$) adj infect\$).tw.

63. or/60-62

64. OSTEOMYELITIS/

65. osteomyeliti\$.tw.

66. or/64-65

67. exp URINARY TRACT INFECTION/

68. ((bladder\$ or genitourin\$ or kidney\$ or pyelo\$ or renal\$ or ureter\$ or ureth\$ or urin\$ or urolog\$ or urogen\$) adj5 infect\$).tw.

69. UTI.tw.

70. ((upper or lower) adj5 urin\$).tw.

- 71. CYSTITIS/
- 72. cystitis\$.tw.
- 73. PYELONEPHRITIS/
- 74. pyelonephriti\$.tw.
- 75. pyonephrosi\$.tw.
- 76. pyelocystiti\$.tw.
- 77. or/67-76
- 78. MUCOCUTANEOUS LYMPH NODE SYNDROME/
- 79. (mucocutaneous adj2 lymph\$).tw.
- 80. mcls.tw.
- 81. (kawasaki adj (disease or syndrome)).tw.
- 82. or/78-81
- 83. or/36,40,44,48,51,54,59,63,66,77,82
- 84. ANTIINFECTIVE AGENT/
- 85. ANTIBIOTIC AGENT/
- 86. PENICILLINS/
- 87. penicillin\$.tw.
- 88. antibiotic\$.tw.
- 89. bacteriocide\$.tw.
- 90. ((antibacterial\$ or antimycobacteria\$ or bacteriocidal\$) adj agent\$).tw.
- 91. or/84-90
- 92. AMOXICILLIN/
- 93. amoxicil\$.tw.
- 94. amoxycil\$.tw.
- 95. amoxil\$.tw.
- 96. or/92-95
- 97. AMOXICILLIN-POTASSIUM CLAVULANATE COMBINATION/
- 98. augmentin\$.tw.
- 99. or/97-98
- 100. AMPICILLIN/
- 101. ampicillin\$.tw.
- 102. penbritin\$.tw.
- 103. or/100-102
- 104. CEFADROXIL/
- 105. cefadroxil\$.tw.
- 106. cephadrox\$.tw.
- 107. or/104-106
- 108. CEPHALEXIN/
- 109. cephalixin\$.tw.

- 110. cefalexin\$.tw.
- 111. cefaclor\$.tw.
- 112. ceporex\$.tw.
- 113. keflex\$.tw.
- 114. or/108-113
- 115. CEFIXIME/
- 116. cefixim\$.tw.
- 117. suprax\$.tw.
- 118. or/115-117
- 119. CEFOTAXIME/
- 120. cefotaxim\$.tw.
- 121. cephotaxim\$.tw.
- 122. claforan\$.tw.
- 123. klaforan\$.tw.
- 124. or/119-123
- 125. CEPHALOSPORINS/
- 126. (cephalospor\$ adj2 (acid\$ or antibiotic\$)).tw.
- 127. cefpirome\$.tw.
- 128. cefrom\$.tw.
- 129. or/125-128
- 130. CEFTIZOXIME/
- 131. cefpodoxim\$.tw.
- 132. ceftizoxim\$.tw.
- 133. orelox\$.tw.
- 134. or/130-133
- 135. CEPHRADINE/
- 136. cefradin\$.tw.
- 137. velosef\$.tw.
- 138. or/135-137
- 139. CEFTAZIDIME/
- 140. ceftazidim\$.tw.
- 141. fortum\$.tw.
- 142. kefadim\$.tw.
- 143. or/139-142
- 144. CEFTRIAXONE/
- 145. ceftriaxon\$.tw.
- 146. rocephin\$.tw.
- 147. or/144-146
- 148. CEFUROXIME/

- 149. cefuroxim\$.tw.
- 150. zinacef\$.tw.
- 151. zinnat\$.tw.
- 152. or/148-151
- 153. GENTAMICINS/
- 154. gentamicin\$.tw.
- 155. cidomycin\$.tw.
- 156. genticin\$.tw.
- 157. or/153-156
- 158. AMIKACIN/
- 159. amikacin\$.tw.
- 160. AMINOGLYCOSIDES/
- 161. (aminoglycoside\$ or aminoglucoside\$).tw.
- 162. TOBRAMYCIN/
- 163. tobramycin\$.tw.
- 164. nebcin\$.tw.
- 165. tobi.tw.
- 166. netilmicin\$.tw.
- 167. or/158-166
- 168. or/91,96,99,103,107,114,118,124,129,134,138,143,147,152,157,167
- 169. ECONOMICS/
- 170. "COSTS AND COST ANALYSIS"/
- 171. COST BENEFIT ANALYSIS/
- 172. COST CONTROL/
- 173. COST SAVINGS/
- 174. COST OF ILLNESS/
- 175. HEALTH CARE COSTS/
- 176. ECONOMIC ASPECTS OF ILLNESS/
- 177. ECONOMICS, PHARMACEUTICAL/
- 178. HEALTH CARE FINANCING/
- 179. FINANCIAL MANAGEMENT/
- 180. HOSPITAL COST/
- 181. SOCIOECONOMIC FACTORS/
- 182. HEALTH RESOURCE ALLOCATION/
- 183. (financ\$ or fiscal\$ or funding).tw.
- 184. (QALY\$ or life?year\$).tw.
- 185. (econom\$ or cost\$).tw.
- 186. pharmacoeconomic\$.tw.
- 187. or/169-186

188. and/33,83,168,187

Appendix F Summary of identified studies

Chapter 5

Review question

The predictive value of the following symptoms and signs, alone or in combination, as initial indications of serious illness:

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and other sounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb
- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

Number of papers identified: 9401

Number of papers weeded out: 8537

Number of papers requested: 211

Number of papers excluded: 142

Number of papers included: 69

Chapter 5

Heart rate

Review question

The predictive value of heart rate, including:

- how heart rate changes with temperature?
- whether heart rate outside the normal range detects serious illness?
- whether heart rate and temperature outside normal range detects serious illness?

Number of papers identified: 193

Number of papers weeded out: 188

Number of papers requested: 5

Number of papers excluded: 0

Number of papers included: 5

Chapter 8

Children 3 months and older

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

Number of papers identified: 619

Number of papers weeded out: 519

Number of papers requested: 46

Number of papers excluded: 31

Number of papers included: 15

Health economics

Number of papers identified: 17

Number of papers weeded out: 14

Number of papers requested: 1

Number of papers excluded: 1

Number of papers included: 0

Chapter 8

Response to antipyretic medication

Review question

What is the predictive value of the clinical response to paracetamol or NSAIDs?

Number of papers identified: 5372

Number of papers weeded out: 5250

Number of papers requested: 19

Number of papers excluded: 5

Number of papers included: 14

Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

Number of papers identified: 1705

Number of papers weeded out: 1699

Number of papers requested: 4

Number of papers excluded: 4

Number of papers included: 0

9.3 Physical and drug interventions

Review question

Effect on fever and associated symptoms of treatment with:

- Paracetamol alone or NSAIDs alone, compared with placebo and with one another
- Alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time
- Paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone.

Number of papers identified: 1732

Number of papers weeded out: 1636

Number of papers requested: 86

Number of papers excluded: 58

Number of papers included: 28

Appendix G Excluded studies

Chapter 5

Review question

What is the value (as shown by likelihood ratios, sensitivity, specificity, positive predictive value and negative predictive value) of the following symptoms and signs, alone or in combination, as initial indications of serious illness?

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and othersounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb
- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

Number of papers identified: 9401

Number of papers weeded out: 8537

Number of papers requested: 211

Number of papers excluded: 142

Number of papers included: 69

Table G.1

Bibliographic information	Reason for exclusion
Akpede,G.O., Abiodun,P.O., Sykes,R.M., Pattern of infections in children under-six years old presenting with convulsions associated with fever of acute onset in a children's emergency room in Benin City, Nigeria, <i>Journal of Tropical Pediatrics</i> , 39, 11-15, 1993	Does not compare signs and symptoms in children with and children without serious illness
Akpede,G.O., Abiodun,P.O., Sykes,R.M., Acute fevers of unknown origin in young children in the tropics, <i>Journal of Pediatrics</i> , 122, 79-81, 1993	Compares signs and symptoms in children with and children without malaria - tropical diseases are not included in the current review
Al-Eissa,Y.A., Lumbar puncture in the clinical evaluation of children with seizures associated with fever, <i>Pediatric Emergency Care</i> , 11, 347-350, 1995	Does not compare signs and symptoms in children with and children without serious illness
Al-Khathlan,N.A., Jan,M.M., Clinical profile of admitted children with febrile seizures, <i>Neurosciences</i> , 10, 30-33, 2005	Does not compare signs and symptoms in children with and children without serious illness
Al-Rashed,A.M., Bacteremia in febrile children under 3 years of age in an emergency department of a university hospital, <i>Saudi Medical Journal</i> , 29, 229-233, 2008	Not a predictive or comparative study
Anderson,A.B., Desisto,M.J., Marshall,P.C., DeWitt,T.G., Duration of fever prior to onset of a simple febrile seizure: a predictor of significant illness and neurologic course, <i>Pediatric Emergency Care</i> , 5, 12-15, 1989	Duration of fever reported is duration of fever prior to seizure - not a comparison of interest for this review
Anga,G., Barnabas,R., Kaminiel,O., Tefuarani,N., Vince,J., Ripa,P., Riddell,M., Duke,T., The aetiology, clinical presentations and outcome of febrile encephalopathy in children in Papua New Guinea, <i>Annals of Tropical Paediatrics</i> , 30, 109-118, 2010	Does not review individual symptoms and signs
Arguedas,A., Abdelnour,A., Soley,C., Jimenez,E., Jimenez,A.L., Ramcharran,D., Porat,N., Dagan,R., Gray,S., Rodgers,G.L., Prospective epidemiologic surveillance of invasive pneumococcal disease and pneumonia in children in San Jose, Costa Rica, <i>Vaccine</i> , 30, 2342-2348, 2012	Does not look at symptoms and signs
Ariffin,H., Navaratnam,P., Lin,H.P., Surveillance study of bacteraemic episodes in febrile neutropenic children, <i>International Journal of Clinical Practice</i> , 56, 237-240, 2002	Does not compare signs and symptoms in children with and children without serious illness
Barbado,F.J., Vazquez,J.J., Pena,J.M., Seoane,J.G., Arnalich,F., Gil,A., Puig,J.G., Vazquez,J.O., Fever of unknown origin: a survey on 133 patients, <i>Journal of Medicine</i> , 15, 185-192, 1984	Does not compare signs and symptoms in children with and children without serious illness
Belongia,E.A., Irving,S.A., Waring,S.C., Coleman,L.A., Meece,J.K., Vandermause,M., Lindstrom,S., Kempf,D., Shay,D.K., Clinical characteristics and 30-day outcomes for influenza A 2009 (H1N1), 2008-2009 (H1N1), and 2007-2008 (H3N2) infections, <i>JAMA</i> , 304, 1091-1098, 2010	Does not compare those with and without serious illness
Berkowitz,C.D., Uchiyama,N., Tully,S.B., Marble,R.D., Spencer,M., Stein,M.T., Orr,D.P., Fever in infants less than two months of age: spectrum of disease and predictors of outcome, <i>Pediatric Emergency Care</i> , 1, 128-135, 1985	Prediction of serious illness included laboratory test results - was not possible to determine predictive value of clinical signs and symptoms alone

Bilavsky,E., shkenazi-Hoffnung,L., Yarden-Bilavsky,H., Amir,J., Livni,G., A search for the 'Holy Grail' in the evaluation of febrile neonates aged 28 days or less: A prospective study, <i>Scandinavian Journal of Infectious Diseases</i> , 43, 264-268, 2011	Include laboratory test results - not possible to separate out clinical signs and symptoms
Bilavsky,E., Shouval,D.S., Yarden-Bilavsky,H., Fisch,N., Ashkenazi,S., Amir,J., A prospective study of the risk for serious bacterial infections in hospitalized febrile infants with or without bronchiolitis, <i>Pediatric Infectious Disease Journal</i> , 27, 269-270, 2008	Compares serious bacterial illness in children with and children without bronchiolitis - does not compare signs and symptoms in children with and children without serious illness
Biswas,R., Dhakal,B., Das,R.N., Shetty,K.J., Resolving diagnostic uncertainty in initially poorly localizable fevers: a prospective study, <i>International Journal of Clinical Practice</i> , 58, 26-28, 2004	Does not compare signs and symptoms in children with and children without serious illness. The included population were older than 14 years.
Blacklock, C; Maydon-White, R; Coad, N; Thompson, M, Which symptoms and clinical features correctly identify serious respiratory infection in children attending a paediatric assessment unit?, <i>Archives of Disease in Childhood</i> , 96, 708-714, 2011	Not all children were febrile and results were not presented as a subgroup analysis. The grouping of illnesses meant that the comparison relevant to the current review (serious illness vs. no/minor illness) could not be made.
Bohnhorst,B., Lange,M., Bartels,D.B., Bejo,L., Hoy,L., Peter,C., Procalcitonin and valuable clinical symptoms in the early detection of neonatal late-onset bacterial infection, <i>Acta Paediatrica, International Journal of Paediatrics</i> , 101, 19-25, 2012	Not all children had fever. No subgroup analysis was available for those that did.
Bonadio,W.A., The history and physical assessments of the febrile infant, <i>Pediatric Clinics of North America</i> , 45, 65-77, 1998	Review with no new data
Bonadio,W.A., Hagen,E., Rucka,J., Shallow,K., Stommel,P., Smith,D., Efficacy of a protocol to distinguish risk of serious bacterial infection in the outpatient evaluation of febrile young infants, <i>Clinical Pediatrics,Clin.Pediatr.</i> , 32, 401-404, 1993	Looks at the Rochester and Milwaukee protocols, both of which include laboratory findings in their criteria
Bonadio,W.A., Hennes,H., Smith,D., Ruffing,R., Melzer-Lange,M., Lye,P., Isaacman,D., Reliability of observation variables in distinguishing infectious outcome of febrile young infants, <i>Pediatric Infectious Disease Journal</i> , 12, 111-114, 1993	Scoring system that is not relevant to this review
Bonadio,W.A., Stremski,E., Shallow,K., Clinical characteristics of children with fever and transient neutropenia who experience serious bacterial infections, <i>Pediatric Emergency Care</i> , 5, 163-165, 1989	Does not compare signs and symptoms in children with and children without serious illness
Bower,J.R., Powell,K.R., Unexplained fever in infants and young children: How to manage, <i>Consultant</i> , 41, 712-715, 2001	Does not compare symptoms and signs in children with and without serious bacterial illness
Brent,A.J., Lakhanpaul,M., Ninis,N., Levin,M., MacFaul,R., Thompson,M., Evaluation of temperature-pulse centile charts in identifying serious bacterial illness: observational cohort study, <i>Archives of Disease in Childhood</i> , 96, 368-373, 2011	Useful data are temperature-pulse centile charts - more relevant to the separate heart rate question
Bressan,S., Andreola,B., Zucchetto,P., Montini,G., Burei,M., Perilongo,G., Da,Dalt L., Procalcitonin as a predictor of renal scarring in infants and young children, <i>Pediatric Nephrology</i> , 24, 1199-1204, 2009	Not a comparison of interest

Bressan,S., Berlese,P., Mion,T., Masiero,S., Cavallaro,A., Da,Dalt L., Bacteremia in feverish children presenting to the emergency department: a retrospective study and literature review, <i>Acta Paediatrica</i> , 101, 271-277, 2012	Does not compare symptoms and signs in children with and children without serious illness. Excludes children that the current review question is interested in (e.g. those who appear ill, those who are irritable).
Brogan,P.A., Raffles,A., The management of fever and petechiae: making sense of rash decisions, <i>Archives of Disease in Childhood</i> , 83, 506-507, 2000	Includes a laboratory test as part of the predictive model - not possible to examine the predictive value of signs and symptoms alone
Byer,R.L., Bachur,R.G., Clinical deterioration among patients with fever and erythroderma, <i>Pediatrics</i> , 118, 2450-2460, 2006	Does not compare signs and symptoms in children with and children without serious illness
Byington,C.L., Reynolds,C.C., Korgenski,K., Sheng,X., Valentine,K.J., Nelson,R.E., Daly,J.A., Osguthorpe,R.J., James,B., Savitz,L., Pavia,A.T., Clark,E.B., Costs and infant outcomes after implementation of a care process model for febrile infants, <i>Pediatrics</i> , 130, e16-e24, 2012	Not relevant to question
Canadian Agency for Drugs and Technologies in Health., Early identification of sepsis: a review of the evidence for clinical indicators and guidelines for management (Structured abstract), <i>Health Technology Assessment Database</i> , -, 2012	Structured abstract. Full article accessed - excluded as does not compare symptoms and signs for detecting serious illness in children with fever. Not all children had fever, does not compare symptoms and signs in combination with fever.
Carrol,E.D., Newland,P., Riordan,F.A., Thomson,A.P., Curtis,N., Hart,C.A., Procalcitonin as a diagnostic marker of meningococcal disease in children presenting with fever and a rash, <i>Archives of Disease in Childhood</i> , 86, 282-285, 2002	Does not compare clinical signs and symptoms in those with and without serious bacterial illness
Caspe,W.B., Chamudes,O., Louie,B., The evaluation and treatment of the febrile infant, <i>Pediatric Infectious Disease</i> , 2, 131-135, 1983	Uses signs and symptoms to distinguish between viral and bacterial infections, not serious and non-serious illness
Chaturvedi,P., Kishore,M., Modified Glasgow Coma Scale to predict mortality in febrile unconscious children, <i>Indian Journal of Pediatrics</i> , 68, 311-314, 2001	Does not compare signs and symptoms in children with and children without serious illness
Chiappini,E., Principi,N., Longhi,R., Tovo,P.A., Becherucci,P., Bonsignori,F., Esposito,S., Festini,F., Galli,L., Lucchesi,B., Mugelli,A., de,Martino M., Writing Committee of the Italian Pediatric Society Panel for the Management of Fever in Children., Management of fever in children: summary of the Italian Pediatric Society guidelines, <i>Clinical Therapeutics</i> , 31, 1826-1843, 2009	Narrative review with no new data
Chin,R.F., Neville,B.G., Peckham,C., Bedford,H., Wade,A., Scott,R.C., NLSTEPSS Collaborative Group., Incidence, cause, and short-term outcome of convulsive status epilepticus in childhood: prospective population-based study, <i>Lancet</i> , 368, 222-229, 2006	Does not compare serious illness in children with and without status epilepticus
Chin,R.F., Neville,B.G., Scott,R.C., Meningitis is a common cause of convulsive status epilepticus with fever, <i>Archives of Disease in Childhood</i> , 90, 66-69, 2005	Does not compare signs and symptoms in children with and children without serious illness

Dagan,R., Powell,K.R., Hall,C.B., Menegus,M.A., Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis, <i>Journal of Pediatrics</i> , 107, 855-860, 1985	Rochester criteria - based on laboratory test results rather than clinical signs and symptoms
Dagan,R., Sofer,S., Phillip,M., Shachak,E., Ambulatory care of febrile infants younger than 2 months of age classified as being at low risk for having serious bacterial infections, <i>Journal of Pediatrics</i> , 112, 355-360, 1988	Laboratory test results rather than clinical signs and symptoms
Deorari,A.K., Chellani,H., Carlin,J.B., Greenwood,P., Prasad,M.S., Satyavani,A., Singh,J., John,R., Taneja,D.K., Paul,P., Meenakshi,M., Kapil,A., Paul,V.K., Weber,M., Clinico-epidemiological profile and predictors of severe illness in young infants (<60 days) reporting to a hospital in North India, <i>Indian Pediatrics</i> , 44, 739-748, 2007	Not all children had fever. Does not link signs and symptoms to the prediction of serious bacterial illness.
Fleming,S., Thompson,M., Stevens,R., Heneghan,C., Pluddemann,A., Maconochie,I., Tarassenko,L., Mant,D., Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: a systematic review of observational studies, <i>Lancet</i> , 377, 1011-1018, 2011	Does not predict serious bacterial infection
Galetto-Lacour,A., Zamora,S.A., Andreola,B., Bressan,S., Lacroix,L., Da,Dalt L., Gervais,A., Validation of a laboratory risk index score for the identification of severe bacterial infection in children with fever without source, <i>Archives of Disease in Childhood</i> , 95, 968-973, 2010	Laboratory test results not covered by the guideline update
Garcia,S., Mintegi,S., Gomez,B., Barron,J., Pinedo,M., Barcena,N., Martinez,E., Benito,J., Is 15 days an appropriate cut-off age for considering serious bacterial infection in the management of febrile infants?, <i>Pediatric Infectious Disease Journal</i> , 31, 455-458, 2012	Does not use symptoms and signs in the prediction of serious illness
Gorelick,M.H., Shaw,K.N., Murphy,K.O., Baker,M.D., Effect of fever on capillary refill time, <i>Pediatric Emergency Care</i> , <i>Pediatr. Emerg. Care</i> , 13, 305-307, 1997	Not all children had fever. There is not a clear link in the results between fever and CRT.
Grupo de Trabajo sobre el Nino Febril de la Sociedad Espanola de Urgencias de Pediatria., [The young febrile child. Results of a multicenter survey]. [Spanish], <i>Anales Espanoles de Pediatria</i> , 55, 5-10, 2001	Spanish language paper
Gupta,D., Mishra,S., Chaturvedi,P., Fast breathing in the diagnosis of pneumonia--a reassessment, <i>Journal of Tropical Pediatrics</i> , <i>J. Trop. Pediatr.</i> , 42, 196-199, 1996	Children did not present with fever
Haj-Hassan,T.A., Thompson,M.J., Mayon-White,R.T., Ninis,N., Harnden,A., Smith,L.F., Perera,R., Mant,D.C., Which early 'red flag' symptoms identify children with meningococcal disease in primary care?, <i>British Journal of General Practice</i> , 61, e97-104, 2011	Not all children had fever. Does not compare signs and symptoms in those with fever.
Hampers,L.C., Spina,L.A., Evaluation and management of pediatric febrile seizures in the emergency department, <i>Emergency Medicine Clinics of North America</i> , 29, 83-93, 2011	Narrative review with no new data
Haq,S.A., Alam,M.N., Hossain,S.M., Ahmed,T., Tahir,M., Value of clinical features in the diagnosis of enteric fever, <i>Bangladesh Medical Research Council Bulletin</i> , 23, 42-46, 1997	All participants were older than 12 years of age. Prediction of enteric/typhoid fever - not a serious illness of interest to the GDG
Henderson,S., A paediatric early warning scoring system for a remote rural area, <i>Nursing Children and Young People</i> , 24, 23-26, 2012	Does not compare symptoms and signs in children with and children without serious illness

Heulitt,M.J., Ablow,R.C., Santos,C.C., O'Shea,T.M., Hilfer,C.L., Febrile infants less than 3 months old: value of chest radiography, <i>Radiology</i> , 167, 135-137, 1988	Does not compare signs and symptoms in children with and children without serious illness
Hiew,T.M., Tan,A.M., Cheng,H.K., Clinical features and haematological indices of bacterial infections in young infants, <i>Singapore Medical Journal</i> , 33, 125-130, 1992	Not all children had fever. The prediction of signs and symptoms in conjunction with fever is not reported.
Huang,G.Y., Ma,X.J., Huang,M., Chen,S.B., Huang,M.R., Gui,Y.H., Ning,S.B., Zhang,T.H., DU,Z.D., Yanagawa,H., Kawasaki,T., Epidemiologic pictures of Kawasaki disease in Shanghai from 1998 through 2002, <i>Journal of Epidemiology</i> , 16, 9-14, 2006	All had Kawasaki disease and does not look at fever + signs and symptoms
Huppler,A.R., Eickhoff,J.C., Wald,E.R., Performance of low-risk criteria in the evaluation of young infants with fever: review of the literature. [31 refs], <i>Pediatrics</i> , 125, 228-233, 2010	Only looks at laboratory criteria
Jaffe,D.M., Fleisher,G.R., Temperature and total white blood cell count as indicators of bacteremia, <i>Pediatrics</i> , 87, 670-674, 1991	White blood cell count and laboratory values rather than clinical symptoms and signs
Jamuna,R., Srinivasan,S., Harish,B.N., Factors predicting occult bacteremia in young children, <i>Indian Journal of Pediatrics</i> , Indian J. Pediatr., 67, 709-711, 2000	Did not look at relevant symptoms/signs
Jaskiewicz,J.A., McCarthy,C.A., Richardson,A.C., White,K.C., Fisher,D.J., Dagan,R., Powell,K.R., Febrile infants at low risk for serious bacterial infection--an appraisal of the Rochester criteria and implications for management. Febrile Infant Collaborative Study Group, <i>Pediatrics</i> , 94, 390-396, 1994	Uses Rochester criteria - includes laboratory results rather than clinical signs and symptoms
Joshi,BatajooR, Rayamajhi,A., Mahaseth,C., Children with first episode of fever with seizure: Is lumbar puncture necessary?, <i>Journal of the Nepal Medical Association</i> , 47, 109-112, 2008	Reports on 'meningeal signs' - these are not clearly defined and the current review is looking at evidence for individual symptoms and signs
Joshi,N., Rajeshwari,K., Dubey,A.P., Singh,T., Kaur,R., Clinical spectrum of fever of unknown origin among Indian children. [27 refs], <i>Annals of Tropical Paediatrics</i> , 28, 261-266, 2008	Does not compare signs and symptoms in children with and children without serious illness
Juntunen,A., Herrgard,E., Mannonen,L., Korppi,M., Linnavuori,K., Vaheri,A., Koskiniemi,M., A major role of viruses in convulsive status epilepticus in children: a prospective study of 22 children, <i>European Journal of Pediatrics</i> , 160, 37-42, 2001	Does not compare signs and symptoms in children with and children without serious illness
Kao,H.C., Huang,Y.C., Chiu,C.H., Chang,L.Y., Lee,Z.L., Chung,P.W., Kao,F.C., Lin,T.Y., Acute hematogenous osteomyelitis and septic arthritis in children, <i>Journal of Microbiology, Immunology and Infection</i> , 36, 260-265, 2003	Children did not present with fever
Karmarkar,S.A., Aneja,S., Khare,S., Saini,A., Seth,A., Chauhan,B.K., A study of acute febrile encephalopathy with special reference to viral etiology, <i>Indian Journal of Pediatrics</i> , 75, 801-805, 2008	Does not compare signs and symptoms in children with and children without serious illness
Kennedy,P.G., A retrospective analysis of forty-six cases of herpes simplex encephalitis seen in Glasgow between 1962 and 1985, <i>Quarterly Journal of Medicine</i> , Q.J.Med., 68, 533-540, 1988	Not all children had fever - this study looks at children with herpes simplex encephalitis rather than at children with fever

Kimia,A., Ben-Joseph,E.P., Rudloe,T., Capraro,A., Sarco,D., Hummel,D., Johnston,P., Harper,M.B., Yield of lumbar puncture among children who present with their first complex febrile seizure, <i>Pediatrics</i> , 126, 62-69, 2010	Does not compare signs and symptoms in children with and children without serious illness
King,C., Evaluation and management of febrile infants in the emergency department, <i>Emergency Medicine Clinics of North America</i> , 21, 89-99, 2003	The review did not present usable data
King,E.A., Slawson,D.C., Tachypnea as a predictor of pneumonia in febrile children, <i>Journal of Family Practice</i> , 42, 25-, 1996	Brief report of Taylor (1995) "Establishing clinically relevant standards for tachypnea in febrile children younger than 2 years" - full article considered separately for inclusion in the review
Klein-Kremer,A., Goldman,R.D., Return visits to the emergency department among febrile children 3 to 36 months of age, <i>Pediatric Emergency Care</i> , 27, 1126-1129, 2011	Does not compare symptoms and signs in children with and without serious illness
Kocher,M.S., Mandiga,R., Zurakowski,D., Barnewolt,C., Kasser,J.R., Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children, <i>Journal of Bone and Joint Surgery - Series A</i> , 86, 1629-1635, 2004	Not all children presented with fever
Krief,W.I., Levine,D.A., Platt,S.L., Macias,C.G., Dayan,P.S., Zorc,J.J., Feffermann,N., Kuppermann,N., Multicenter RSV-SBI Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics., Influenza virus infection and the risk of serious bacterial infections in young febrile infants, <i>Pediatrics</i> , 124, 30-39, 2009	Compares children with influenza to those without influenza. Does not link clinical signs and symptoms to serious illness
Kuppermann,N., Fleisher,G.R., Jaffe,D.M., Predictors of occult pneumococcal bacteremia in young febrile children, <i>Annals of Emergency Medicine</i> , 31, 679-687, 1998	Does not compare signs and symptoms in children with and children without serious illness
Lacour,A.G., Zamora,S.A., Gervais,A., A score identifying serious bacterial infections in children with fever without source, <i>Pediatric Infectious Disease Journal</i> , 27, 654-656, 2008	Uses laboratory tests as predictors
Laman,M., Manning,L., Hwaiwhange,I., Vince,J., Aipit,S., Mare,T., Warrel,J., Karunajeewa,H., Siba,P., Mueller,I., Davis,T.M., Lumbar puncture in children from an area of malaria endemicity who present with a febrile seizure, <i>Clinical Infectious Diseases</i> , 51, 534-540, 2010	Compares outcome in children with simple or complex seizures - not a relevant comparison
Leonard,P.A., Beattie,T.F., Is measurement of capillary refill time useful as part of the initial assessment of children?, <i>European Journal of Emergency Medicine</i> , 11, 158-163, 2004	Not all children had fever
Levine,D.A., Platt,S.L., Dayan,P.S., Macias,C.G., Zorc,J.J., Krief,W., Schor,J., Bank,D., Fefferman,N., Shaw,K.N., Kuppermann,N., Multicenter RSV-SBI Study Group of the Pediatric Emergency Medicine Collaborative Research Committee of the American Academy of Pediatrics., Risk of serious bacterial infection in young febrile infants with respiratory syncytial virus infections, <i>Pediatrics</i> , 113, 1728-1734, 2004	Compares children with respiratory syncytial virus to those without respiratory syncytial virus. Does not link clinical signs and symptoms to serious illness
Lorber,J., Sunderland,R., Lumbar puncture in children with convulsions associated with fever, <i>Lancet</i> , 1, 785-786, 1980	Reported on duration of convulsion - not relevant to this review

Luaces-Cubells,C., Mintegi,S., Garcia-Garcia,J.J., Astobiza,E., Garrido-Romero,R., Velasco-Rodriguez,J., Benito,J., Procalcitonin to detect invasive bacterial infection in non-toxic-appearing infants with fever without apparent source in the emergency department, <i>Pediatric Infectious Disease Journal</i> , 31, 645-647, 2012	Included in PCT vs CRP question. Not relevant to the current review.
Lucero,M.G., Tupasi,T.E., Gomez,M.L., Beltran,G.L., Crisostomo,A.U., Romano,V.V., Rivera,L.M., Respiratory rate greater than 50 per minute as a clinical indicator of pneumonia in Filipino children with cough, <i>Reviews of Infectious Diseases,Rev.Infect.Dis.</i> , 12 Suppl 8, S1081-S1083, 1990	Population was did not include Children with fever
Luginbuhl,L.M., Newman,T.B., Pantell,R.H., Finch,S.A., Wasserman,R.C., Office-based treatment and outcomes for febrile infants with clinically diagnosed bronchiolitis, <i>Pediatrics</i> , 122, 947-954, 2008	Compares signs and symptoms for children with and without bronchiolitis - not a serious illness of interest to the GDG
Lumsden,D.E., de la Morandiere,K.P., Best evidence topic report. Rigors in febrile children may be associated with a higher incidence of serious bacterial infection. [1 refs], <i>Emergency Medicine Journal</i> , 24, 663-, 2007	Summary of a study. Original study (Tal, 1997) reviewed separately.
Maayan-Metzger,A., Mazkereth,R., Kuint,J., Fever in healthy asymptomatic newborns during the first days of life, <i>Archives of Disease in Childhood: Fetal and Neonatal Edition</i> , 88, F312-F314, 2003	Compares characteristics of children with and children without fever - prediction of fever rather than serious illness
Machado,B.M., Cardoso,D.M., De,PaulisM, Escobar,A.M.D.U., Gilio,A.E., Fever without source: Evaluation of a guideline, <i>Jornal de Pediatria</i> , 85, 426-432, 2009	The presence of toxemia was evaluated when the children were not febrile
Mahabee-Gittens,E.M., Grupp-Phelan,J., Brody,A.S., Donnelly,L.F., Bracey,S.E., Duma,E.M., Mallory,M.L., Slap,G.B., Identifying children with pneumonia in the emergency department, <i>Clinical Pediatrics</i> , 44, 427-435, 2005	Not all children had fever. All children had cough.
Manzano,S., Bailey,B., Gervais,A., Cousineau,J., Delvin,E., Girodias,J.B., Markers for bacterial infection in children with fever without source, <i>Archives of Disease in Childhood</i> , 96, 440-446, 2011	Use of the visual analogue scale - not relevant to the current review
Manzano,S., Bailey,B., Girodias,J.B., Galetto-Lacour,A., Cousineau,J., Delvin,E., Impact of procalcitonin on the management of children aged 1 to 36 months presenting with fever without source: a randomized controlled trial, <i>American Journal of Emergency Medicine</i> , 28, 647-653, 2010	Does not use signs and symptoms to predict serious illness. Excluded children that were diagnosed with the SBIs of interest (UTI, pneumonia, etc).
Marom,R., Sakran,W., Antonelli,J., Horovitz,Y., Zarfin,Y., Koren,A., Miron,D., Quick identification of febrile neonates with low risk for serious bacterial infection: an observational study, <i>Archives of Disease in Childhood Fetal and Neonatal Edition</i> , 92, F15-F18, 2007	Did not assess individual symptoms/signs. Scoring system not relevant to this review
Massin,M.M., Montesanti,J., Lepage,P., Management of fever without source in young children presenting to an emergency room, <i>Acta Paediatrica</i> , 95, 1446-1450, 2006	Does not compare signs and symptoms in children with and children without serious illness
Mazzi,E., Bartos,A.E., Carlin,J., Weber,M.W., Darmstadt,G.L., Bolivia Clinical Signs Study Group., Clinical signs predicting severe illness in young infants (<60 days) in Bolivia, <i>Journal of Tropical Pediatrics</i> , 56, 307-316, 2010	Not all of the illnesses predicted were serious bacterial illnesses
McCarthy,P.L., Dolan,T.F.,Jr., Hyperpyrexia in children. Eight-year emergency room experience, <i>American Journal of Diseases of Children</i> , 130, 849-851, 1976	Does not compare signs and symptoms in children with and children without serious illness

McCarthy,P.L., Lembo,R.M., Fink,H.D., Observation, history, and physical examination in diagnosis of serious illnesses in febrile children <=24 months, <i>Journal of Pediatrics</i> ,J.Pediatr., 110, 26-30, 1987	Not looking at individual symptoms and signs. Not a scoring system of interest
Millichap,J.J., Gordon,Millichap J., Methods of investigation and management of infections causing febrile seizures, <i>Pediatric Neurology</i> , 39, 381-386, 2008	Compares infections in complex and simple seizures - does not compare signs and symptoms of children with and children without serious illness
Mintegi,S., Benito,J., Astobiza,E., Capape,S., Gomez,B., Eguireun,A., Well appearing young infants with fever without known source in the emergency department: are lumbar punctures always necessary?, <i>European Journal of Emergency Medicine</i> , 17, 167-169, 2010	Does not compare signs and symptoms in children with and children without serious illness
Mintegi,S., Benito,J., Pijoan,J.I., Maranon,R., Penalba,A., Gonzalez,A., Munoz,G., Luaces,C., Claret,G., Occult pneumonia in infants with high fever without source: a prospective multicenter study, <i>Pediatric Emergency Care</i> , 26, 470-474, 2010	Laboratory test results
Mintegi,S., Gomez,B., Urrea,E., Romero,A., Paniagua,N., Lopez,E., Benito,J., Use of urine dipstick evaluating young infants with fever without a source and positive urine culture, <i>Pediatric Infectious Disease Journal</i> , 30, 1103-1105, 2011	Does not compare symptoms and signs in those with and without serious illness
Morley,C.J., Thornton,A.J., Cole,T.J., Fowler,M.A., Hewson,P.H., Symptoms and Signs in Infants Younger Than 6 Months of Age Correlated With the Severity of Their Illness, <i>Pediatrics</i> , 88, 1119-1124, 1991	Fever was not an inclusion criterion in the study. Temperature was not reported as a baseline characteristic or a result.
Mustafa,B., Hani,A.W.A., Chem,Y.K., Mariam,M., Khairul,A.H., Rasid,K.A., Chua,K.B., Epidemiological and clinical features of dengue versus other acute febrile illnesses amongst patients seen at government polyclinics, <i>Medical Journal of Malaysia</i> , 65, 293-298, 2010	Study was unavailable
Nguyen,C.T.E., Clavel,V., Major,P., Hervouet-Zeiber,C., Di,LiddoL., Mattimoe,C., Bernard-Bonnin,A.C., Febrile seizures: How do current clinical practices compare with literature guidelines?, <i>Paediatrics and Child Health</i> , 16, 40A, 2011	Abstract only. Does not look at the link between symptoms and signs and serious illness.
Nijman,R.G., Thompson,M., van,Veen M., Perera,R., Moll,H.A., Oostenbrink,R., Derivation and validation of age and temperature specific reference values and centile charts to predict lower respiratory tract infection in children with fever: prospective observational study, <i>BMJ</i> , 345, e4224-, 2012	Does not compare symptoms and signs in children with and children without serious illness
Oostenbrink,R., Moons,K.G., Donders,A.R., Grobbee,D.E., Moll,H.A., Prediction of bacterial meningitis in children with meningeal signs: reduction of lumbar punctures, <i>Acta Paediatrica</i> , 90, 611-617, 2001	Not all children had fever
Oostenbrink,R., Moons,K.G., rksen-Lubsen,A.G., Grobbee,D.E., Moll,H.A., A diagnostic decision rule for management of children with meningeal signs, <i>European Journal of Epidemiology</i> ,Eur.J.Epidemiol., 19, 109-116, 2004	Not all children had fever. The study does not look at the presence of fever with other signs and symptoms.
Osborn,L.M., Bolus,R., Temperature and fever in the full-term newborn, <i>Journal of Family Practice</i> , 20, 261-264, 1985	Does not compare signs and symptoms in children with and children without serious illness. Not all children presented with fever

Osman,O., Brown,D., Beattie,T., Midgley,P., Management of febrile children in a paediatric emergency department, Health Bulletin, 60, 33-39, 2002	Not all children had fever. The results for height of temperature were not clearly reported. The age of the children was not reported in the paper.
Otieno,H., Were,E., Ahmed,I., Charo,E., Brent,A., Maitland,K., Are bedside features of shock reproducible between different observers?, Archives of Disease in Childhood,Arch.Dis.Child., 89, 977-979, 2004	Not all children had fever
Pancharoen,C., Chansongsakul,T., Bhattarakosol,P., Causes of fever in children with first febrile seizures: how common are human herpesvirus-6 and dengue virus infections?, Southeast Asian Journal of Tropical Medicine and Public Health, 31, 521-523, 2000	Does not compare signs and symptoms in children with and children without serious illness
Paquette,K., Cheng,M.P., McGillivray,D., Lam,C., Quach,C., Is a lumbar puncture necessary when evaluating febrile infants (30 to 90 days of age) with an abnormal urinalysis?, Pediatric Emergency Care, 27, 1057-1061, 2011	Does not compare symptoms and signs in those with and without serious illness
Pasic,S., Minic,A., Djuric,P., Micic,D., Kuzmanovic,M., Sarjanovic,L., Markovic,M., Fever of unknown origin in 185 paediatric patients: a single-centre experience, Acta Paediatrica, 95, 463-466, 2006	Does not compare signs and symptoms in children with and children without serious illness
Phelps,K.E., Steele,R.W., Fever and stiff neck, Clinical Pediatrics, 51, 193-196, 2012	Case report on one child
Ploin,D., Gillet,Y., Morfin,F., Fouilhoux,A., Billaud,G., Liberas,S., Denis,A., Thouvenot,D., Fritzell,B., Lina,B., Floret,D., Influenza burden in febrile infants and young children in a pediatric emergency department, Pediatric Infectious Disease Journal, 26, 142-147, 2007	Not all children presented with fever. Predicting influenza - not an illness of interest to the GDG
Pluddemann,A., Price,C.P., Thompson,M., Wolstenholme,J., Heneghan,C., Primary care diagnostic technology update: point-of-care testing for glycosylated haemoglobin, British Journal of General Practice, 61, 139-140, 2011	Review with no new data. Does not compare signs and symptoms in children with and children without serious illness
Pomeroy,S.L., Holmes,S.J., Dodge,P.R., Feigin,R.D., Seizures and other neurologic sequelae of bacterial meningitis in children, New England Journal of Medicine, 323, 1651-1657, 1990	Does not compare signs and symptoms in children with and children without serious illness
Press,S., Association of hyperpyrexia with serious disease in children, Clinical Pediatrics, 33, 19-25, 1994	Does not compare signs and symptoms in children with and children without serious illness
Pusic,M.V., Clinical management of fever in children younger than three years of age, Paediatrics and Child Health, 12, 469-472, 2007	Narrative review with no new data - outlines management strategies rather than diagnosis
Ramakrishnan,K., Mathew,K.N., Thomas,K., Causes of fever in febrile seizures, Indian Journal of Pediatrics, 49, 367-369, 1982	Does not compare signs and symptoms in children with and children without serious illness
Rampersad,A., Mukundan,D., Fever, Current Opinion in Pediatrics, 21, 139-144, 2009	Review with no new data
Ray,J.G., Screening and active management reduced perinatal complications more than routine care in gestational diabetes, ACP Journal Club, 143, 65-, 2005	Commentary on gestational diabetes
Razak,M., Ismail,M.M., Omar,A., A review of haematogenous osteomyelitis in children in Kuala Lumpur Hospital, Medical Journal of Malaysia, 53 Suppl A, 83-85, 1998	Not all had fever (80%). All children were included because they had haematogenous osteomyelitis.

Redd,S.C., Vreuls,R., Metsing,M., Mohobane,P.H., Patrick,E., Moteetee,M., Clinical signs of pneumonia in children attending a hospital outpatient department in Lesotho, Bulletin of the World Health Organization,Bull.World Health Organ., 72, 113-118, 1994	Children did not present with fever
Richet,H., Casalta,J.P., Thuny,F., Merrien,J., Harle,J.R., Weiller,P.J., Habib,G., Raoult,D., Development and assessment of a new early scoring system using non-specific clinical signs and biological results to identify children and adult patients with a high probability of infective endocarditis on admission, Journal of Antimicrobial Chemotherapy, 62, 1434-1440, 2008	Does not link signs and symptoms to serious bacterial illness. Not all participants had fever.
Riordan,A.F., Marzouk,O., Thomson,A.P., Sills,J.A., Hart,A.C., Prospective validation of the glasgow meningococcal septicaemia prognostic score. Comparison with other scoring methods, European Journal of Pediatrics,Eur.J.Pediatr., 161, 531-537, 2002	Not all children had fever
Ronfani,L., Vilarim,J.N., Dragovich,D., Bacalhau,A.F., Cattaneo,A., Signs of severe bacterial infection in neonates, Journal of Tropical Pediatrics, 45, 48-51, 1999	Not all children had fever. Fever is not reported in conjunction with other signs and symptoms for predicting serious bacterial infection.
Rossi,L.N., Brunelli,G., Duzioni,N., Rossi,G., Lumbar puncture and febrile convulsions, Helvetica Paediatrica Acta, 41, 19-24, 1986	Does not compare signs and symptoms in children with and children without serious illness
Shacham,S., Kozer,E., Bahat,H., Mordish,Y., Goldman,M., Bulging fontanelle in febrile infants: is lumbar puncture mandatory?, Archives of Disease in Childhood, 94, 690-692, 2009	Does not report enough data in comparing those with a serious bacterial infection and those without. Only reports that none of the 'good' or 'excellent' appearance children had bacterial meningitis (does not report how many ill appearing children had bacterial meningitis. Makes a comparison between aseptic meningitis and normal CSF, which is not relevant to the current review). Laboratory test results were not used in all children, and so the study authors suggest caution in a bacterial vs. viral diagnosis.
Shamo'on,H., Hawamdah,A., Haddadin,R., Jmeian,S., Detection of pneumonia among children under six years by clinical evaluation, Eastern Mediterranean Health Journal, 10, 482-487, 2004	Children did not present with fever
Shiva,F., Hashemian,H.R., Febrile seizures: clinical course and diagnostic evaluation, JPMA - Journal of the Pakistan Medical Association, 48, 276-277, 1998	Does not compare signs and symptoms in children with and children without serious illness
Singh,R.R., Chaudhary,S.K., Bhatta,N.K., Khanal,B., Shah,D., Clinical and etiological profile of acute febrile encephalopathy in eastern Nepal, Indian Journal of Pediatrics, 76, 1109-1111, 2009	Does not link clinical signs and symptoms to serious illness
Steiner,M.J., DeWalt,D.A., Byerley,J.S., Is this child dehydrated?, JAMA, 291, 2746-2754, 2004	The included children did not all have fever
Sur,D.K., Bukont,E.L., Evaluating fever of unidentifiable source in young children, American Family Physician, 75, 1805-1811, 2007	Narrative review with no new data

Surpure,J.S., Hyperpyrexia (temperature greater than 40 C) in children, JACEP, 8, 130-133, 1979	Does not compare signs and symptoms in children with and children without serious illness
Thompson,M., Van den,Bruel A., Verbakel,J., Lakhanpaul,M., Haj-Hassan,T., Stevens,R., Moll,H., Buntinx,F., Berger,M., Aertgeerts,B., Oostenbrink,R., Mant,D., Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care, Health Technology Assessment (Winchester, England), 16, 1-100, 2012	Published after the current review was started - individual studies were assessed for inclusion in the current review
Thompson,M., van,denBruelA, Verbakel,J., Lakhanpaul,M., Haj-Hassan,T., Stevens,R., Moll,H., Buntinx,F., Berger,M., Aertgeerts,B., Oostenbrink,R., Mant,D., Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care, Health Technology Assessment, 16, 1-99, 2012	Not all children had fever. The individual studies from this systematic review were reviewed separately for inclusion.
Thompson,M.J., Ninis,N., Perera,R., Mayon-White,R.T., Phillips,C., Bailey,L., Harnden,A., Mant,D., Levin,M.J., Clinical recognition of meningococcal disease in children and adolescents, Lancet, 367, 397-403, 2006	Children did not all present with fever
Tibby,S.M., Hatherill,M., Murdoch,I.A., Capillary refill and core-peripheral temperature gap as indicators of haemodynamic status in paediatric intensive care patients, Archives of Disease in Childhood,Arch.Dis.Child., 80, 163-166, 1999	Not a population of interest
Tseng,C.F., Fu,Y.C., Fu,L.S., Betau,H., Chi,C.S., Clinical spectrum of Kawasaki disease in infants, Chung Hua i Hsueh Tsa Chih - Chinese Medical Journal, 64, 168-173, 2001	All had Kawasaki disease therefore not predictive
Tunkel,A.R., Scheld,W.M., Acute bacterial meningitis, Lancet, 346, 1675-1680, 1995	Narrative review. Not all children had fever.
Van den,Bruel A., Aertgeerts,B., Bruyninckx,R., Aerts,M., Buntinx,F., Signs and symptoms for diagnosis of serious infections in children: a prospective study in primary care, British Journal of General Practice, 57, 538-546, 2007	Does not review individual symptoms and signs
Van den,Bruel A., Bruyninckx,R., Vermeire,E., Aerssens,P., Aertgeerts,B., Buntinx,F., Signs and symptoms in children with a serious infection: a qualitative study, BMC Family Practice, 6, 36-, 2005	Included children are not presenting with fever. Series of case reports. Not a predictive study.
Van den,Bruel A., Haj-Hassan,T., Thompson,M., Buntinx,F., Mant,D., European Research Network on Recognising Serious Infection investigators., Diagnostic value of clinical features at presentation to identify serious infection in children in developed countries: a systematic review. [53 refs], Lancet, 375, 834-845, 2010	Review with no meta-analysis. Included studies considered separately for inclusion in the NCC review.
Van,DenBruelA, Thompson,M.J., Haj-Hassan,T., Stevens,R., Moll,H., Lakhanpaul,M., Mant,D., Diagnostic value of laboratory tests in identifying serious infections in febrile children: Systematic review, BMJ, 342, -, 2011	Uses laboratory test results rather than clinical signs and symptoms
Walsh-Kelly,C., Nelson,D.B., Smith,D.S., Losek,J.D., Melzer-Lange,M., Hennes,H.M., Glaeser,P.W., Clinical predictors of bacterial versus aseptic meningitis in childhood, Annals of Emergency Medicine,Ann.Emerg.Med., 21, 910-914, 1992	Not all children had fever (around 50% in infants and 15% in other children)
Waskerwitz,S., Berkelhamer,J.E., Outpatient bacteremia: clinical findings in children under two years with initial temperatures of 39.5 degrees C or higher, Journal of Pediatrics, 99, 231-233, 1981	Does not look at relevant symptoms or signs

Wilkinson,M., Bulloch,B., Smith,M., Prevalence of occult bacteremia in children aged 3 to 36 months presenting to the emergency department with fever in the postpneumococcal conjugate vaccine era, Academic Emergency Medicine, 16, 220-225, 2009	Does not compare signs and symptoms in children with and children without serious illness
Wilson,D., Assessing and managing the febrile child, Nurse Practitioner, 20, 59-74, 1995	Review with no new data
Yamamoto,L.T., Wigder,H.N., Fligner,D.J., Rauen,M., Dershewitz,R.A., Relationship of bacteremia to antipyretic therapy in febrile children, Pediatric Emergency Care, 3, 223-227, 1987	Does not compare signs and symptoms in children with and children without serious illness
Yarden-Bilavsky,H., Bilavsky,E., Amir,J., Ashkenazi,S., Livni,G., Serious bacterial infections in neonates with fever by history only versus documented fever, Scandinavian Journal of Infectious Diseases, 42, 812-816, 2010	Compares the incidence of serious illness with documented fever compared to fever by history only - not a comparison of interest to the GDG
Yilmaz,H.L., Yildizdas,R.D., Alparslan,N., Ozcan,K., Yaman,A., Kibar,F., Screening tools for bacteraemia in a selected population of febrile children, Annals of the Academy of Medicine, Singapore, 37, 192-199, 2008	A white blood cell count of $\leq 5000/\text{mm}^3$ or $\geq 15000/\text{mm}^3$ was an entry requirement for the study - this review does not look at the use of laboratory tests.

Chapter 5

Heart rate

Review question

The predictive value of heart rate, including:

- how heart rate changes with temperature?
- whether heart rate outside the normal range detects serious illness?
- whether heart rate and temperature outside normal range detects serious illness?

No studies were excluded

Chapter 8

Children 3 months and older

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

Table G.2

Study	Reason for exclusion
Alnader,M.F., Dasoky,H.A., Al-hamiedeen,N., Is C-reactive protein a valuable marker for severe bacterial infection?, Rawal Medical Journal, 37, 152-154, 2012	Foral publication process for the paper is unclear.
Bhatnagar,S., Beig,F.K., Malik,A., Adenosine deaminase and C-reactive protein in cerebrospinal fluid for differential diagnosis of tubercular meningitis in children, Indian Journal of Clinical Biochemistry, 23, 299-301, 2008	Includes children with confirmed diagnoses over 5 years of age
Bilavsky,E., Yarden-Bilavsky,H., Ashkenazi,S., Amir,J., C-reactive protein as a marker of serious bacterial infections in hospitalized febrile infants, Acta Paediatrica, 98, 1776-1780, 2009	Children are already hospitalised so outside the guideline population
Bleeker,S.E., rksen-Lubsen,G., Grobbee,D.E., Donders,A.R.T., Moons,K.G.M., Moll,H.A., Validating and updating a prediction rule for serious bacterial infection in patients with fever without source, Acta Paediatrica, International Journal of Paediatrics, 96, 100-104, 2007	Prediction rules for SBI using combination of factors.
Bressan,S., Andreola,B., Cattelan,F., Zangardi,T., Perilongo,G., Da,Dalt L., Predicting severe bacterial infections in well-appearing febrile neonates: laboratory markers accuracy and duration of fever, Pediatric Infectious Disease Journal, 29, 227-232, 2010	Does not include PCT test
Butbul-Aviel,Y., Koren,A., Halevy,R., Sakran,W., Procalcitonin as a diagnostic aid in osteomyelitis and septic arthritis, Pediatric Emergency Care, 21, 828-832, 2005	Children presenting with specific systems of arthritis.
Centre for Reviews and Dissemination., Accuracy of the procalcitonin test in the diagnosis of occult bacteremia in paediatrics: a systematic review and meta-analysis (;Provisional abstract);, Database of Abstracts of Reviews of Effects, -, 2012	Review protocol only
Chang,W.S., Chiu,N.C., Chi,H., Li,W.C., Huang,F.Y., Comparison of the characteristics of culture-negative versus culture-positive septic arthritis in children, Journal of Microbiology, Immunology and Infection, 38, 189-193, 2005	Not relevant to the question
Chen,C.J., Lo,Y.F., Huang,M.C., Chung,R.L., Tang,R.B., Wu,K.G., A model for predicting risk of serious bacterial infection in febrile infants younger than 3 months of age, Journal of the Chinese Medical Association: JCMA, 72, 521-526, 2009	Mathematical model no clinical data
England,R.J., Crabbe,D.C.G., Delayed diagnosis of appendicitis in children treated with antibiotics, Pediatric Surgery International, 22, 541-545, 2006	Not relevant to the question
Galetto-Lacour,A., Zamora,S.A., Andreola,B., Bressan,S., Lacroix,L., Da,Dalt L., Gervais,A., Validation of a laboratory risk index score for the identification of severe bacterial infection in children with fever without source, Archives of Disease in Childhood, 95, 968-973, 2010	It uses the same population as in Andreola 2007.

Garin,E.H., Olavarria,F., Araya,C., Broussain,M., Barrera,C., Young,L., Diagnostic significance of clinical and laboratory findings to localize site of urinary infection, <i>Pediatric Nephrology</i> , 22, 1002-1006, 2007	Not relevant to the research question
Huang,M.Y., Gupta-Malhotra,M., Huang,J.J., Syu,F.K., Huang,T.Y., Acute-phase reactants and a supplemental diagnostic aid for Kawasaki disease, <i>Pediatric Cardiology</i> , 31, 1209-1213, 2010	Not relevant to the question
Jaksic,E., Bogdanovic,R., Artiko,V., Saranovic,D.S., Petrasinovic,Z., Petrovic,M., Bojic,L., Pavlovic,S., Paripovic,A., Antonovic,O., Lezaic,V.D., Saranovic,D., Petrovic,N., Obradovic,V., Diagnostic role of initial renal cortical scintigraphy in children with the first episode of acute pyelonephritis, <i>Annals of Nuclear Medicine</i> , 25, 37-43, 2011	Not relevant to question
Lacour,A.G., Zamora,S.A., Gervais,A., A score identifying serious bacterial infections in children with fever without source, <i>Pediatric Infectious Disease Journal</i> , 27, 654-656, 2008	It combines data from Lacour 2001 and Lacour 2003, which are already included in the review
Manzano,S., Bailey,B., Girodias,J.B., Galetto-Lacour,A., Cousineau,J., Delvin,E., Impact of procalcitonin on the management of children aged 1 to 36 months presenting with fever without source: a randomized controlled trial, <i>American Journal of Emergency Medicine</i> , 28, 647-653, 2010	Investigates the impact of PCT measurement on antibiotic use
Mintegi,S., Benito,J., Pijoan,J.I., Maranon,R., Penalba,A., Gonzalez,A., Munoz,G., Luaces,C., Claret,G., Occult pneumonia in infants with high fever without source: a prospective multicenter study, <i>Pediatric Emergency Care</i> , 26, 470-474, 2010	Relevant data were not reported
Nahum,E., Livni,G., Schiller,O., Bitan,S., Ashkenazi,S., Dagan,O., Role of C-reactive protein velocity in the diagnosis of early bacterial infections in children after cardiac surgery, <i>Journal of Intensive Care Medicine</i> , 27, 191-196, 2012	Children already in hospital for cardiac surgery so outside the review population. Potential interaction for surgery and other treatments.
Papaevangelou,V., Papassotiriou,I., Sakou,I., Ferentinos,G., Liapi,G., Kyrka,A., Konstantopoulos,A., Evaluation of a quick test for C-reactive protein in a pediatric emergency department, <i>Scandinavian Journal of Clinical and Laboratory Investigation</i> , 66, 717-721, 2006	Methods of measuring CRP not included in review
Peltola,V., Toikka,P., Irjala,K., Mertsola,J., Ruuskanen,O., Discrepancy between total white blood cell counts and serum C-reactive protein levels in febrile children, <i>Scandinavian Journal of Infectious Diseases</i> , 39, 560-565, 2007	Study pre-defined cut-offs to compared WBC and CRP
Reitzenstein,J.E., Yamamoto,L.G., Mavoori,H., Similar erythrocyte sedimentation rate and C-reactive protein sensitivities at the onset of septic arthritis, osteomyelitis, acute rheumatic fever, <i>Pediatric Reports</i> , 2, 32-35, 2010	The study population was an inpatient cohort
Rudensky,B., Sirota,G., Erlichman,M., Yinnon,A.M., Schlesinger,Y., Neutrophil CD64 expression as a diagnostic marker of bacterial infection in febrile children presenting to a hospital emergency department, <i>Pediatric Emergency Care</i> , 24, 745-748, 2008	Not relevant to question
Sanders,S., Barnett,A., Correa-Velez,I., Coulthard,M., Doust,J., Systematic Review of the Diagnostic Accuracy of C-Reactive Protein to Detect Bacterial Infection in Nonhospitalized Infants and Children with Fever, <i>Journal of Pediatrics</i> , 153, 570-574, 2008	Systematic review - relevant individual studies were included

Shin,S.H., Choi,C.W., Lee,J.A., Kim,E.K., Choi,E.H., Kim,H.S., Kim,B.I., Choi,J.H., Risk factors for serious bacterial infection in febrile young infants in a community referral hospital, Journal of Korean Medical Science, 24, 844-848, 2009	The participants had obvious signs of localised infections
Thompson,A., Mannix,R., Bachur,R., Acute pediatric monoarticular arthritis: distinguishing lyme arthritis from other etiologies, Pediatrics, 123, 959-965, 2009	Lyme disease is not endemic in UK
Thompson,M., van,denBrielA, Verbakel,J., Lakhanpaul,M., Haj-Hassan,T., Stevens,R., Moll,H., Buntinx,F., Berger,M., Aertgeerts,B., Oostenbrink,R., Mant,D., Systematic review and validation of prediction rules for identifying children with serious infections in emergency departments and urgent-access primary care, Health Technology Assessment, 16, 1-99, 2012	Individual studies included in our review; review mentioned in text, but not formally reviewed.
Van den,Briel A., Thompson,M.J., Haj-Hassan,T., Stevens,R., Moll,H., Lakhanpaul,M., Mant,D., Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review, BMJ, 342, d3082-, 2011	Papers included in this review already included in our review. Review mentioned in text of our review, but not formally reviewed.
Van,DenBrielA, Thompson,M.J., Haj-Hassan,T., Stevens,R., Moll,H., Lakhanpaul,M., Mant,D., Diagnostic value of laboratory tests in identifying serious infections in febrile children: Systematic review, BMJ, 342, -, 2011	Systematic review - relevant individual studies have been included
Velasco-Zuniga,R., Trujillo-Wurttele,J.E., Fernandez-Arribas,J.L., Serrano-Carro,B., Campo-Fernandez,N., Puente-Montes,S., Predictive factors of low risk for bacteremia in infants with urinary tract infection, Pediatric Infectious Disease Journal, 31, 642-645, 2012	Not relevant to the question
Verboon-Macielek,M.A., Thijsen,S.F.T., Hemels,M.A.C., Menses,M., Van,LoonA, Krediet,T.G., Gerards,L.J., Fleer,A., Voorbij,H.A.M., Rijkers,G.T., Inflammatory mediators for the diagnosis and treatment of sepsis in early infancy, Pediatric Research, 59, 457-461, 2006	Potentially biased population
Wander,K., Brindle,E., O'connor,K.A., Sensitivity and specificity of C-reactive protein and alpha(1) -acid glycoprotein for episodes of acute infection among children in kilimanjaro, tanzania, American Journal of Human Biology, 24, 565-568, 2012	Type of infection could not be confirmed

Health economics

Table G.3

Study	Reason for exclusion
Phillips,R., Wade,R., Myers,L., Hardman,M., Sutton,A., Stewart,L., A systematic review of prognostic serum markers in febrile neutropenic episodes in children and young people undergoing treatment for malignant disease (Protocol for a systematic review) (Structured abstract), Health Technology Assessment Database, -, 2012	Protocol only. No data presented.

Chapter 8

Response to antipyretic medication

Review question

What is the predictive value of the clinical response to paracetamol or NSAIDs?

Table G.4

Study	Reason for exclusion
Kramer,M.S., Naimark,L.E., Roberts-Brauer,R., McDougall,A., Leduc,D.G., Risks and benefits of paracetamol antipyresis in young children with fever of presumed viral origin, <i>Lancet</i> , 337, 591-594, 1991	Does not report required outcomes
Lesko,S.M., O'Brien,K.L., Schwartz,B., Vezina,R., Mitchell,A.A., Invasive group A streptococcal infection and nonsteroidal antiinflammatory drug use among children with primary varicella, <i>Pediatrics</i> , 107, 1108-1115, 2001	Not relevant to this question, but included in another question.
Mackowiak,P.A., Diagnostic implications and clinical consequences of antipyretic therapy, <i>Clinical Infectious Diseases</i> , 31, S230-S233, 2000	Non-systematic review of evidence
McErlean,M.A., Bartfield,J.M., Kennedy,D.A., Gilman,E.A., Stram,R.L., Raccio-Robak,N., Home antipyretic use in children brought to the emergency department, <i>Pediatric Emergency Care</i> , 17, 249-251, 2001	Does not address study question
Richardson,A.C., Roghmann,K.J., White,K.C., Use of clinical observation scales following antipyretic therapy to predict serious illness in febrile children, <i>American Journal of Diseases of Children</i> ,Am.J.Dis.Child., 144, 435-, 1990	Not relevant to question

Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

Table G.5

Study	Reason for exclusion
Hoover,L., AAP reports on the use of antipyretics for fever in children, American Family Physician, 85, 518-519, 2012	General comment paper; not a review
Pereira,G.L., Dagostini,J.M., Dal Pizzol,T.S., Alternating antipyretics in the treatment of fever in children: a systematic review of randomized clinical trials, Jornal de Pediatria, 88, 289-296, 2012	All papers already included in NCCs own review
Section,onClinicalPharmacologyandTherapeutics, Committee,onDrugs, Sullivan,J.E., Farrar,H.C., Fever and antipyretic use in children, Pediatrics, 127, 580-587, 2011	General literature review; not a systematic review
Senel,S., Erkek,N., Karacan,C.D., Comparison of acetaminophen and ketoprofen in febrile children: a single dose randomized clinical trial, Indian Journal of Pediatrics, 79, 213-217, 2012	Ketoprofen not licenced in the UK and was not included as a treatment for review.

9.3 Physical and drug interventions

Review question

Effect on fever and associated symptoms of treatment with:

- Paracetamol alone or NSAIDs alone, compared with placebo and with one another
- Alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time
- Paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone.

Table G.6

Study	Reason for exclusion
Aksoylar,S., Aksit,S., Caglayan,S., Yaprak,I., Bakiler,R., Cetin,F., Evaluation of sponging and antipyretic medication to reduce body temperature in febrile children, Acta Paediatrica Japonica, 39, 215-217, 1997	Physical methods not included in review
Amdekar,Y.K., Desai,R.Z., Antipyretic activity of ibuprofen and paracetamol in children with pyrexia, British Journal of Clinical Practice, 39, 140-143, 1985	It could not be established if this was a randomised study or not
Ashraf,E., Ford,L., Geetha,R., Cooper,S., Safety profile of ibuprofen suspension in young children, Inflammopharmacology, 7, 219-225, 1999	Included in Southy review
Baker MD, Fosarelli PD, Carpenter RO., Childhood fever: correlation of diagnosis with temperature response to acetaminophen., Pediatrics , 80, 315-318, 1987	Not relevant to question
Baker RC, Tiller T, Bausher JC, et al., Severity of disease correlated with fever reduction in febrile infants., Pediatrics , 83, 1016-1019, 1989	Not relevant to question

Bertin,L., Pons,G., d'Athis,P., Duhamel,J.F., Maudelonde,C., Lasfargues,G., Guillot,M., Marsac,A., Debregeas,B., Olive,G., A randomized, double-blind, multicentre controlled trial of ibuprofen versus acetaminophen and placebo for symptoms of acute otitis media in children, <i>Fundamental and Clinical Pharmacology</i> , 10, 387-392, 1996	Main focus is not fever. Outcomes of interest not reported in usable format. Only useful for adverse events and already included in Pierce and Southey systematic reviews.
Brown,R.D., Wilson,J.T., Kearns,G.L., Eichler,V.F., Johnson,V.A., Bertrand,K.M., Single-dose pharmacokinetics of ibuprofen and acetaminophen in febrile children, <i>Journal of Clinical Pharmacology</i> , 32, 231-241, 1992	No outcomes of interest reported
Carley,S., Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Paracetamol or ibuprofen in febrile children. [15 refs], <i>Journal of Accident and Emergency Medicine</i> , 16, 137-139, 1999	Short report review
Catti,A., Monti,T., Treatment of infants with acute upper respiratory tract inflammation. A double-blind comparison between nimesulide and paracetamol suppositories, <i>Clinical Trials Journal</i> , 27, 327-335, 1990	Nimesulide not licenced in the UK
Celebi,S., Hacimustafaoglu,M., Aygun,D., Arisoy,E.S., Karali,Y., Akgoz,S., Citak Kurt,A.N., Seringec,M., Antipyretic effect of ketoprofen, <i>Indian Journal of Pediatrics</i> , 76, 287-291, 2009	Ketoprofen not licenced in UK
Del Vecchio,M.T., Sundel,E.R., Alternating antipyretics: is this an alternative?, <i>Pediatrics</i> , 108, 1236-1237, 2001	Letter to editor
Duhamel,J.F., Le,Gall E., Dalphin,M.L., Payen-Champenois,C., Antipyretic efficacy and safety of a single intravenous administration of 15 mg/kg paracetamol versus 30 mg/kg propacetamol in children with acute fever due to infection, <i>International Journal of Clinical Pharmacology and Therapeutics</i> , 45, 221-229, 2007	Compares types of paracetamol
Gianiorio,P., Zappa,R., Sacco,O., Fregonese,B., Scaricabarozzi,I., Rossi,G.A., Antipyretic and anti-inflammatory efficacy of nimesulide vs paracetamol in the symptomatic treatment of acute respiratory infections in children, <i>Drugs</i> , 46 Suppl 1, 204-207, 1993	Nimesilude not used in UK
Goldstein,L.H., Berlin,M., Berkovitch,M., Kozer,E., Effectiveness of oral vs rectal acetaminophen: a meta-analysis, <i>Archives of Pediatrics and Adolescent Medicine</i> , 162, 1042-1046, 2008	Route of administration
Goyal,P.K., Chandra,J., Unnikrishnan,G., Kumari,S., Passah,S.M., Double blind randomized comparative evaluation of nimesulide and paracetamol as antipyretics, <i>Indian Pediatrics</i> , 35, 519-522, 1998	Nimesulide not licenced in the UK
Hay,A.D., Costelloe,C., Redmond,N.M., Montgomery,A.A., Fletcher,M., Hollinghurst,S., Peters,T.J., Paracetamol plus ibuprofen for the treatment of fever in children (PITCH): randomised controlled trial.[Erratum appears in BMJ. 2009;339:b3295], <i>BMJ</i> , 337, a1302-, 2008	Summary of larger HTA report already included
Heubi,J.E., Barbacci,M.B., Zimmerman,H.J., Therapeutic misadventures with acetaminophen: hepatotoxicity after multiple doses in children.[see comment]. [44 refs], <i>Journal of Pediatrics,J.Pediatr.</i> , 132, 22-27, 1998	Case study reports.
Hopchet,L., Kulo,A., Rayyan,M., Verbesselt,R., Vanhole,C., de Hoon,J.N., Allegaert,K., Does intravenous paracetamol administration affect body temperature in neonates?, <i>Archives of Disease in Childhood</i> , 96, 301-304, 2011	Only 6 infants with fever assessed.

Houry,D., Ernst,A., Weiss,S., Ledbetter,M., Ketorolac versus acetaminophen for treatment of acute fever in the emergency department, Southern Medical Journal, 92, 1171-1173, 1999	Ketoprofen not recommended in children
Joshi,Y.M., Sovani,V.B., Joshi,V.V., Navrange,J.R., Benakappa,D.G., Shivananda,P., Sankaranarayanan,V.S., Comparative evaluation of the antipyretic efficacy of ibuprofen and paracetamol, Indian Pediatrics, 27, 803-806, 1990	Not an RCT
Kanabar,D., Dale,S., Rawat,M., A review of ibuprofen and acetaminophen use in febrile children and the occurrence of asthma-related symptoms. [32 refs], Clinical Therapeutics, 29, 2716-2723, 2007	Safety not being examined
Karbasi,S.A., Modares-Mosadegh,M., Golestan,M., Comparison of antipyretic effectiveness of equal doses of rectal and oral acetaminophen in children, Jornal de Pediatria, 86, 228-232, 2010	Route of administration not being examined
Keinanen,S., Hietula,M., Simila,S., Kouvalainen,K., Antipyretic therapy. Comparison of rectal and oral paracetamol, European Journal of Clinical Pharmacology, 12, 77-80, 1977	Compares route of administration rather than treatments.
Khubchandani,R.P., Ghatikar,K.N., Keny,S., Usgaonkar,N.G., Choice of antipyretic in children, Journal of the Association of Physicians of India, 43, 614-616, 1995	Data cannot be extracted on comparisons of interest
Kidon,M.I., Kang,L.W., Chin,C.W., Hoon,L.S., Hugo,V.B., Nonsteroidal anti-inflammatory drug hypersensitivity in preschool children, Allergy, Asthma and Clinical Immunology, 3, 114-122, 2007	General literature review
Kokki,H., Ketoprofen pharmacokinetics, efficacy, and tolerability in pediatric patients, Paediatric Drugs, 12, 313-329, 2010	Ketoprofen not recommended in this age-group.
Kokki,H., Kokki,M., Ketoprofen versus paracetamol (acetaminophen) or ibuprofen in the management of fever: results of two randomized, double-blind, double-dummy, parallel-group, repeated-dose, multicentre, phase III studies in children, Clinical Drug Investigation, 30, 375-386, 2010	Ketoprofen not recommended in children
Lal,A., Gomber,S., Talukdar,B., Antipyretic effects of nimesulide, paracetamol and ibuprofen-paracetamol, Indian Journal of Pediatrics, Indian J. Pediatr., 67, 865-870, 2000	Focus of study was not comparison of interest. Data not reported in usable format.
Leroy,S., Marc,E., Bavoux,F., Treluyer,J.M., Gendrel,D., Breart,G., Pons,G., Chalumeau,M., Hospitalization for severe bacterial infections in children after exposure to NSAIDs: A prospective adverse drug reaction reporting study, Clinical Drug Investigation, 30, 179-185, 2010	Aim of study was unclear.
Lesko,S.M., Mitchell,A.A., An assessment of the safety of pediatric ibuprofen. A practitioner-based randomized clinical trial, JAMA, 273, 929-933, 1995	Included in Southy review
Mackowiak,P.A., Diagnostic implications and clinical consequences of antipyretic therapy, Clinical Infectious Diseases, 31, S230-S233, 2000	Not relevant to question
Magni,A.M., Scheffer,D.K., Bruniera,P., Antipyretic effect of ibuprofen and dipyron in febrile children, Jornal de Pediatria, 87, 36-42, 2011	Dipyron not used in UK
Maron,J.J., Ickes,A.C., The antipyretic effectiveness of acetaminophen suppositories versus tablets: a double-blind study, Current Therapeutic Research, Clinical and Experimental, 20, 45-52, 1976	Study examined route of administration.
Marriott,S.C., Stephenson,T.J., Hull,D., Pownall,R., Smith,C.M., Butler,A., A dose ranging study of ibuprofen suspension as an antipyretic, Archives of Disease in Childhood, 66, 1037-1041, 1991	No comparison with placebo or paracetamol

Mayoral,C.E., Marino,R.V., Rosenfeld,W., Greensher,J., Alternating antipyretics: is this an alternative?, <i>Pediatrics</i> , 105, 1009-1012, 2000	Survey of clinicians not an intervention study.
Mazur LJ, Jones TM, Kozinetz CA., Temperature response to acetaminophen and risk of occult bacteremia: a case-control study., <i>J Pediatr</i> , 115, 888-91, 1989	Not relevant to question
Meremikwu,Martin M., Oyolita,Angela, Paracetamol versus placebo or physical methods for treating fever in children, <i>Cochrane Database of Systematic Reviews</i> , -, 2010	Has not been edited since 2004. Individual studies will be included in the review.
Nabulsi,M., Is combining or alternating antipyretic therapy more beneficial than monotherapy for febrile children?, <i>BMJ</i> , 340, 92-93, 2010	Comment and literature review
Nabulsi,M., Tamim,H., Sabra,R., Mahfoud,Z., Malaeb,S., Fakih,H., Mikati,M., Equal antipyretic effectiveness of oral and rectal acetaminophen: a randomized controlled trial [ISRCTN11886401], <i>BMC Pediatrics</i> , 5, 35-, 2005	Examines the route of administration
Offringa,M., Newton,R., Prophylactic drug management for febrile convulsions in children, <i>Cochrane Database of Systematic Reviews</i> , -, 2007	Does not address the study question
Pardo,J., Daza,R., Chumbes,O., Loayza,I., Huicho,L., Antipyretic efficacy and tolerability of oral ibuprofen, oral dipyron and intramuscular dipyron in children: A randomized controlled trial, <i>Sao Paulo Medical Journal</i> , 124, 135-140, 2006	Dipyron not used in UK
Perrott,D.A., Piira,T., Goodenough,B., Champion,G.D., Efficacy and safety of acetaminophen vs ibuprofen for treating children's pain or fever: A Meta-analysis, <i>Archives of Pediatrics and Adolescent Medicine</i> , 158, 521-526, 2004	Meta-analysis included in 2007 guideline. Individual studies included in 2012 guideline.
Polidori,G., Titti,G., Pieragostini,P., Comito,A., Scaricabarozzi,I., A comparison of nimesulide and paracetamol in the treatment of fever due to inflammatory diseases of the upper respiratory tract in children, <i>Drugs</i> , 46 Suppl 1, 231-233, 1993	Nimesulide banned in UK
Purssell,E., Treating fever in children: paracetamol or ibuprofen?, <i>British Journal of Community Nursing</i> , Br J Community Nurs, 7, 316-320, 2002	Out of date. Individual studies will be included in meta-analysis.
Scolnik,D., Kozer,E., Jacobson,S., Diamond,S., Young,N.L., Comparison of oral versus normal and high-dose rectal acetaminophen in the treatment of febrile children, <i>Pediatrics</i> , 110, 553-556, 2002	Examined route of administration, not comparison of treatments
Sheth,U.K., Gupta,K., Paul,T., Pispati,P.K., Measurement of antipyretic activity of ibuprofen and paracetamol in children, <i>Journal of Clinical Pharmacology</i> , 20, 672-675, 1980	Figures not presented in a format that could be used in analysis
Simila,S., Kouvalainen,K., Keinanen,S., Oral antipyretic therapy, <i>Scandinavian Journal of Rheumatology</i> , 5, 81-83, 1976	Not an RCT - no evidence of randomisation
Strengell,T., Uhari,M., Tarkka,R., Uusimaa,J., Alen,R., Lautala,P., Rantala,H., Antipyretic agents for preventing recurrences of febrile seizures: randomized controlled trial, <i>Archives of Pediatrics and Adolescent Medicine</i> , 163, 799-804, 2009	Diclofenac used in all groups, so cannot isolate effect of other treatments.
Torrey SB, Henretig F, Fleisher G, et al., Temperature response to antipyretic therapy in children: relationship to occult bacteremia., <i>Am J Emerg Med</i> , 3, 190-2, 1985	Not relevant to question
Ugazio,A.G., Guarnaccia,S., Berardi,M., Renzetti,I., Clinical and pharmacokinetic study of nimesulide in children, <i>Drugs</i> , 46 Suppl 1, 215-218, 1993	Nimesulide not used in UK

utret-Leca,E., souda-Grimaldi,L., Maurage,C., Jonville-Bera,A.P., Upper gastrointestinal complications associated with NSAIDs in children, Therapie, 62, 173-176, 2007	Case reports
Vernon,S., Bacon,C., Weightman,D., Rectal paracetamol in small children with fever, Archives of Disease in Childhood, 54, 469-470, 1979	Examines the route of administration
Walson,P.D., Jones,J., Chesney,R., Rodarte,A., Antipyretic efficacy and tolerability of a single intravenous dose of the acetaminophen prodrug propacetamol in children: a randomized, double-blind, placebo-controlled trial, Clinical Therapeutics, 28, 762-769, 2006	Compares types of paracetamol
Weisse,M.E., Miller,G., Brien,J.H., Fever response to acetaminophen in viral vs. bacterial infections, Pediatric Infectious Disease Journal, 6, 1091-1094, 1987	Not relevant to question
Wilson,J.T., Helms,R., Pickering,B.D., Donahue,L., Brown,R.D., Acetaminophen controlled-release sprinkles versus acetaminophen immediate-release elixir in febrile children, Journal of Clinical Pharmacology, 40, 360-369, 2000	Examines the route of administration
Yaffe,S.J., Comparative efficacy of aspirin and acetaminophen in the reduction of fever in children, Archives of Internal Medicine, 141, 286-292, 1981	Non-systematic literature review.
Yamamoto LT, Wigder HN, Fligner DJ, et al., Relationship of bacteremia to antipyretic therapy in febrile children, Pediatr Emerg Care, 3, 223-227, 1987	Not relevant to question
Yoon,J.S., Jeong,D.C., Oh,J.W., Lee,K.Y., Lee,H.S., Koh,Y.Y., Kim,J.T., Kang,J.H., Lee,J.S., The effects and safety of dexibuprofen compared with ibuprofen in febrile children caused by upper respiratory tract infection, British Journal of Clinical Pharmacology, 66, 854-860, 2008	Dexipirofen not used in UK

Appendix H Evidence tables

The evidence tables are presented in a separate file

Appendix I GRADE profiles

These are the complete GRADE profiles which accompany the abbreviated versions in the full guideline. These include details of the quality assessment and additional footnoted information which accompanies the main findings. The GRADE findings (evidence profiles) are presented with the same table numbers as the abbreviated tables in the main text of the full guideline to assist cross-referencing.

Chapter 5

Review question

What is the value (as shown by likelihood ratios, sensitivity, specificity, positive predictive value and negative predictive value) of the following symptoms and signs, alone or in combination, as initial indications of serious illness?

- abnormal skin or mucosal colour (for example, pallor or cyanosis)
- appearing ill to a healthcare professional or parent/carer
- altered responsiveness or cry
- altered breathing (for example, nasal flaring, grunting, chest indrawing)
- abnormal respiratory rate, pulmonary (lung) crackles and othersounds
- oxygen desaturation
- dehydration
- prolonged capillary refill time, cold hands and feet
- poor feeding
- persistent fever (5 days or more)
- height of fever
- limb or joint swelling
- unwillingness to bear weight or use a limb

- bulging fontanelle
- rash (blanching or non-blanching)
- focal neurological signs
- focal seizures
- new lumps
- neck stiffness
- vomiting
- status epilepticus (prolonged or continuous fits).

Table I5.3 GRADE profile for evaluation of colour

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Colour (cyanotic or pale or flushed/mottled)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	36 (20 to 53) ^a	40 (31 to 49) ^a	16 (8 to 24) ^a	67 (55 to 78) ^a	0.6 (0.4 to 1.0) ^a	1.6 (1.1 to 2.3) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	9 (5 to 14) ^a	92 (90 to 93) ^a	11 (6 to 16) ^a	90 (89 to 92) ^a	1.1 (0.7 to 1.8) ^a	1.0 (0.9 to 1.0) ^a	Low	Prospective	Very serious ^{b, f}	NA	No serious	No serious	Yes ^{d, g}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether all children received the same test to confirm serious infection^c Some results were uninterpretable, indeterminable or intermediate test results^d Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

^e Included children were aged 2 weeks to 1 year old. Children were included if they had a rectal temperature greater than or equal to 38°C. The study was conducted in a paediatric emergency ward of a hospital in the Netherlands. Children were self-referred or referred by a GP.

^f The study authors report that not all eligible infants were enrolled

^g Included children were less than 3 months old. Infants were included if they had auxiliary, rectal or tympanic temperatures equal to or greater than 38°C in the office or in the previous 24 hours at home. The study was based in a GP's office in the USA.

Table I5.4 GRADE profile for evaluation of social cues

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Decreased social interaction														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	24 (17 to 30) ^a	74 (71 to 76) ^a	9 (6 to 11) ^a	90 (88 to 92) ^a	0.9 (0.7 to 1.2) ^a	1.0 (0.9 to 1.1) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b The study authors report that not all eligible infants were enrolled

^c It is not clear whether all participants received the same test to confirm serious illness

^d Included children were less than 3 months old. Included infants had auxiliary, rectal or tympanic temperatures equal to or greater than 38°C in the office or in the previous 24 hours at home. The study was based in a GP's office in the USA.

^e Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

Table I5.5 GRADE profile for evaluation of 'appears ill to a healthcare professional'

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
At least mildly unwell (includes mildly unwell, moderately unwell, and very unwell)														
<i>For detecting urinary tract infection, pneumonia or bacteraemia</i>														
1 (Craig, 2010)	12807	74 (72 to 77) ^a	42 (41 to 43) ^a	9 (9 to 10) ^a	95 (95 to 96) ^a	1.3 (1.2 to 1.3) ^a	0.6 (0.5 to 0.7) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g, h}
At least moderately ill or moderately unwell (includes moderately ill/unwell and very ill/unwell)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	58 (41 to 74) ^a	70 (61 to 78) ^a	37 (24 to 51) ^a	84 (76 to 92) ^a	1.9 (1.3 to 2.9) ^a	0.6 (0.4 to 0.9) ^a	Low	Prospective	Very serious ^{c, i}	NA	No serious	No serious	Yes ^{f, j}
<i>For detecting urinary tract infection, pneumonia or bacteraemia</i>														
1 (Craig, 2010)	12807	22 (20 to 25) ^a	92 (91 to 92) ^a	17 (15 to 19) ^a	94 (93 to 94) ^a	2.7 (2.4 to 3.0) ^a	0.8 (0.8 to 0.9) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g, h}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	38 (30 to 45) ^a	65 (62 to 67) ^a	10 (8 to 13) ^a	91 (89 to 92) ^a	1.1 (0.9 to 1.3) ^a	1.0 (0.8 to 1.1) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^e
<i>For detecting occult infections</i>														
1 (Pantell, 2004)	3066	NC	NC	NC	NC	NC	NC	Low	Prospective	Very serious ^{c, k, l}	NA	No serious	NA	Yes ^{f, h, m, n}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Not well-appearing														
<i>For detecting serious bacterial infection</i>														
1 (Gomez, 2010)	1018	26 (8 to 44) ^a	96 (95 to 97) ^a	13 (3 to 22) ^a	98 (97 to 99) ^a	6.2 (2.9 to 13.1) ^a	0.8 (0.6 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, o}	NA	No serious	No serious	Yes ^{h, p, q}
Appears unwell														
<i>For detecting serious bacterial infection</i>														
1 (Nijman, 2012)	1255	1 (0 to 4) ^a	97 (96 to 98) ^a	6 (0 to 15) ^a	89 (88 to 91) ^a	0.6 (0.1 to 2.5) ^a	1.0 (1.0 to 1.0) ^a	Very low	Prospective	Very serious ^{c, d, o, l}	NA	Serious ^r	No serious	Yes ^{h, s}
Poor appearance														
<i>For detecting serious bacterial infection</i>														
1 (Chen, 2009)	135	35 (19 to 51) ^a	82 (75 to 90) ^a	40 (22 to 58) ^a	79 (71 to 87) ^a	2.0 (1.1 to 3.6) ^a	0.8 (0.6 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, o, l}	NA	No serious	No serious	Yes ^{h, t}
Ill appearance														
<i>For detecting serious illness</i>														
1 (McCarthy, 1985)	103	54 (35 to 73) ^a	90 (83 to 96) ^a	64 (44 to 84) ^a	85 (77 to 93) ^a	5.2 (2.5 to 10.9) ^a	0.5 (0.3 to 0.8) ^a	Very low	Prospective	Very serious ^{b, c, l}	NA	No serious	Serious ^u	Yes ^{h, v}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting invasive bacterial disease</i>														
1 (Baker, 1989)	190	47 (21 to 72) ^a	90 (80 to 99) ^a	64 (35 to 92) ^a	81 (70 to 93) ^a	4.6 (1.6 to 13.3) ^a	0.6 (0.4 to 1.0) ^a	Very low	Prospective	Very serious ^{l, o}	NA	Serious ^w	Serious ^u	Yes ^{f, h, x}
<i>For detecting serious invasive bacteraemia</i>														
1 (Mandl, 1997)	411	100 (60 to 100)	88 (86 to 91)	11 (1 to 23)	100 (97 to 100)	8.6 (6.6 to 11.2) ^a	NC	Very low	Prospective and retrospective	Very serious ^{b, l, o, y}	NA	Serious ^z	Serious ^u	Yes ^{f, h, aa, ab}
<i>For detecting serious bacterial infection</i>														
1 (Schwartz, 2009)	449	21 (12 to 29) ^a	90 (87 to 93) ^a	33 (20 to 45) ^a	82 (79 to 86) ^a	2.0 (1.2 to 3.4) ^a	0.9 (0.8 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, l, o}	NA	No serious	No serious	Yes ^{h, ac}
1 (Shin, 2009)	221	37 (22 to 51) ^a	69 (62 to 76) ^a	22 (12 to 32) ^a	82 (76 to 88) ^a	1.2 (0.7 to 1.9) ^a	0.9 (0.7 to 1.2) ^a	Low	Prospective	Very serious ^{d, l, o}	NA	No serious	No serious	Yes ^{h, ad}
<i>For detecting urinary tract infection</i>														
1 (Shaw, 1998)	2411	49 (38 to 60) ^a	72 (71 to 74) ^a	6 (4 to 7) ^a	98 (97 to 98) ^a	1.8 (1.4 to 2.2) ^a	0.7 (0.6 to 0.9) ^a	Low	Prospective	Very serious ^{f, l}	NA	No serious	No serious	Yes ^{h, ae}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Very ill or very unwell appearance														
<i>For detecting urinary tract infection, pneumonia or bacteraemia</i>														
1 (Craig, 2010)	12807	3 (2 to 3) ^a	100 (100 to 100) ^a	45 (33 to 58) ^a	93 (93 to 93) ^a	10.6 (6.5 to 17.3) ^a	1.0 (1.0 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g, h}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	4 (1 to 7) ^a	97 (97 to 98) ^a	14 (4 to 24) ^a	90 (89 to 92) ^a	1.5 (0.6 to 3.4) ^a	13.6 (3.5 to 23.8) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^e
<i>For detecting occult infections</i>														
1 (Pantell (2004)	3066	NC	NC	NC	NC	NC	NC	Low	Prospective	Very serious ^{c, k, l}	NA	No serious	NA	Yes ^{f, h, m, af}
Severely ill														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	33 (17 to 49) ^a	90 (85 to 96) ^a	52 (31 to 73) ^a	81 (74 to 88) ^a	3.5 (1.6 to 7.5) ^a	0.7 (0.6 to 0.9) ^a	Low	Prospective	Very serious ^{c, i}	NA	No serious	No serious	Yes ^{f, j}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Toxicity														
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	33 (7 to 60) ^a	97 (94 to 99) ^a	33 (7 to 60) ^a	97 (94 to 99) ^a	10.1 (3.5 to 28.8) ^a	0.7 (0.5 to 1.0) ^a	Very low	Prospective	Very serious ^{d, l, ag}	NA	No serious	Serious ^{ah}	Yes ^{f, h, aa, ai}
Suspicious physical findings														
<i>For detecting meningitis</i>														
1 (Joffe, 1983)	241	23 (16 to 30) ^a	97 (94 to 100) ^a	91 (81 to 100) ^a	52 (45 to 59) ^a	8.5 (2.7 to 27.2) ^a	0.8 (0.7 to 0.9) ^a	Very low	Retrospective	Very serious ^{b, c, o, l, aj}	NA	Serious ^{ak}	No serious	Yes ^{h, aa, al}

NA Not applicable

NC Not calculable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^c It is not clear whether all children received the same test to confirm serious infection

^d It is not clear whether the test to confirm serious infection was independent of the signs and symptoms

^e Included children were less than 5 years old. Included children had a measured axillary temperature of greater than or equal to 38°C; parental report of a temperature of greater than or equal to 38°C measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. The study was undertaken in a hospital in Australia.

^f Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

^g Results are reported per illness rather than per child – some children were included more than once for different illnesses

^h It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

ⁱ Some results were uninterpretable, indeterminable or intermediate test results

^j Included children were between 2 weeks and 1 year old. Included children had a rectal temperature equal to or greater than 38°C. This study took place in a paediatric emergency ward of a hospital in the Netherlands. Children were self referred or referred by a GP.

- ^k It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected
- ^l It is unclear whether the results of the test used to confirm serious illness were interpreted without knowledge of the signs or symptoms
- ^m Included children were 3 months old or younger. Included children had a temperature of 38°C or greater either at home or in the clinician's office. Undertaken in a GP's office in the USA.
- ⁿ Results reported in the paper: adjusted OR 1.79 (0.95 to 3.38), $P = 0.07$. Data on diagnostic accuracy or that would allow diagnostic accuracy data to be calculated was not reported in the study.
- ^o It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection
- ^p Included children aged less than 90 days. Included temperatures greater or equal to 38°C at home or at presentation. Undertaken in a paediatric emergency department in Spain.
- ^q Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated
- ^r Included children up to 16 years old (83% of children were 5 years and under)
- ^s Included children aged 1 month to 16 years. Included children with a temperature of 38.5°C or higher, recent high fever, or fever as a reason for referral. Undertaken in the emergency department of a children's hospital in the Netherlands.
- ^t Included children aged under 3 months. Included children had a rectal temperature of 38°C or higher. The study was undertaken in a hospital in Taiwan.
- ^u The difference between the lower and upper confidence intervals is 40% or greater for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value
- ^v Included children aged 24 months and younger. Included children had a temperature of 38.3°C or higher. The study was undertaken in an emergency room in the USA.
- ^w Included children were aged 3 months to 15 years (54% of children were younger than 2 years)
- ^x Included children aged 3 months to 15 years. Included children with a presence or history of fever greater than 38°C. It took place in a hospital medical centre in the USA
- ^y Is it not clearly reported how many children were enrolled retrospectively and how many were enrolled prospectively into the study
- ^z Included children up to and including 18 years of age (58% of children were aged between 3 and 36 months)
- ^{aa} It was unclear whether the period between the reference test and the signs and symptoms being recorded was short enough to be reasonably sure that the illness did not resolve before the reference test was undertaken
- ^{ab} Included children up to 18 years of age. Included children with a temperature equal to or greater than 38°C. It was undertaken in a hospital setting in the USA.
- ^{ac} Included children were neonates (not defined). Included children with a rectal temperature of 38°C or higher. Undertaken in a paediatric emergency room in Israel.
- ^{ad} Included children were under 3 months old. Included children had an axillary temperature of 38°C or higher. The study was undertaken in a hospital in South Korea.
- ^{ae} Included boys younger than 1 year and girls younger than 2 years. Included children with a temperature equal to or greater than 38.3°C. It took place in the emergency department in the USA.
- ^{af} Results reported in the paper: adjusted OR 8.90 (3.34 to 23.69), $P < 0.001$. Data on diagnostic accuracy or that would allow diagnostic accuracy data to be calculated was not reported in the study.
- ^{ag} The selection criteria for the children included in the study were not clearly described
- ^{ah} The difference between the upper and lower confidence intervals is 40% or greater for one, two or three of sensitivity, specificity, positive predictive value or negative predictive value
- ^{ai} Included children 6 months to 5 years. Fever was not defined. The study was undertaken in the paediatric ward of a hospital in Iran.
- ^{aj} It is unclear whether the spectrum of children included in the study was representative of those who would be seen in practice
- ^{ak} Included children up to the age of 6 years
- ^{al} Included children between 6 months and 6 years. Fever was not defined. The study was undertaken in two hospitals in the USA.

Table I5.6 GRADE profile for evaluation of awake

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Drowsy on history or examination														
<i>For detecting serious illness</i>														
1 (Hewson, 2000)	313	51 (40 to 61) ^a	84 (79 to 89) ^a	55 (44 to 66) ^a	82 (77 to 87) ^a	3.2 (2.2 to 4.6) ^b	0.6 (0.5 to 0.7) ^b	Low	Prospective	Very serious ^{c, d, e}	NA	No serious ^s	No serious ^s	Yes ^{f, g, h}
Increased sleepiness														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	34 (26 to 41) ^b	74 (71 to 76) ^b	12 (9 to 15) ^b	91 (90 to 93) ^b	1.3 (1.0 to 1.6) ^b	0.9 (0.8 to 1.0) ^b	Low	Prospective	Very serious ⁱ	NA	No serious	No serious ^s	Yes ^{g, j, k}
Drowsiness														
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	25 (1 to 50) ^b	100 (100 to 100) ^b	100 (100 to 100) ^b	96 (94 to 99) ^b	NC ^b	0.8 (0.5 to 1.0) ^b	Very low	Prospective	Very serious ^{e, l}	NA	No serious	Serious ^m	Yes ^{g, h, n}
1 (Oftringa, 1992)	92	25 (1 to 50) ^b	74 (64 to 84) ^b	14 (0 to 29) ^b	85 (76 to 94) ^b	1.0 (0.3 to 2.8) ^b	1.0 (0.7 to 1.4) ^b	Very low	Retrospective	Very serious ^{c, d, e, i, l, o}	NA	Serious ^p	Serious ^m	Yes ^{g, h, q}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Drowsiness at home														
<i>For detecting meningitis</i>														
1 (Offringa, 1992)	92	30 (12 to 49) ^b	94 (89 to 100) ^b	64 (35 to 92) ^b	80 (72 to 89) ^b	5.3 (1.7 to 16.3) ^b	0.7 (0.6 to 1.0) ^b	Very low	Retrospective	Very serious ^{c, d, e, j, l, o,}	NA	Serious ^p	Serious ^m	Yes ^{g, h, q}
Postictal drowsiness														
<i>For detecting meningitis</i>														
1 (Batra, 2011)	199	60 (17 to 100) ^b	96 (93 to 99) ^b	27 (1 to 54) ^b	99 (97 to 100) ^b	14.6 (5.4 to 39.0) ^b	0.4 (0.1 to 1.2) ^b	Very low	Retrospective	Very serious ^{c, d, e, j, l}	NA	Serious	Serious ^m	Yes ^{g, h, r, s}

NA Not applicable

^a Confidence intervals calculated by the NCC-WCH based on results reported in the study

^b Calculated by the NCC-WCH based on results reported in the study

^c Not all of the children received the same test to confirm serious illness

^d It is not clear if the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious infection

^e It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms

^f Fever was not defined. Included children aged 1 to 26 weeks. This study took place in an emergency department in Australia.

^g Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

^h It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

ⁱ It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^j The study authors report that not all eligible infants were enrolled

^k Included axillary, rectal or tympanic temperature of 38°C or greater at presentation or 24 hours previously. Included children aged 3 months or younger. Study was undertaken at GP's offices in Australia.

^l It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

^m The confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%

ⁿ Fever was not defined. Included children aged 6 months to 5 years. Study undertaken in the paediatric ward of a hospital in Iran

^o It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^p Included children aged from 3 months to 6 years

^q Fever was not defined. Included children aged 3 months to 6 years. Study was undertaken in the emergency room of a hospital Netherlands

^r Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated

^s Fever was not defined. Included children aged 6 to 18 months. Study undertaken in a paediatric casualty ward in India

Table I5.7 GRADE profile for evaluation of decreased activity

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Decreased activity														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	17 (12 to 23) ^a	82 (80 to 84) ^a	9 (6 to 12) ^a	90 (89 to 92) ^a	0.9 (0.7 to 1.3) ^a	1.0 (0.9 to 1.1) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}
Decreased activity level during examination														
<i>For detecting bacteraemia</i>														
1 (Crain, 1982)	175	NC	NC	NC	NC	NC	NC	Modest	Prospective	Serious ^f	NA	No serious	NA	Yes ^{e, g}
Looking around the room (moderately impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	21 (7 to 35) ^a	69 (60 to 78) ^a	18 (6 to 30) ^a	73 (64 to 82) ^a	0.7 (0.3 to 1.4) ^a	1.1 (0.9 to 1.4) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Looking around the room (severely impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	30 (15 to 46) ^a	92 (87 to 97) ^a	56 (33 to 79) ^a	81 (73 to 88) ^a	3.9 (1.7 to 9.0) ^a	0.8 (0.6 to 1.0) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}
Moving arms and legs spontaneously (moderately impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	27 (12 to 42) ^a	78 (70 to 86) ^a	28 (13 to 44) ^a	77 (69 to 85) ^a	1.2 (0.6 to 2.4) ^a	0.9 (0.7 to 1.2) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}
Moving arms and legs spontaneously (severely impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	24 (10 to 39) ^a	96 (93 to 100) ^a	67 (40 to 93) ^a	80 (73 to 87) ^a	6.4 (2.0 to 19.8) ^a	0.8 (0.6 to 1.0) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}
Reaching for objects (moderately impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	15 (3 to 27) ^a	77 (69 to 85) ^a	17 (3 to 31) ^a	74 (66 to 83) ^a	0.7 (0.3 to 1.6) ^a	1.1 (0.9 to 1.3) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Reaching for objects (severely impaired)														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	30 (15 to 46) ^a	90 (85 to 96) ^a	50 (28 to 72) ^a	81 (73 to 88) ^a	3.2 (1.5 to 7.0) ^a	0.8 (0.6 to 1.0) ^a	Low	Prospective	Very serious ^{f, h}	NA	No serious	No serious	Yes ^{e, i}
Lethargy														
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	17 (6 to 29) ^a	72 (65 to 79) ^a	13 (4 to 22) ^a	78 (72 to 85) ^a	0.6 (0.3 to 1.2) ^a	1.2 (1.0 to 1.4) ^a	Low	Prospective	Very serious ^{j, k, l}	NA	No serious	No serious	Yes ^{m, n}
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	42 (14 to 70) ^a	95 (92 to 97) ^a	28 (7 to 48) ^a	97 (95 to 99) ^a	7.8 (3.3 to 18.2) ^a	0.6 (0.4 to 1.0) ^a	Very low	Prospective	Very serious ^{j, o}	NA	No serious	Serious ^p	Yes ^{e, m, q}
<i>For detecting bacteraemia</i>														
1 (Crocker, 1985)	201	14 (1 to 27) ^a	78 (72 to 84) ^a	10 (1 to 18) ^a	85 (79 to 90) ^a	0.7 (0.3 to 1.7) ^a	1.1 (0.9 to 1.3) ^a	Low	Prospective	Very serious ^{f, k}	NA	No serious	No serious	Yes ^{e, j, p, r}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b The authors report that not all eligible infants were enrolled in the study^c It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection^d Included children aged 3 months or younger. Included axillary, rectal or tympanic temperature of 38°C or greater at presentation or 24 hours previously. Study was undertaken at GP's offices in Australia.^e Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

^f It is not clear whether all children received the same test to confirm serious infection

^g Included children 8 weeks old and younger. Included temperatures of 38°C and greater. The study was undertaken in a paediatric emergency room in the USA.

^h Some results were uninterpretable, indeterminable or intermediate test results

ⁱ Included children aged 2 week to 1 year old. Included temperatures of 38°C or greater. Undertaken in a paediatric emergency ward of a hospital in the Netherlands. Self referred or referred by general practitioner.

^j It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms

^k It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection

^l It is unclear whether the test to confirm serious illness is independent of the child's symptoms and signs

^m It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

ⁿ Included children aged less than 3 months. Included axillary temperature of 38°C or higher. Undertaken in outpatients clinic in South Korea.

^o It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

^p The confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%

^q Included children aged 6 months to 5 years. Fever not defined. Undertaken in a paediatric ward of a hospital in Iran.

^r Included children aged 6 months to 2 years. Included temperature of 39.4°C and higher. Undertaken in an emergency department of a hospital in the USA.

Table I5.8 GRADE profile for evaluation of no smile and/or abnormal cry

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Cry														
<i>For detecting serious bacterial infection</i>														
1 (Craig, 2010)	15781	43 (40 to 45) ^a	68 (67 to 68) ^a	9 (9 to 10) ^a	94 (93 to 94) ^a	1.3 (1.2 to 1.4) ^a	0.9 (0.8 to 0.9) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e, f}
<i>For detecting bacteraemia</i>														
1 (Crain, 1982)	175	NR ^k	NR ^k	NR ^k	NR ^k	NR ^k	NR ^k	Low	Prospective	Very serious ^{g, h}	NA	No serious	NA	Yes ^{d, e, i}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Abnormal cry														
<i>For detecting bacteraemia</i>														
1 (Pantell, 2004)	3066	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	Low	Prospective	Very serious ^{b, c, g, h}	NA	No serious	NA	Yes ^{d, e, j}

NA Not applicable

NR Not reported

^a Calculated by the NCC-WCH based on results reported in the study

^b Not all of the children were tested for the presence of a serious illness

^c Not all of the children received the same test to confirm serious illness

^d It was unclear whether the period between noting the child's signs and symptoms and the tests to confirm serious illness was short enough to be reasonably sure that the illness did not change or resolve

^e It is unclear whether the same data was available when the test results were interpreted would be available when the test is used in practice

^f Included children were under 5 years. Children were included if they had an axillary temperature/parental report of a temperature $\geq 38^{\circ}\text{C}$. The study was conducted in the emergency department of a hospital in Australia. Results are reported per illness rather than per child – some children were included more than once for different illnesses.

^g Selection criteria for inclusion into the study were not clearly described

^h It is unclear whether the results of the test to confirm serious illness was undertaken without knowledge of the child's signs and symptoms

ⁱ Included children were 8 weeks old or younger. Included temperatures were a rectal temperature of 38°C or greater. Undertaken in a paediatric emergency room of a hospital in USA.

^j Included children were 3 months old or younger. Included temperatures were 38°C or greater at home or in the clinician's office. Undertaken in GP's office in the USA.

^k Text in the study paper stated that crying is not significantly associated with bacteraemia

^l Adjusted OR 2.23 (95% CI 1.16 to 4.29), $P < 0.02$

Table I5.9 GRADE profile for evaluation of irritability

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Irritability														
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	34 (20 to 49) ^a	63 (56 to 70) ^a	18 (10 to 27) ^a	80 (73 to 87) ^a	0.9 (0.6 to 1.5) ^a	1.0 (0.8 to 1.3) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}
<i>For detecting bacteraemia</i>														
1 (Crain, 1982)	175	NR ^g	NR ^g	NR ^g	NR ^g	NR ^g	NR ^g	Low	Prospective	Very serious ^{a, b}	NA	No serious	NA	Yes ^{e, h, i}
1 (Crocker, 1985)	201	64 (47 to 82) ^j	55 (48 to 62) ^j	19 (11 to 27) ^j	91 (85 to 96) ^j	1.4 (1.0 to 2.0) ^j	0.7 (0.4 to 1.1) ^j	Low	Prospective	Very serious ^{c, k, l}	NA	No serious	No serious	Yes ^{e, h, m}
<i>For detecting urinary tract infection</i>														
1 (Morris, 2007)	98	NR ⁿ	NR ⁿ	NR ⁿ	NR ⁿ	NR ⁿ	NR ⁿ	Low	Prospective	Very serious ^{a, d, k}	NA	No serious	NA	Yes ^{e, h, o, p}
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	58 (30 to 86) ^j	86 (82 to 90) ^j	17 (6 to 29) ^j	98 (96 to 100) ^j	4.2 (2.3 to 7.3) ^j	0.5 (0.2 to 0.9) ^j	Low	Prospective	Very serious ^{a, c, l}	NA	No serious	Serious ^q	Yes ^{e, h, o, r}
<i>For detecting viral meningitis or non-specific meningitis</i>														
1 (Gomez, 2012)	309	24 (15 to 32) ^j	78 (72 to 84) ^j	34 (23 to 45) ^j	68 (62 to 74) ^j	1.1 (0.7 to 1.7) ^j	1.0 (0.9 to 1.1) ^j		Retrospective	Very serious ^{b, c, d, k}	NA	No serious	No serious	Yes ^{e, s}

^a The selection criteria for including children in the study were not clearly described

^b It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's signs and symptoms

^c It is not clear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness

^d It is not clear whether the test to confirm serious illness was independent of the child's signs and symptoms

^e It is not clear whether the same clinical data were available as would be available in practice

^f Included children aged less than 3 months. Included those with an axillary temperature of 38°C or higher. Undertaken in an outpatients clinic in South Korea.

^g Text in the paper stated that irritability is not significantly associated with bacteraemia

^h It is not clear if the period of time between assessing the child's signs and symptoms and performing the test to confirm serious illness is short enough

ⁱ Included children aged 8 weeks old and younger. Included children with rectal temperatures of 38°C and higher. The study was undertaken in a paediatric emergency room in the USA.

^j Calculated by the NCC-WCH based on results reported in the study

^k It is not clear whether all children received the same test to confirm serious illness

^l It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's signs and symptoms

^m Included children aged 6 months to 2 years. Included children with temperatures of 39.4°C and higher. Undertaken in an emergency department of a hospital in the USA.

ⁿ Text in the paper stated that irritability is not predictive of urinary tract infection

^o The sign or symptom was not described in enough detail to allow another clinician to make the same diagnosis

^p Included children less than 36 months. Included children with an axillary temperature greater than 37.2°C. The study was undertaken in the children's outpatients department in a hospital in Papua New Guinea.

^q The difference between the lower and upper confidence intervals is greater than 40% for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value

^r Included children aged 6 months to 5 years. Fever was not defined. The study was undertaken in the paediatric ward of a hospital in Iran.

^s Included children aged younger than 90 days. Included children with a temperature of 38.0°C or greater at home or upon arrival at the ED. Undertaken in a paediatric emergency department in Spain.

Table I5.10 GRADE profile for evaluation of decreased consciousness/coma

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Decreased consciousness														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2001)	231	3 (1 to 6) ^a	91 (84 to 99) ^a	55 (25 to 84) ^a	24 (18 to 30) ^a	0.4 (0.1 to 1.3) ^a	1.1 (1.0 to 1.1) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g}	NA	No serious ^h	Serious ^h	Yes ^{i, j}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Coma														
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	8 (0 to 24) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	96 (93 to 98) ^a	NC	0.9 (0.8 to 1.1) ^a	Mode rate	Prospective	Serious ^k	NA	No serious	No serious	Yes ^{i, l}
1 (Offringa, 1992)	92	26 (8 to 44) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	80 (72 to 89) ^a	NC	0.7 (0.6 to 0.9) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g, m}	NA	Serious ⁿ	No serious	Yes ^{i, o, p}
Unrousable coma														
<i>For detecting meningitis</i>														
1 (Akpede, 1992)	522	22 (5 to 40) ^a	94 (92 to 96) ^a	15 (3 to 27) ^a	97 (95 to 98) ^a	3.9 (1.7 to 9.1) ^a	0.8 (0.7 to 1.0) ^a	Low	Prospective	Serious ^{b, f, g}	NA	Serious ⁿ	No serious	Yes ^{i, q}

NA Not applicable

NC Not calculable

^a Calculated by the NCC-WCH based on data reported in the study^b It is unclear whether the children who were included in the study were representative of those that will receive the test in practice^c It is unclear whether the test used to confirm serious illness would classify the illness correctly^d It is unclear whether all of the children received the same test to confirm serious illness^e It is unclear whether the test to confirm serious illness was independent of the signs and symptoms^f It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness^g It is unclear whether the results of the test to confirm serious illness were interpreted without knowledge of the signs and symptoms^h The confidence intervals were 40% or greater for one, two or three of sensitivity, specificity, positive predictive value or negative predictive valueⁱ It is unclear whether the same clinical data were available when the test results were interpreted as would be available when the test is used in practice^j Included children aged 1 to 36 months. Fever was not defined. Undertaken at two children's hospitals in the Netherlands.^k The selection criteria were not clearly described

^l Included children were aged from 6 months to 5 years. Temperature was not used as an inclusion criterion, but children were those hospitalised after a fever associated seizure. Undertaken in the paediatric department of a hospital in Iran.

^m It is unclear whether the whole sample (or a random selection of the sample) received the test to confirm serious illness

ⁿ Children were included that were 6 years old

^o Not enough detail was reported on the test to confirm serious illness for it to be replicated by a different healthcare professional

^p Included children were 3 months to 6 years old. Temperature was not used as an inclusion criterion, but children had had a first episode of seizure associated with fever. Undertaken in the emergency room of two hospitals in the Netherlands.

^q Included children were 1 month to 6 years old. Included rectal temperatures of 38°C or higher. Children had had convulsions associated with fever and had a fever duration of less than 7 days. Undertaken in a paediatric emergency department in Nigeria.

Table I5.11 GRADE profile for evaluation of restlessness

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Restlessness														
<i>For detecting serious illness</i>														
1 (Nademi, 2001)	141	76 (62 to 88)	43 (33 to 52)	35 (25 to 45)	81 (70 to 91)	1.3 (1.0 to 1.7) ^a	0.6 (0.3 to 1.0) ^a	Very low	Prospective	Very serious ^{b, c, d, e}	NA	Serious ^f	No serious	Yes ^{g, h}

NA Not applicable

^a Calculated by the NCC based on data reported in the study

^b It is unclear whether all children received the same reference test

^c It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness

^d It is unclear whether the results of test to confirm serious illness were interpreted without knowledge of the signs and symptoms

^e Not enough detail on the definition of the sign or symptom was provided to allow another healthcare professional to make the same diagnosis

^f Included children up to 16 years old (mean age was 3.3 years)

^g It is unclear whether the same clinical data would be available when the test results were interpreted as would be available when the test is used in practice

^h Included children from 8 days to 16 years old. Included those with a temperature of 38°C or higher. Undertaken in the paediatric assessment unit of two hospitals in England.

Table I5.12 GRADE profile for evaluation of tachypnoea

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Tachypnea														
<i>For detecting pneumonia</i>														
1 (Taylor, 1995)	572	74 (70 to 77)	77 (77 to 80)	20 (17 to 23)	97 (96 to 99)	3.2 (2.5 to 4.0) ^a	0.3 (0.2 to 0.6) ^a	Low	Prospective	Very serious ^{b, c, d, e}	NA	No serious	No serious	Yes ^{f, g}
Elevated respiratory rate														
<i>For detecting bacteraemia</i>														
1 (Craig, 2010)	12807	11 (3 to 19) ^a	85 (84 to 86) ^a	1 (0 to 1) ^a	100 (99 to 100) ^a	0.7 (0.4 to 1.5) ^a	1.0 (1.0 to 1.1) ^a	Low	Prospective	Very serious ^{c, d, h}	NA	No serious	No serious	Yes ^{f, i, j, k}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It was not clear if the reference standard was likely to classify the target condition correctly^c It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection^d It is not clear whether all children received the same test to confirm serious infection^e It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection^f It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study^g Included children were less than 2 years old. Included children had a temperature of 38°C or greater. Study undertaken in the emergency department of a children's hospital in the USA.^h It is not clear whether the test to confirm serious infection was independent of the signs and symptomsⁱ Included children were less than 5 years old. Included children had a measured axillary temperature of greater than or equal to 38°C; parental report of a temperature of greater than or equal to 38°C measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever (10th revision of the international classification of diseases, Australian modification codes R50, R50.0, R50.1, R50.9 and R56.0), as determined by a triage nurse. The study was undertaken in a hospital in Australia.^j Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician^k Results are reported per illness rather than per child – some children were included more than once for different illnesses

Table I5.13 GRADE profile for evaluation of crackles

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Chest crackles														
<i>For detecting pneumonia, urinary tract infection and bacteraemia</i>														
1 (Craig, 2010)	12807	19 (17 to 22) ^a	93 (92 to 93) ^a	17 (15 to 19) ^a	1 (1 to 1) ^a	2.6 (2.3 to 2.9) ^a	0.9 (0.8 to 0.9) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}
Abnormal chest sounds														
<i>For detecting pneumonia, urinary tract infection and bacteraemia</i>														
1 (Craig, 2010)	12807	29 (27 to 32) ^a	85 (85 to 86) ^a	13 (12 to 15) ^a	94 (94 to 94) ^a	2.0 (1.8 to 2.2) ^a	0.8 (0.8 to 0.9) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}
Crepitations														
<i>For detecting serious bacterial illness</i>														
1 (Bleeker, 2001)	231	2 (0 to 5) ^a	93 (87 to 100) ^a	50 (15 to 85) ^a	24 (19 to 30) ^a	0.3 (0.1 to 1.3) ^a	1.0 (1.0 to 1.1) ^a	Very low	Retrospective	Very serious ^{c, d, h, i, j}	NA	Serious ^k	No serious	Yes ^{g, l, m}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection^c It is not clear whether all children received the same test to confirm serious infection^d It is unclear whether the results of the test used to confirm serious illness were interpreted without knowledge of the signs or symptoms^e Included children were less than 5 years old. Included children had a measured auxiliary temperature of greater than or equal to 38°C; parental report of a temperature of greater than or equal to 38°C measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever (10th revision of the international classification of diseases, Australian modification codes R50, R50.0, R50.1, R50.9 and R56.0), as determined by a triage nurse. The study was undertaken in a hospital in Australia.^f Results are reported per illness rather than per child – some children were included more than once for different illnesses^g It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^h It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

ⁱ It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^j It is not clear whether the test to confirm serious infection was independent of the signs and symptoms

^k Included children from 8 days to 16 years of age (mean: 3.3 years)

^l Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated

^m Included temperatures of 38°C or greater. Included children aged 1 to 36 months. Undertaken in the emergency department of two hospitals in the Netherlands.

Table I5.14 GRADE profile for evaluation of respiratory symptoms

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Respiratory distress														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	3066	4 (1 to 8) ^a	92 (90 to 93) ^a	5 (1 to 9) ^a	90 (88 to 91) ^a	0.5 (0.2 to 1.1) ^a	1.0 (1.0 to 1.1) ^a	Mode rate	Prospective	Serious ^b	NA	No serious	No serious	Yes ^{c, d}
Breathing difficulty														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	26 (23 to 28) ^a	87 (87 to 88) ^a	13 (12 to 15) ^a	94 (93 to 94) ^a	2.0 (1.8 to 2.2) ^a	0.9 (0.8 to 0.9) ^a	Mode rate	Prospective	Serious ^{b, e, f}	NA	No serious	No serious	Yes ^{c, g}
Breathing difficulty or chest wall recession														
<i>For detecting serious illness</i>														
1 (Hewson, 2000)	313	NR/NC	65 (NR/NC)	41 (NR/NC)	82 (NR/NC)	NR/NC	NR/NC	Mode rate	Prospective	Serious ^{e, h, i}	NA	No serious	No serious	Yes ^{c, j}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Shortness of breath														
<i>For detecting serious bacterial infection</i>														
1 (Njiman, 2012)	1255	27 (20 to 35) ^a	88 (86 to 90) ^a	21 (15 to 27) ^a	91 (90 to 93) ^a	2.2 (1.6 to 3.1) ^a	0.8 (0.7 to 0.9) ^a	Very low	Prospective	Very serious ^{e, f, h, i}	NA	Serious ^k	No serious	Yes ^{c, l}
Respiratory symptoms														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	70 (67 to 72) ^a	28 (27 to 28) ^a	7 (7 to 7) ^a	92 (91 to 93) ^a	1.0 (0.9 to 1.0) ^a	1.1 (1.0 to 1.2) ^a	Modest	Prospective	Serious ^{b, e, f}	NA	No serious	No serious	Yes ^{c, g, m}

NA Not applicable

NR/NC Not reported/not calculable

^a Results calculated by the NCC-WCH based on results reported in the study

^b It is not clear if the whole sample of children (or a random sample) received a test to confirm serious illness

^c It is not clear whether the same clinical data were available when the test results were interpreted as would be available in practice

^d Included children were aged 3 months or younger. Included those with an auxiliary, rectal or tympanic temperature of 38°C or higher at presentation or in the 24 hours prior to presentation. Undertaken in GPs offices in the USA.

^e It is not clear whether all children received the same test to confirm serious illness

^f It is not clear whether the test to confirm serious illness was independent of the clinical signs and symptoms

^g Included children were under 5 years old. Included those with one or more of the following elements: a measured auxiliary temperature of 38°C or higher; parental report of a temperature of 38°C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in the emergency department of a children's hospital in Australia.

^h It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness.

ⁱ It is unclear whether the results of the test to confirm serious illness were interpreted without knowledge of the signs and symptoms

^j Includes children aged 1 to 26 weeks. Temperature was not an inclusion criterion, but the results reported here are for a subgroup of febrile infants. Undertaken in the emergency department of one children's hospital and the emergency departments of two general hospitals in Australia.

^k Included children aged up to 16 years (83% were 5 years or younger)

^l Included children aged 1 month to 16 years. Included those with a temperature of 38.5°C or higher, recent high fever or fever as a reason for referral. Undertaken in the emergency department of a children's hospital in the Netherlands.

^m Not enough detail regarding the measurement of the sign or symptom was provided to allow another healthcare provider to repeat the measurement

Table I5.15 GRADE profile for evaluation of nasal symptoms

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Purulent nasal discharge														
<i>For detecting serious bacterial illness</i>														
1 (Bleeker, 2001)	231	20 (14 to 26) ^a	53 (41 to 66) ^a	56 (44 to 69) ^a	18 (13 to 24) ^a	0.4 (0.3 to 0.7) ^a	1.5 (1.2 to 1.9) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g}	NA	No serious	No serious	Yes ^{h, i}
Upper respiratory tract infection or runny nose														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	5 (2 to 8) ^a	90 (88 to 91) ^a	5 (2 to 8) ^a	90 (88 to 91) ^a	0.5 (0.2 to 1.0) ^a	1.1 (1.0 to 1.1) ^a	Modest	Prospective	Serious ^j	NA	No serious	No serious	Yes ^{i, k}
Mild upper respiratory tract infection symptoms														
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	5 (0 to 11) ^a	72 (65 to 79) ^a	4 (0 to 9) ^a	76 (69 to 82) ^a	0.2 (0.0 to 0.7) ^a	1.3 (1.2 to 1.5) ^a	Low	Prospective	Very serious ^{e, f, g}	NA	No serious	No serious	Yes ^{i, l}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is unclear whether the spectrum of children is representative of those who will receive the test in practice

^c It is unclear whether the test to confirm serious illness is likely to confirm serious illness

^d It is unclear whether all of the children received the same test to confirm serious illness

^e It is unclear whether the test to confirm serious illness is independent of the clinical signs and symptoms

^f It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness

^g It is unclear whether the results of the test to confirm serious illness were interpreted without knowledge of the signs and symptoms

^h Included children aged between 1 and 36 months. Temperature was not specified as an inclusion criterion, but only those with 'acute fever' were included. Undertaken in a children's hospital in the Netherlands.

ⁱ It is not clear whether the same clinical data were available when the test results were interpreted as would be available in practice

^j It is not clear if the whole sample of children (or a random sample) received a test to confirm serious illness

^k Included children were aged 3 months or younger. Included those with an auxiliary, rectal or tympanic temperature of 38°C or higher at presentation or in the 24 hours prior to presentation. Undertaken in GPs offices in the USA.

^l Included children aged less than 3 months. Included those with an axillary temperature of 38°C or higher. Undertaken in an outpatients clinic in South Korea.

Table I5.16 GRADE profile for evaluation of wheeze

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Audible wheeze														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	8 (7 to 10) ^a	94 (93 to 94) ^a	9 (7 to 11) ^a	93 (92 to 93) ^a	1.3 (1.1 to 1.6) ^a	1.0 (1.0 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}
Stridor														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	1 (1 to 2) ^a	98 (98 to 98) ^a	5 (2 to 7) ^a	93 (92 to 93) ^a	0.6 (0.4 to 1.1) ^a	1.0 (1.0 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children or a random sample of the children were given a test to confirm serious illness

^c It is not clear whether all children received the same test to confirm serious illness

^d It is not clear whether the test to confirm serious illness was independent of the clinical signs and symptoms

^e It is not clear whether the clinical data available when the test results were interpreted are what would be available when the test is used in practice

^f Included children aged under 5 years. Included those with one or more of the following elements: a measured auxiliary temperature of 38°C or higher; parental report of a temperature of 38°C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in a children's emergency department of a hospital in Australia.

Table I5.17 GRADE profile for evaluation of chest findings/abnormal chest sounds

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Abnormal chest sounds														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	8 (7 to 10) ^a	94 (93 to 94) ^a	9 (7 to 11) ^a	93 (92 to 93) ^a	1.3 (1.1 to 1.6) ^a	1.0 (1.0 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}
Chest findings														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	2 (0 to 4)	95 (94 to 96)	4 (0 to 8)	90 (89 to 92)	0.4 (0.1 to 1.2)	1.0 (1.0 to 1.1)	Mode rate	Prospective	Serious ^b	NA	No serious	No serious	Yes ^{e, g, h}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children or a random sample of the children were given a test to confirm serious illness

^c It is not clear whether all children received the same test to confirm serious illness

^d It is not clear whether the test to confirm serious illness was independent of the clinical signs and symptoms

^e It is not clear whether the clinical data available when the test results were interpreted are what would be available when the test is used in practice

^f Included children aged under 5 years. Included those with one or more of the following elements: a measured auxiliary temperature of 38°C or higher; parental report of a temperature of 38°C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in a children's emergency department of a hospital in Australia.

^g Not enough detail was provided on the measurement of the sign or symptom so that another healthcare professional could make the same diagnosis

^h Included children were aged 3 months or younger. Included those with an auxiliary, rectal or tympanic temperature of 38°C or higher at presentation or in the 24 hours prior to presentation. Undertaken in GPs offices in the USA.

Table I5.18 GRADE profile for evaluation of cough

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Cough														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	58 (55 to 61) ^a	46 (46 to 47) ^a	8 (7 to 8) ^a	93 (93 to 94) ^a	1.1 (1.0 to 1.1) ^a	0.9 (0.9 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	1 (0 to 2) ^a	98 (98 to 99) ^a	4 (0 to 11) ^a	90 (89 to 92) ^a	0.4 (0.1 to 2.7) ^a	1.0 (1.0 to 1.0) ^a	Mode rate	Prospective	Serious ^b	NA	No serious	No serious	Yes ^{e, g}
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	15 (4 to 27) ^a	63 (55 to 70) ^a	9 (2 to 15) ^a	76 (69 to 83) ^a	0.4 (0.2 to 0.9) ^a	1.3 (1.1 to 1.6) ^a	Very low	Prospective	Very serious ^{b, c, d, h, i, j}	NA	Serious ^k	No serious	Yes ^{e, l}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether all of the children or a random sample of the children were given a test to confirm serious illness^c It is not clear whether all children received the same test to confirm serious illness^d It is not clear whether the test to confirm serious illness was independent of the clinical signs and symptoms^e It is not clear whether the clinical data available when the test results were interpreted are what would be available when the test is used in practice^f Included children aged under 5 years. Included those with one or more of the following elements: a measured auxiliary temperature of 38°C or higher; parental report of a temperature of 38°C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in a children's emergency department of a hospital in Australia.^g Included children were aged 3 months or younger. Included those with an auxiliary, rectal or tympanic temperature of 38°C or higher at presentation or in the 24 hours prior to presentation. Undertaken in GPs' offices in the USA.^h It is not clear whether the spectrum of children was representative of those who would receive the test in practiceⁱ It is not clear whether the clinical signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness^j It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the clinical signs and symptoms

^k Included children aged up to 16 years old^l Included children aged from 1 month to 16 years. Included those with a rectal temperature above 38°C at some time within 24 hours before inclusion. Undertaken in a hospital in Denmark.**Table I5.19** GRADE profile for evaluation of poor feeding

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Poor intake														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2001)	231	36 (29 to 44) ^a	74 (63 to 85) ^a	81 (72 to 90) ^a	28 (21 to 35) ^a	1.4 (0.9 to 2.3) ^a	0.9 (0.7 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g}	NA	No serious	No serious	Yes ^{h, i, j}
Poor feeding														
<i>For detecting serious disease</i>														
1 (Nademi, 2001)	141	78 (65 to 90)	43 (33 to 52)	36 (25 to 45)	83 (72 to 92)	1.4 (1.1 to 1.7) ^a	0.5 (0.3 to 0.9) ^a	Very low	Prospective	Very serious ^{d, e, f, g}	NA	Serious ^k	No serious	Yes ^{h, i, l, m}
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	27 (13 to 40) ^a	63 (56 to 70) ^a	15 (7 to 23) ^a	78 (71 to 85) ^a	0.7 (0.4 to 1.2) ^a	1.2 (0.9 to 1.4) ^a	Low	Prospective	Very serious ^{e, f, g}	NA	No serious	No serious	Yes ^{i, n}
Decreased feeding														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	37 (29 to 44) ^a	63 (60 to 65) ^a	9 (7 to 12) ^a	90 (88 to 92) ^a	1.0 (0.8 to 1.2) ^a	1.0 (0.9 to 1.1) ^a	Low	Prospective	Very serious ^{o, p}	NA	No serious	No serious	Yes ^{h, q}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

^c It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^d Not all of the children received the same test to confirm serious illness

^e It is not clear if the child's signs and symptoms formed part of the test for serious illness

^f It is not clear if the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious infection

^g It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms

^h Not enough detail was provided in the study paper to allow the sign or symptom to be detected by a different clinician

ⁱ It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^j Included children aged 1 to 36 months. Included temperatures equal to or greater than 38°C. Undertaken in the emergency department of two children's hospitals in the Netherlands.

^k Included children from 8 days to 16 years of age (mean: 3.3 years)

^l Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated

^m Included children aged 8 days to 16 years. Included temperature of 38°C or greater. Study undertaken in a paediatric assessment unit of a hospital in the UK.

ⁿ Included children aged less than 3 months. Included those with an axillary temperature of 38°C or higher. Undertaken in an outpatients clinic in South Korea.

^o The study authors report that not all eligible infants were enrolled

^p It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^q Included children were less than 3 months old. Included infants had auxiliary, rectal or tympanic temperatures equal to or greater than 38°C in the office or in the previous 24 hours at home. The study was based in a GP's office in the USA.

Table I5.20 GRADE profile for evaluation of capillary refill time

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Capillary refill time of 2 to 3 seconds														
<i>For detecting pneumonia, urinary tract infection and bacteraemia</i>														
1 (Craig, 2010)	12807	10 (8 to 11) ^a	96 (96 to 96) ^a	17 (14 to 19) ^a	93 (93 to 94) ^a	2.6 (2.1 to 3.1) ^a	0.9 (0.9 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}
Capillary refill time of > 3 seconds														
<i>For detecting pneumonia, urinary tract infection and bacteraemia</i>														
1 (Craig, 2010)	12807	1 (1 to 2) ^a	100 (100 to 100) ^a	35 (22 to 49) ^a	93 (92 to 93) ^a	7.0 (3.9 to 12.7) ^a	1.0 (1.0 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection^c Not all of the children received the same test to confirm serious illness^d It is not clear whether the test to confirm serious infection was independent of the signs and symptoms^e Included children were less than 5 years old. Included children had a measured auxiliary temperature of greater than or equal to 38°C; parental report of a temperature of greater than or equal to 38°C measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever (10th revision of the international classification of diseases, Australian modification codes R50, R50.0, R50.1, R50.9 and R56.0), as determined by a triage nurse. The study was undertaken in a hospital in Australia.^f Results are reported per illness rather than per child – some children were included more than once for different illnesses^g It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

Table I5.21 GRADE profile for evaluation of reduced urine output

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Reduced urine output														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	17 (11 to 23) ^a	86 (85 to 88) ^a	12 (8 to 16) ^a	91 (89 to 92) ^a	1.2 (0.8 to 1.8) ^a	1.0 (0.9 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g, h}
Poor micturition														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2001)	231	33 (26 to 40) ^a	79 (69 to 90) ^a	83 (74 to 92) ^a	28 (22 to 35) ^a	1.6 (0.9 to 2.8) ^a	0.8 (0.7 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, i, j}	NA	No serious	No serious	Yes ^{e, g, k}

NA Not applicable

^a Calculated by NCC-WCH based on results reported in the study^b Selection criteria for inclusion in the study were not clearly described^c Not all of the children (or a random sample of the children) received a test to confirm serious illness^d Not all children received the same test to confirm serious illness^e It is unclear whether the period between noting a child's signs and symptoms and performing the test to confirm serious illness was short enough to be reasonably sure that the target condition did not change between the two tests^f Not enough details were provided on the signs and symptoms to ensure the findings could be replicated by another healthcare professional^g It is not clear whether the same clinical data available when the test results were interpreted would be available when the test is used in practice^h Included children were 3 months or younger. Infants were included if they had an axillary, rectal or tympanic temperature $\geq 38^{\circ}\text{C}$ in the office or in the previous 24 hours at home. The study was conducted in GPs' offices in the USA.ⁱ It is unclear whether the child's signs and symptoms were interpreted without knowledge of the results of the test to confirm serious illness^j It is unclear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's signs and symptoms^k Not enough detail on the test used to confirm serious illness was reported in the study

Table I5.22 GRADE profile for evaluation of duration of fever

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Fever duration > 12 hours														
<i>For detecting serious bacterial infection</i>														
1 (Pratt, 2007)	119	44 (22 to 67) ^a	19 (15 to 22) ^a	2 (1 to 3) ^a	90 (85 to 96) ^a	0.5 (0.3 to 0.9) ^a	3.0 (1.9 to 4.7) ^a	Very low	Prospective	Very serious ^{b, c, d}	NA	No serious	Serious ^e	Yes ^{f, g, h}
<i>For detecting bacteraemia</i>														
1 (Haddon, 1999)	534	65 (42 to 87) ^a	38 (29 to 48) ^a	15 (7 to 23) ^a	87 (77 to 97) ^a	1.0 (0.7 to 1.5) ^a	0.9 (0.5 to 1.8) ^a	Very low	Prospective	Very serious ^{d, i, j, k}	NA	No serious	Serious ^e	Yes ^{f, l}
Fever duration ≥ 24 hours														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	19 (13 to 25) ^a	90 (89 to 92) ^a	17 (11 to 22) ^a	91 (90 to 93) ^a	1.9 (1.3 to 2.7) ^a	0.9 (0.8 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, m, n}	NA	No serious	No serious	Yes ^{f, g, o}
<i>For detecting bacteraemia</i>														
1 (Teach, 1997)	6619	60 (53 to 67) ^a	28 (27 to 30) ^a	2 (2.00 to 3) ^a	96 (95 to 97) ^a	0.8 (0.7 to 0.9) ^a	1.4 (1.2 to 1.7) ^a	Very low	Retrospective	Very serious ^{d, i, p, q}	NA	No serious	No serious	Yes ^{g, r}
Fever duration >24 hours														
<i>For detecting serious bacterial infection</i>														
1 (Andreola, 2007)	408	52 (42 to 62) ^a	31 (26 to 36) ^a	18 (14 to 23) ^a	69 (61 to 76) ^a	0.8 (0.6 to 0.9) ^a	1.5 (1.2 to 2.0) ^a	Low	Prospective	Very serious ^{d, i, s}	NA	No serious	No serious	Yes ^{g, t}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Fever duration \geq 2 days														
<i>For detecting bacteraemia</i>														
1 (Teach, 1997)	6619	18 (12 to 23) ^a	74 (73 to 75) ^a	2 (1 to 3) ^a	97 (96 to 97) ^a	0.7 (0.5 to 0.9) ^a	1.1 (1.0 to 1.2) ^a	Very low	Retrospective	Very serious ^{d, i, p, q}	NA	No serious	No serious	Yes ^{g, r}
Fever duration > 48 hours														
<i>For detecting serious bacterial infection</i>														
1 (Berger, 1996)	138	39 (23 to 56) ^a	82 (75 to 89) ^a	41 (24 to 58) ^a	81 (74 to 89) ^a	2.2 (1.2 to 3.9) ^a	0.7 (0.6 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d, i}	NA	No serious	No serious	Yes ^{f, g, u}
1 (Trautner, 2006)	103	NR/NC ^v	NR/NC ^v	NR/NC ^v	NR/NC ^v	NR/NC ^v	NR/NC ^v	Low	Prospective	Serious ^{d, i, s}	NA	Serious ^w	NA	Yes ^{g, x, y}
Fever duration \geq 72 hours														
<i>For detecting urinary tract infection</i>														
1 (Salleeh, 2010)	818	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	Very low	Prospective	Very serious ^{c, d, i, aa}	NA	Serious ^{ab}	NA	Yes ^{g, ac, ad}
Fever duration > 3 days														
<i>For detecting serious bacterial infection</i>														
1 (Factor, 2001)	669	25 (21 to 30) ^a	85 (81 to 89) ^a	69 (61 to 76) ^a	47 (42 to 51) ^a	1.7 (1.2 to 2.3) ^a	0.9 (0.8 to 0.9) ^a	Low	Prospective	Very serious ^{c, d, i, s, ae}	NA	No serious	No serious	Yes ^{g, af}

NA Not applicable

NC Not calculable

NR Not reported

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^c It is not clear whether all children received the same test to confirm serious infection

^d It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection

^e The difference between the highest and lowest confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%

^f It was unclear whether the period between the reference test and the signs and symptoms being recorded was short enough to be reasonably sure that the illness did not resolve before the reference test was undertaken

^g It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^h Included children were 1 to 36 months old. Included children had a temperature equal to or greater than 39°C (reported or documented). The study was conducted in a hospital in USA.

ⁱ It is unclear whether the results of the test used to confirm serious illness were interpreted without knowledge of the signs or symptoms

^j Uninterpretable, indeterminate or intermediate test results were reported for some children

^k Withdrawals from the study were not explained

^l Included children were 3 to 36 months old. Included children had a temperature equal to or greater than 39°C recorded in the emergency department. The study was based in the emergency department of a hospital in Australia.

^m The selection criteria were not clearly described

ⁿ Some eligible infants were not enrolled

^o Included children were less than or equal 3 months. Included infants had an auxiliary, rectal or tympanic temperature greater than or equal to 38 degrees in the office or at home. The study was based In GPs offices in USA.

^p Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated

^q Study authors report that it is possible the duration of fever data is not accurate as it was reliant on the caregivers' recall of the day on which the fever began

^r Included children were 3 to 36 months old with an initial recorded temperature of greater than or equal to 39°C. The subjects were part of a multicenter trial conducted in USA.

^s It is not clear whether the test to confirm serious infection was independent of the signs and symptoms

^t Included children aged less than 3 years. Included those with fever, although fever was not defined. Undertaken in an emergency department in Italy.

^u Included children were 2 weeks to 1 year old with a temperature greater than or equal to 38°C. The study was based in the paediatric emergency ward of a hospital in the Netherlands.

^v OR 1.04 (95% CI 0.35 to 3.12)

^w Included children up to 18 years old

^x Included children less than 18 years old with a temperature greater than or equal to 41.1°C. The study was conducted in a paediatric emergency department in USA.

^y Results reported in the study: OR 1.04 (0.35 to 3.12) (compared to duration < 24 hours). Data on diagnostic accuracy or data that would allow diagnostic accuracy data to be calculated was not reported.

^z RR 1.6 (95% 1.2 to 2.1), $P = 0.002$

^{aa} It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^{ab} This study reported on bag urinalysis results rather than urinary tract infection specifically

^{ac} Included children were 3 to 36 months with a temperature greater than or equal to 38°C recorded in the emergency department or by parental report. The study was based in a paediatric emergency department in Canada.

^{ad} Results reported in the study: RR 1.6 (1.2 to 2.1), $p = 0.002$ (compared to duration < 2 days). Data on diagnostic accuracy or data that would allow diagnostic accuracy data to be calculated was not reported.

^{ae} It is unclear whether the spectrum of participants is representative of those that will present for assessment in practice

^{af} Included children aged 2 to 59 months. Included those with an axillary temperature of 38°C or more. Undertaken in an outpatient department and emergency room in Bangladesh.

Table I5.23 GRADE profile for comparison of duration of fever

Number of studies	Duration of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	With SBI (Mean)	Without SBI (Mean)	P value							
Duration of fever										
For detecting serious bacterial infection										
1 (Hsiao, 2006)	26.5 hours (SD 41.5)	18.6 hours (SD 21.7)	P < 0.001	High	Prospective	No serious	NA	No serious	NA	Yes ^a
1 (Bleeker, 2007)	2.5 days (SD 2.6)	2.6 days (SD 2.3)	NR	High	Prospective	No serious	NA	No serious	NA	Yes ^b
1 (Lacour, 2001)	Median 27 hours (range 2 to 140)	Median 24 hours (range 2 to 140)	P = 0.02	High	Prospective	No serious	NA	No serious	NA	Yes ^c
1 (Galletto-Lacour, 2003)	Median 48 hours (range 6 to 140)	Median 24 hours (range 1 to 140)	P = 0.026	High	Prospective	No serious	NA	No serious	NA	Yes ^c
1 (Olaciregui, 2009)	18.62 hours (SD 35.8)	13.81 hours (SD 26)	P = 0.26	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^d
1 (Bleeker, 2001)	2.6 days (SD 2.2)	3.2 days (SD 2.8)	P < 0.15	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^e

Number of studies	Duration of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	With SBI (Mean)	Without SBI (Mean)	P value							
1 (Fouzas, 2010)	Median 14 hours (IQR 6 to 29)	Median 14 hours (IQR 6 to 27)	P = 0.49	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^f
<i>For detecting meningococcal disease</i>										
1 (Nielsen, 2001)	Median 21 hours (IQR/range NR)	Median 24 hours (IQR/range NR)	P not significant	Low	Prospective	Serious ^g	NA	Serious ^h	NA	Yes ⁱ

IQR Interquartile range, NA Not applicable, NR Not reported, SD standard deviation

^a Included children were 57 to 180 days old (2 to 6 months) with a rectal temperature of greater than 37.9°C. The study was based in a children's hospital in USA.

^b Included children were 1 to 36 months with a temperature greater than or equal to 38°C. The study was based in 2 paediatric teaching hospitals in the Netherlands.

^c Included children were 7 days to 36 months with a rectal temperature greater than 38°C. The study was conducted in the emergency department of a children's hospital in Switzerland.

^d Included children were 4 to 90 days old with a rectal temperature greater than 38°C. The study was based in an emergency department in Spain.

^e Included children were 1 to 36 months. Included children had acute fever without apparent source (cut off not defined). The study was based in 2 paediatric teaching hospitals in the Netherlands.

^f Included children were 29 to 89 days with a rectal temperature greater than 38°C. The study was based in a tertiary care paediatric unit in Greece.

^g 10 of the 39 cases of meningococcal disease were probable rather than confirmed.

^h Included children up to 16 years old

ⁱ Included children were greater than 1 month and less than 16 years with a rectal temperature greater than 38°C at some time within the 24 hours before inclusion. The study was conducted in the paediatric department of a hospital in Denmark.

Table I5.24 GRADE profile for evaluation of height of fever in children younger than 3 months

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature $\geq 38.0^{\circ}\text{C}$														
<i>For detecting serious bacterial infection</i>														
1 (Stanley, 2005)	5279	100 (100 to 100) ^a	0 (0 to 0) ^a	9 (8 to 10) ^a	NC	1.0 (1.0 to 1.0) ^a	NC	Very low	Retrospective	Very serious b, c, d	NA	No serious	No serious	Yes ^{e, f}
<i>For detecting sepsis</i>														
1 (Weber, 2003)	3303	NR/NC ^g	NR/NC ^g	NR/NC ^g	NR/NC ^g	NR/NC ^g	NR/NC ^g	Low	Prospective	Very serious b, c, d, h	NA	No serious	NA	Yes ^{e, i}
<i>For detecting meningitis</i>														
1 (Weber, 2003)	3303	NR/NC ^j	NR/NC ^j	NR/NC ^j	NR/NC ^j	NR/NC ^j	NR/NC ^j	Low	Prospective	Very serious b, c, d, h	NA	No serious	NA	Yes ^{e, i}
Temperature $> 39.0^{\circ}\text{C}$														
<i>For detecting urinary tract infection</i>														
1 (Zorc, 2005)	1025	37 (27 to 47) ^a	81 (78 to 83) ^a	16 (11 to 21) ^a	93 (91 to 95) ^a	2.0 (1.4 to 2.6) ^a	0.8 (0.7 to 0.9) ^a	Modest	Prospective	Serious c, d, k	NA	No serious	No serious	Yes ^{e, l, m}
Temperature $\geq 39.5^{\circ}\text{C}$														
<i>For detecting serious bacterial infection</i>														
1 (Zarkesh, 2011)	202	24 (10 to 37) ^a	76 (70 to 83) ^a	19 (8 to 30) ^a	81 (75 to 87) ^a	1.0 (0.5 to 1.9) ^a	1.0 (0.8 to 1.2) ^a	Low	Retrospective	Serious b, d, h	NA	No serious	No serious	Yes ^{e, n}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting occult bacteraemia, urinary tract infection, or bacteraemia</i>														
1 (Gomez, 2010)	1018	26 (8 to 44) ^a	91 (89 to 93) ^a	6 (1 to 11) ^a	98 (97 to 99) ^a	2.8 (1.4 to 5.8) ^a	0.8 (0.6 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, o}
Temperature $\geq 40.0^{\circ}\text{C}$														
<i>For detecting bacterial meningitis, bacteraemia, urinary tract infection, or salmonella enteritis</i>														
1 (Bonadio, 1994)	356	21 (7 to 35) ^a	96 (94 to 98) ^a	35 (14 to 56) ^a	92 (89 to 95) ^a	5.3 (2.3 to 12.3) ^a	0.8 (0.7 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, p}
Temperature $> 40.0^{\circ}\text{C}$														
<i>For detecting serious bacterial infection</i>														
1 (Stanley, 2005)	5279	7 (5 to 10) ^a	99 (99 to 99) ^a	38 (28 to 48) ^a	91 (91 to 92) ^a	6.1 (4.1 to 9.3) ^a	0.9 (0.9 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f}

NA Not applicable, NC Not calculable, NR/NC Not reported/Not calculable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all children received the same test to confirm serious infection

^c It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection

^d It is unclear whether the results of the test used to confirm serious illness were interpreted without knowledge of the signs or symptoms

^e It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^f Included children aged under 3 months. Included those with a temperature of 38°C or higher. Undertaken in a paediatric emergency department in the USA.

^g OR 3.6 (95% CI 2.6 to 5.1)

^h It is unclear whether the results of the test to confirm serious illness included the assessment of symptoms and signs

ⁱ Included children aged 0 to 59 days. Temperature was not an inclusion criterion. Undertaken in hospitals and outpatient clinics in Ethiopia, The Gambia, Papua New Guinea, and Philippines

^j OR 11.8 (95% CI 5.7 to 24.6)

^k One third of eligible infants were not enrolled - missed infants had a lower rate of urinary tract infection than enrolled infants

Feverish illness in children (appendices)

^l Results reported in the study: OR 7.4 (95% CI 3.0 to 18.5). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^m Included children aged 60 days or younger. Included those with a temperature of 38°C or higher. Undertaken in eight paediatric emergency departments in the USA.

ⁿ Includes children aged 28 days or younger. Included those with a rectal temperature of 38.5°C or higher measured in the emergency room. Undertaken in a hospital in Iran.

^o Included children aged under 90 days. Included those with a temperature of 38°C or higher at home or at presentation. Undertaken in an emergency department in Spain.

^p Includes children aged 8 to 12 weeks. Included those with a temperature of 38°C or higher. Undertaken in the emergency department of a children's hospital in the USA.

Table I5.25 GRADE profile for evaluation of height of fever in all ages up to 5 years, including those less than 3 months

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature $\geq 37.4^{\circ}\text{C}$														
<i>For detecting urinary tract infection</i>														
1 (Shettigar, 2011)	334	100 (100 to 100) ^a	0 (0 to 0) ^a	8 (5 to 11) ^a	NC	1.0 (1.0 to 1.0) ^a	NC	Mode rate	Prospective	Serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}
Temperature $\geq 37.5^{\circ}\text{C}$														
<i>For detecting serious bacterial infection</i>														
1 (Brent, 2011)	1716	61 (49 to 72)	65 (62 to 67)	7 (5 to 9)	2 (2 to 3)	1.7 (0.7 to 4.5)	0.6 (0.2 to 1.6)	Very low	Prospective	Very serious ^{b, c, f}	NA	Serious ^g	No serious	Yes ^h
<i>For detecting malaria or meningitis</i>														
1 (Owusu-Ofori, 2004)	608	75 (67 to 83) ^a	21 (8 to 34) ^a	74 (66 to 82) ^a	22 (8 to 35) ^a	0.9 (0.8 to 1.1) ^a	1.2 (0.6 to 2.4) ^a	Low	Prospective	Serious ^{b, c, i}	NA	Serious ^g	No serious	Yes ^{d, j}
<i>For detecting serious illness</i>														
1 (Yeboah-Antwi, 2008)	685	NR/NC ^k	NR/NC ^k	NR/NC ^k	NR/NC ^k	NR/NC ^k	NR/NC ^k	Low	Prospective	Very serious ^{b, c, f, l}	NA	No serious	NA	Yes ^{d, m, n, o}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Yeboah-Antwi, 2008)	685	NR/NC ^p	NR/NC ^p	NR/NC ^p	NR/NC ^p	NR/NC ^p	NR/NC ^p	Low	Prospective	Very serious b, c, f, l	NA	No serious	NA	Yes ^d , m, n, q
1 (Yeboah-Antwi, 2008)	685	NR/NC ^r	NR/NC ^r	NR/NC ^r	NR/NC ^r	NR/NC ^r	NR/NC ^r	Low	Prospective	Very serious b, c, f, l	NA	No serious	NA	Yes ^d , m, n, s
<i>For detecting severe illness requiring hospitalisation</i>														
1 (YICSSG, 2008)	8889	NR/NC ^t	NR/NC ^t	NR/NC ^t	NR/NC ^t	NR/NC ^t	NR/NC ^t	Low	Prospective	Very serious b, c, f, u	NA	No serious	NA	Yes ^d , v, w
1 (YICSSG, 2008)	8889	NR/NC ^x	NR/NC ^x	NR/NC ^x	NR/NC ^x	NR/NC ^x	NR/NC ^x	Low	Prospective	Very serious b, c, f, u	NA	No serious	NA	Yes ^d , v, y
1 (YICSSG, 2008)	8889	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	NR/NC ^z	Low	Prospective	Very serious b, c, f, u	NA	No serious	NA	Yes ^d , v, aa
Temperature > 37.5°C														
<i>For detecting meningitis</i>														
1 (Wells, 2001)	218	79 (63 to 95)	55 (48 to 62)	18 (11 to 25)	95 (88 to 100)	1.7 (1.3 to 2.3) ^a	0.4 (0.2 to 0.8) ^a	Low	Prospective	Serious b, c, f, i	NA	Serious ^g	No serious	Yes ^d , ab

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature $\geq 38.0^{\circ}\text{C}$														
<i>For detecting pneumonia, urinary tract infection or bacteraemia</i>														
1 (Craig, 2010)	12807	85 (83 to 87) ^a	22 (22 to 23) ^a	8 (7 to 8) ^a	95 (94 to 96) ^a	1.1 (1.1 to 1.1) ^a	0.7 (0.6 to 0.8) ^a	Low	Prospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, ac}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	100 (100 to 100) ^a	0 (0 to 0) ^a	10 (8 to 11) ^a	NC	1.0 (1.0 to 1.0) ^a	NC	Mode rate	Prospective	Serious ^{ad}	NA	No serious	No serious	Yes ^{d, ae}
<i>For detecting bacteraemia or bacterial meningitis</i>														
1 (Pantell, 2004)	3066	90 (83 to 98) ^a	29 (28 to 31) ^a	3 (2 to 3) ^a	99 (99 to 100) ^a	1.3 (1.2 to 1.4) ^a	0.3 (0.2 to 0.7) ^a	Low	Prospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, af}
<i>For detecting serious bacterial infection</i>														
1 (Stanley, 2005)	5279	100 (100 to 100) ^a	0 (0 to 0) ^a	9 (8 to 10) ^a	NC	1.0 (1.0 to 1.0) ^a	NC	Very low	Retrospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, ag}
<i>For detecting sepsis</i>														
1 (Weber, 2003)	3303	NR/NC ^{ah}	NR/NC ^{ah}	NR/NC ^{ah}	NR/NC ^{ah}	NR/NC ^{ah}	NR/NC ^{ah}	Low	Prospective	Very serious b, c, f, ai	NA	No serious	NA	Yes ^{d, aj}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting meningitis</i>														
1 (Weber, 2003)	3303	NR/NC ^{ak}	NR/NC ^{ak}	NR/NC ^{ak}	NR/NC ^{ak}	NR/NC ^{ak}	NR/NC ^{ak}	Low	Prospective	Very serious b, c, f, ai	NA	No serious	NA	Yes ^{d, aj}
Temperature $\geq 38.4^{\circ}\text{C}$														
<i>For detecting urinary tract infection</i>														
1 (Shettigar, 2011)	334	78 (62 to 93)	41 (36 to 47)	10 (6 to 15)	95 (92 to 99)	1.3 (1.1 to 1.6)	0.5 (0.3 to 1.1)	Mode rate	Prospective	Serious b, c	NA	No serious	No serious	Yes ^{d, e}
Temperature $\geq 38.5^{\circ}\text{C}$														
<i>For detecting serious bacterial infection</i>														
1 (Brent, 2011)	1716	38 (27 to 50)	85 (83 to 86)	9 (6 to 13)	97 (96 to 98)	2.5 (1.1 to 5.7)	0.7 (0.3 to 1.7)	Very low	Prospective	Very serious b, c, f	NA	Serious ^g	No serious	Yes ^h
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	77 (71 to 84) ^a	38 (35 to 40) ^a	12 (10 to 14) ^a	94 (92 to 96) ^a	1.2 (1.1 to 1.4) ^a	0.6 (0.5 to 0.8) ^a	Mode rate	Prospective	Serious ^{ad}	NA	No serious	No serious	Yes ^{d, ae}
<i>For detecting bacteraemia or bacterial meningitis</i>														
1 (Pantell, 2004)	3066	61 (48 to 73) ^a	69 (67 to 71) ^a	4 (3 to 5) ^a	99 (98 to 99) ^a	2.0 (1.6 to 2.4) ^a	0.6 (0.4 to 0.8) ^a	Low	Prospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, af}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature > 38.5°C														
<i>For detecting meningitis</i>														
1 (Wells, 2001)	218	58 (39 to 78)	81 (75 to 86)	27 (15 to 40)	94 (88 to 100)	3.1 (2.0 to 4.8) ^a	0.5 (0.3 to 0.8) ^a	Low	Prospective	Serious ^{b, c, f, i}	NA	Serious ^g	No serious	Yes ^{d, ab}
Temperature ≥ 39.0°C														
<i>For detecting urinary tract infection</i>														
1 (Shaw, 1998)	2411	79 (70 to 88) ^a	33 (31 to 35) ^a	9 (3 to 5) ^a	98 (97 to 99) ^a	1.2 (1.0 to 1.3) ^a	0.6 (0.4 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c}	NA	No serious	No serious	Yes ^{d, al}
1 (Newman, 2002)	1666	40 (32 to 47) ^a	74 (72 to 76) ^a	14 (11 to 17) ^a	92 (90 to 94) ^a	1.5 (1.2 to 1.9) ^a	0.8 (0.7 to 0.9)	Mode rate	Prospective	Serious ^{ad}	NA	No serious	No serious	Yes ^{d, ae}
<i>For detecting serious infection</i>														
1 (Thompson, 2009)	700	27 (22 to 32)	87 (84 to 91)	41 (30 to 51) ^a	82 (78 to 85) ^a	2.1 (1.5 to 2.9)	0.8 (0.8 to 0.9)	Low	Prospective	Serious ^c	NA	Serious ^{am}	No serious	Yes ^{d, an}
<i>For detecting pneumonia, urinary tract infection or bacteraemia</i>														
1 (Craig, 2010)	12807	54 (51 to 57) ^a	58 (58 to 59) ^a	9 (9 to 10) ^a	94 (94 to 95) ^a	1.3 (1.2 to 1.4) ^a	0.8 (0.7 to 0.8) ^a	Low	Prospective	Very serious ^{b, c, f}	NA	No serious	No serious	Yes ^{d, ac}
<i>For detecting bacteraemia or bacterial meningitis</i>														
1 (Pantell, 2004)	3066	16 (7 to 26) ^a	90 (88 to 91) ^a	3 (1 to 5) ^a	98 (97 to 99) ^a	1.6 (0.9 to 2.8) ^a	0.9 (0.8 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, f}	NA	No serious	No serious	Yes ^{d, af}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature > 39.0°C														
<i>For detecting serious disease</i>														
1 (Nademi, 2001)	141	14 (3 to 25)	82 (74 to 89)	25 (7 to 42)	70 (61 to 78)	0.8 (0.3 to 1.9) ^a	1.0 (0.9 to 1.2) ^a	Very low	Prospective	Very serious b, c, f	NA	Serious ^{am}	No serious	Yes ^{d, ao}
<i>For detecting bacteraemia or bacterial meningitis</i>														
1 (Pantell, 2004)	3066	43 (31 to 55) ^a	81 (79 to 82) ^a	4 (3 to 6) ^a	99 (98 to 99) ^a	2.2 (1.7 to 3.0) ^a	0.7 (0.6 to 0.9) ^a	Low	Prospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, af}
<i>For detecting urinary tract infection</i>														
1 (Zorc, 2005)	1025	37 (27 to 47) ^a	81 (78 to 83) ^a	16 (11 to 21) ^a	93 (91 to 95) ^a	2.0 (1.4 to 2.6) ^a	0.8 (0.7 to 0.9) ^a	Moderate	Prospective	Serious b, c, ap	NA	No serious	No serious	Yes ^{d, o, aq}
Temperature ≥ 39.1°C														
<i>For detecting pneumonia, urinary tract infection, meningitis, or bacteraemia</i>														
1 (Rudinsky, 2009)	985	83 (75 to 88)	18 (16 to 21)	13 (11 to 15) ^a	88 (83 to 92) ^a	1.0 (0.9 to 1.1)	0.9 (0.6 to 1.4)	Low	Prospective	Very serious b, c, f, u, ar	NA	No serious	No serious	Yes ^{d, as}
<i>For detecting bacteraemia, bacterial meningitis, urinary tract infection, or pneumonia</i>														
1 (Alpert, 1990)	152	100 (100 to 100) ^a	0 (0 to 0) ^a	14 (9 to 18) ^a	NC	1.0 (1.0 to 1.0) ^a	NC	Very low	Retrospective	Very serious b, c, f, ar	NA	No serious	No serious	Yes ^{d, at, au}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature > 39.3°C														
<i>For detecting urinary tract infection</i>														
1 (Shettigar, 2011)	334	33 (16 to 51) ^a	85 (81 to 89) ^a	16 (6 to 26) ^a	93 (91 to 96) ^a	2.2 (1.2 to 3.9) ^a	0.8 (0.6 to 1.0) ^a	Mode rate	Prospective	Serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}
Temperature ≥ 39.4°C														
<i>For detecting pneumonia, urinary tract infection, meningitis, or bacteraemia</i>														
1 (Rudinsky, 2009)	985	67 (59 to 75)	36 (33 to 39)	14 (11 to 16) ^a	88 (85 to 91) ^a	1.1 (0.9 to 1.2)	0.9 (0.7 to 1.2)	Low	Prospective	Very serious ^{b, c, f, u, ar}	NA	No serious	No serious	Yes ^{d, as}
Temperature ≥ 39.5°C														
<i>For detecting serious bacterial infection</i>														
1 (Zarkesh, 2011)	202	24 (10 to 37) ^a	76 (70 to 83) ^a	19 (8 to 30) ^a	81 (75 to 87) ^a	1.0 (0.5 to 1.9) ^a	1.0 (0.8 to 1.2) ^a	Low	Retrospective	Serious ^{c, f, ai}	NA	No serious	No serious	Yes ^{d, av}
<i>For detecting occult bacteraemia, urinary tract infection, or bacteraemia</i>														
1 (Gomez, 2010)	1018	26 (8 to 44) ^a	91 (89 to 93) ^a	6 (1 to 11) ^a	98 (97 to 99) ^a	2.8 (1.4 to 5.8) ^a	0.8 (0.6 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, f}	NA	No serious	No serious	Yes ^{d, aw}
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	19 (13 to 25) ^a	92 (91 to 94) ^a	21 (15 to 28) ^a	91 (90 to 93) ^a	2.5 (1.8 to 3.6) ^a	0.9 (0.8 to 0.9) ^a	Mode rate	Prospective	Serious ^{ad}	NA	No serious	No serious	Yes ^{d, ae}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting bacteraemia or bacterial meningitis</i>														
1 (Pantell, 2004)	3066	NR/NC ^{ax}	NR/NC ^{ax}	NR/NC ^{ax}	NR/NC ^{ax}	NR/NC ^{ax}	NR/NC ^{ax}	Low	Prospective	Very serious b, c, f	NA	No serious	NA	Yes ^{d, af, ay}
Temperature > 39.5°C														
<i>For detecting serious disease</i>														
1 (Nademi, 2001)	141	7 (0 to 15)	93 (87 to 98)	30 (1 to 58)	71 (63 to 78)	1.0 (0.3 to 3.8) ^a	1.0 (0.9 to 1.1) ^a	Very low	Prospective	Very serious b, c, f	NA	Serious ^{am}	No serious	Yes ^{d, ao}
Temperature ≥ 40.0°C														
<i>For detecting bacterial meningitis, bacteraemia, urinary tract infection, or salmonella enteritis</i>														
1 (Bonadio, 1994)	356	21 (7 to 35) ^a	96 (94 to 98) ^a	35 (14 to 56) ^a	92 (89 to 95) ^a	5.3 (2.3 to 12.3) ^a	0.8 (0.7 to 1.0) ^a	Very low	Retrospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, az}
<i>For detecting pneumonia, urinary tract infection, meningitis, or bacteraemia</i>														
1 (Rudinsky, 2009)	985	29 (22 to 38)	70 (67 to 73)	13 (9 to 16) ^a	87 (84 to 89) ^a	1.0 (0.8 to 1.3)	1.0 (0.9 to 1.1)	Low	Prospective	Very serious b, c, f, u, ar	NA	No serious	No serious	Yes ^{d, as}
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12807	15 (13 to 17) ^a	89 (89 to 90) ^a	10 (8 to 11) ^a	93 (93 to 94) ^a	1.4 (1.2 to 1.6) ^a	1.0 (0.9 to 1.0) ^a	Low	Prospective	Very serious b, c, f	NA	No serious	No serious	Yes ^{d, ac}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Temperature > 40.0°C														
<i>For detecting serious bacterial infection</i>														
1 (Stanley, 2005)	5279	7 (5 to 10) ^a	99 (99 to 99) ^a	38 (28 to 48) ^a	91 (91 to 92) ^a	6.1 (4.1 to 9.3) ^a	0.9 (0.9 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, f}	NA	No serious	No serious	Yes ^{d, ag}
Temperature ≥ 40.1°C														
<i>For detecting bacteraemia, bacterial meningitis, urinary tract infection, or pneumonia</i>														
1 (Alpert, 1990)	152	71 (55 to 87) ^a	34 (27 to 41) ^a	14 (9 to 20) ^a	88 (81 to 95) ^a	1.1 (0.8 to 1.4) ^a	0.9 (0.5 to 1.5) ^a	Very low	Retrospective	Very serious ^{b, c, f, ar}	NA	No serious	No serious	Yes ^{d, at, au}
Temperature ≥ 41.1°C														
<i>For detecting bacteraemia, bacterial meningitis, urinary tract infection, or pneumonia</i>														
1 (Alpert, 1990)	152	45 (28 to 63) ^a	69 (62 to 75) ^a	18 (10 to 27) ^a	89 (84 to 94) ^a	1.4 (0.9 to 2.2) ^a	0.8 (0.6 to 1.1) ^a	Very low	Retrospective	Very serious ^{b, c, f, ar}	NA	No serious	No serious	Yes ^{d, at, au}

NA Not applicable, NR/NC Not reported/Not calculable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is unclear whether the signs and symptoms were interpreted without knowledge of the results of the test to confirm serious infection

^c It is unclear whether the results of the test used to confirm serious illness were interpreted without knowledge of the signs or symptoms

^d It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^e Included children aged under 5 years. Included those with an axillary temperature of 37.4°C or greater within 24 hours of admission. Undertaken in a hospital in India.

^f It is not clear whether all children received the same test to confirm serious infection

^g Included children aged up to 15 years old

^h Included children aged 1 month to 15 years old. Temperature was not specified as an inclusion criterion. Undertaken in an emergency department of a hospital in the UK.

ⁱ It is unclear whether the spectrum of children included in the study were representative of those who will be assessed in practice

^j Included children aged 3 months to 15 years. Temperature was not specified as an inclusion criterion. Undertaken in a hospital in Ghana.

^k OR 7.4 (95% CI 3.0 to 18.5)

^l It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^m Not enough detail was provided in the study paper to allow the test used to confirm serious illness to be replicated

ⁿ Included children aged younger than 2 months. Temperature was not specified as an inclusion criterion. Undertaken in a hospital in Ghana.

^o Results reported in the study: OR 7.4 (95% CI 3.0 to 18.5). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^p OR 11.1 (95% CI 5.2 to 24.1)

^q Results reported in the study: OR 11.1 (95% CI 5.2 to 24.1). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^r OR 7.4 (95% CI 2.8 to 19.5)

^s Results reported in the study: OR 7.4 (95% CI 2.8 to 19.5). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^t OR 4.7 (95% CI 2.8 to 8.0)

^u Uninterpretable, indeterminate or intermediate test results were reported for some children

^v Included children aged younger than 60 days. Temperature was not specified as an inclusion criterion. Undertaken in hospitals and outpatient clinics in Bangladesh, Bolivia, Ghana, India, Pakistan and South Africa.

^w Results reported in the study: OR 4.7 (2.8 to 8.0). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^x OR 7.5 (95% CI 5.0 to 11.4)

^y Results reported in the study: OR 7.5 (5.0 to 11.4). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^z OR 3.4 (95% CI 2.4 to 4.9)

^{aa} Results reported in the study: OR 3.4 (2.4 to 4.9) ($P < 0.0001$). Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^{ab} Included children aged up to 15 years old with a non-blanching rash. Temperature was not specified as an inclusion criterion. Undertaken in an accident and emergency department in the UK.

^{ac} Included children aged under 5 years. 'Febrile illness' was defined as any illness with one or more of the following: a measured axillary temperature of $\geq 38^{\circ}\text{C}$; parental report of a temperature of $\geq 38^{\circ}\text{C}$ measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in an emergency department in Australia.

^{ad} It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^{ae} Included children aged 3 months or younger. Included those with an auxiliary, rectal or tympanic temperature of 38°C at presentation or in previous 24 hours at home. Undertaken in GPs offices in the USA.

^{af} Included children 3 months or younger. Included those with a temperature of 38°C or higher either at home or in the clinicians office. Undertake in GPs offices in the USA.

^{ag} Included children aged under 3 months. Included those with a temperature of 38°C or higher. Undertaken in a paediatric emergency department in the USA.

^{ah} OR 3.6 (95% CI 2.6 to 5.1)

^{ai} It is unclear whether the test to confirm serious illness was independent of the symptoms and signs

^{aj} Included children were aged 0 to 59 days. Temperature was not specified as an inclusion criterion. Undertaken in hospitals and outpatient clinics in Ethiopia, The Gambia, Papua New Guinea, and Philippines

^{ak} OR 11.8 (95% CI 5.7 to 24.6)

^{al} Includes boys under 1 year of age and girls under 2 years. Includes those with a temperature of 38.3°C or higher. Undertaken in an emergency department in the USA. Ak Included children up to 16 years old

^{am} Includes children aged up to 16 years

^{an} Includes children aged between 3 months and 16 years. Temperature was not specified as an inclusion criterion. Undertaken in a paediatric assessment unit of a hospital in the UK.

^{ao} Includes children aged 8 days to 16 years. Includes those with a temperature of 38°C or higher. Undertaken in a hospital in the UK.

^{ap} One third of eligible infants were not enrolled - missed infants had a lower rate of urinary tract infection than enrolled infants

^{aq} Included children aged 60 days or younger. Included those with a temperature of 38°C or higher. Undertaken in eight paediatric emergency departments in the USA.

^{ar} The selection criteria were not clearly described

^{as} Includes children aged less than 3 months. Includes temperature of 100.4°F or higher at home or at presentation. Undertaken in an emergency departments in the USA.

^{at} It was unclear whether the period between the reference test and the signs and symptoms being recorded was short enough to be reasonably sure that the illness did not resolve before the reference test was undertaken

^{au} Includes children aged 3 to 36 months. Includes temperatures of 41.1°C or higher. Undertaken in an emergency department of a children's hospital in the USA.

^{av} Includes children aged 28 days or younger. Included those with a rectal temperature of 38.5°C or higher measured in the emergency room. Undertaken in a hospital in Iran.

^{aw} Included children aged under 90 days. Included those with a temperature of 38°C or higher at home or at presentation. Undertaken in an emergency department in Spain.

^{ax} Adjusted OR 3.61 (95% CI 1.40 to 9.25)

^{ay} Results reported in the study: adjusted OR 3.61 (1.40 to 9.25), $P = 0.02$. Data on diagnostic accuracy, or data that would allow diagnostic accuracy data to be calculated, was not reported.

^{az} Includes children aged 8 to 12 weeks. Included those with a temperature of 38°C or higher. Undertaken in the emergency department of a children's hospital in the USA.

Table I5.26 GRADE profile for comparison of height of fever in children with and without serious illness – all ages up to 5 years

Number of studies	Height of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	With SBI (Degrees C, mean)	Without SBI (Degrees C, mean)	P value							
Height of fever										
For detecting serious bacterial infection										
1 (Baskin, 1992)	39.0 (SD 0.6)	38.9 (SD 0.6)	P = 0.01	High	Prospective	No serious	NA	No serious	NA	Yes ^a
1 (Galetto-Lacour, 2003)	Median 39.4 (38.3 to 41)	Median 39.5 (38 to 40.8)	P value 'not significant'	High	Prospective	No serious	NA	No serious	NA	Yes ^b
1 (Hsiao, 2006)	38.4 (SD 0.8)	38.5 (SD 1.0)	P = 0.178	High	Prospective	No serious	NA	No serious	NA	Yes ^c

Number of studies	Height of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	With SBI (Degrees C, mean)	Without SBI (Degrees C, mean)	P value							
1 (Lacour, 2001)	39.1 (SD 0.2)	39.0 (SD 0.1)	P value 'not significant'	High	Prospective	No serious	NA	No serious	NA	Yes ^d
1 (Shin, 2009)	38.7 (SD 0.5)	38.6 (SD 0.4)	P = 0.34	High	Prospective	No serious	NA	No serious	NA	Yes ^e
1 (Andreola, 2007)	39.2 (SD 0.8)	39.0 (SD 0.8)	P = 0.004	Moderate	Prospective	Serious ^f	NA	No serious	NA	Yes ^g
1 (Fouzaz, 2010)	Median 38.5 (IQR 38.1 to 39.0)	Median 38.5 (IQR 38.1 to 38.8)	P = 0.22	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^h
1 (Nijman, 2011)	Median 39.3 (IQR 38.6 to 39.8)	Median 38.9 (IQR 38.1 to 39.6)	P < 0.000	Moderate	Prospective	No serious	NA	Serious ⁱ	NA	Yes ^j
1 (Olaciregui, 2009)	38.23 (SD 0.82)	38.23 (SD 0.64)	P = 0.58	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^k
1 (Maniaci, 2008)	38.9 (SD 0.72)	38.6 (SD 0.45)	P = 0.003	Low	Prospective and retrospective	Serious ^l	NA	No serious	NA	Yes ^m
1 (Nguyen, 1984)	39.9 (SD 0.96)	39.1 (SD 3.0)	P > 0.2	Low	Retrospective	No serious	NA	Serious ⁿ	NA	Yes ^o

Feverish illness in children (appendices)

Number of studies	Height of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	With SBI (Degrees C, mean)	Without SBI (Degrees C, mean)	P value							
For detecting bacteraemia										
1 (Crocker, 1985)	40.0 (SD 0.4)	40.1 (SD 0.3)	P value 'not significant'	High	Prospective	No serious	NA	No serious	NA	Yes ^p
1 (Haddon, 1999)	39.7 (SD 0.39)	39.7 (SD 0.55)	P = 0.91	High	Prospective	No serious	NA	No serious	NA	Yes ^q
1 (Singhi, 1992)	38.8 (SD 0.3)	38.8 (SD 0.15)	NR	High	Prospective	No serious	NA	No serious	NA	Yes ^r
1 (Singhi, 1992)	38.7 (SD 0.2)	38.8 (SD 0.15)	NR	High	Prospective	No serious	NA	No serious	NA	Yes ^r
1 (Teach, 1997)	40.0 (SD 0.61)	39.8 (SD 0.55)	P < 0.001	High	Prospective	No serious	NA	No serious	NA	Yes ^s
1 (Stathakis, 2007)	39.0 (SD 0.9)	38.8 (SD 1.0)	P = 0.80	Moderate	Retrospective	No serious	NA	No serious	NA	Yes ^t
For detecting meningococcal disease										
1 (Nielsen, 2001)	Median 40 (IQR/range not reported)	Median 39 (IQR/range not reported)	P < 0.01	High	Prospective	Serious ^u	NA	Serious ⁱ	NA	Yes ^v

Number of studies	Height of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	With SBI (Degrees C, mean)	Without SBI (Degrees C, mean)	P value							
For detecting pneumonia, urinary tract infection, meningitis, or bacteraemia										
1 (Rudinsky, 2009)	103.3F (SD 1.2)	103.2F (SD 1.2)	P = 0.26	Moderate	Prospective	Serious ^w	NA	No serious	NA	Yes ^x
For detecting urinary tract infection										
1 (Singhi, 1992)	38.8 (SD 0.1)	38.8 (SD 0.15)	NR	High	Prospective	No serious	NA	No serious	NA	Yes ^r

NA Not applicable, NR Not reported, SD standard deviation

^a Includes children aged between 28 and 90 days old. Includes those with a rectal temperature of 38°C or higher at presentation, or a parental history of an equivalent rectal temperature. Undertaken in an emergency department in the USA.

^b Includes children aged from 7 days to 36 months. Includes those with a temperature of 38°C or higher. Undertaken in a hospital in Switzerland.

^c Includes children aged between 2 and 6 months old. Includes those with a rectal temperature higher than 37.9°C. Undertaken in the emergency departments of a children's hospital in the USA.

^d Includes children aged from 7 days to 36 months. Includes those with a rectal temperature higher than 38°C. Undertaken in a hospital in Switzerland.

^e Includes children aged less than 3 months. Includes those with an axillary temperature of 38°C or higher. Undertaken in a hospital in South Korea.

^f Not all children had blood culture performed to confirm serious illness

^g Includes children aged less than 3 years. Includes children with a fever, although fever was not defined. Undertaken in a hospital in Italy.

^h Includes children aged 29 to 89 days old. Includes those with a rectal temperature higher than 38°C. Undertaken in a tertiary care paediatric unit in Greece.

ⁱ Children were aged up to 16 years old

^j Included children aged 1 month to 16 years old. Included those with a temperature higher than 38.5°C, a recent high fever or fever as a reason for referral. Undertaken in the emergency department of a children's hospital in the Netherlands.

^k Includes children aged between 4 and 90 days old. Includes those with a rectal temperature greater than 38°C. Undertaken in an emergency department in Spain.

^l It is not clearly reported how many children were retrospectively recruited

^m Includes children aged 90 days or younger. Includes those with a temperature of 38°C or higher. Undertaken in a hospital in the USA.

ⁿ Includes children up to 16.5 years old (mean 33.9 months)

^o Includes children aged between 1 month and 16.5 years with fever and petechiae (fever not defined). Undertaken in a medical centre in the USA.

^p Includes children aged between 6 months and 2 years. Includes those with a rectal temperature of 39.4°C. Undertaken in a hospital in the USA.

^q Includes children aged between 3 and 36 months. Includes those with a temperature by tympanic thermometry of 39°C or higher. Undertaken in an emergency department in Australia.

Feverish illness in children (appendices)

^r Includes children aged between 1 month and 3 years. Includes those with an axillary temperature of higher than 38.5°C or a rectal temperature of 39°C or higher. Excluded those whose fever had lasted for 3 days or more. Undertaken at a hospital in India.

^s Included children aged from 90 days to 36 months old. Includes those with an initially recorded temperature of 39°C or higher. Undertaken as part of a multicentre study in the USA.

^t Includes children aged 3 to 36 months old. Includes those with a core temperature of 38°C or above measured by tympanic thermometer. Undertaken in a paediatric emergency department in Australia.

^u 10 of the 39 cases of meningococcal disease were probable rather than confirmed

^v Includes children aged from 1 month to 16 years. Includes those with a rectal temperature above 38°C at presentation or in the 24 hours prior to presentation. Undertaken at a hospital in Denmark.

^w The study authors report possible errors in the data from incomplete medical records. They also report that it is possible that the case definition of pneumonia overestimated the number of cases of pneumonia.

^x Includes children aged less than 3 months. Includes those with a temperature of 100.4°F or higher at home or at presentation. Undertaken in an emergency department in the USA.

Table I5.27 GRADE profile for evaluation of bulging fontanelle

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bulging fontanelle														
<i>For detecting serious bacterial illness</i>														
1 (Bleeker, 2001)	231	5 (2 to 9) ^a	90 (82 to 97) ^a	60 (35 to 85) ^a	24 (18 to 30) ^a	0.5 (0.2 to 1.4) ^a	1.1 (1.0 to 1.2) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g}	NA	No serious	Serious ^h	Yes ^{i, j}
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	8 (0 to 24) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	96 (93 to 98) ^a	NC	0.9 (0.8 to 1.1) ^a	Low	Prospective	Very serious ^{b, g}	NA	No serious	No serious	Yes ^{i, k}
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12807	1 (0 to 1) ^a	100 (100 to 100) ^a	19 (7 to 31) ^a	93 (92 to 93) ^a	3.0 (1.4 to 6.5) ^a	1.0 (1.0 to 1.0) ^a	Low	Prospective	Very serious ^{d, l, m}	NA	No serious	No serious	Yes ^{i, n}

NA Not applicable, NC Not calculable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

^c It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^d Not all of the children received the same test to confirm serious illness

^e It is not clear if the child's signs and symptoms formed part of the test to confirm serious illness

^f It is not clear if the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious infection

^g It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms

^h The difference between the lower and upper confidence intervals is greater than 40% for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value

ⁱ It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^j Includes children aged 1 to 36 months. Includes temperatures equal to or greater than 38°C. Undertaken in the emergency department of two children's hospitals in the Netherlands

^k Included children aged 6 months to 5 years. Fever was not defined, included children with seizure associated with fever. Undertaken in the paediatric department of a hospital in Iran.

^l It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^m It is not clear if the test to confirm serious illness was independent of the child's signs and symptoms

ⁿ Included children were less than 5 years old. Included children had a measured axillary temperature of greater than or equal to 38°C; parental report of a temperature of greater than or equal to 38°C measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever (10th revision of the international classification of diseases, Australian modification codes R50, R50.0, R50.1, R50.9 and R56.0), as determined by a triage nurse. The study was undertaken in a hospital in Australia.

Table I5.28 GRADE profile for evaluation of neck stiffness

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Nuchal rigidity														
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	8 (0 to 24) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	96 (93 to 98) ^a	NC	0.9 (0.8 to 1.1) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e}
1 (Offringa, 1992)	92	48 (27 to 68) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	85 (77 to 93) ^a	NC	0.5 (0.4 to 0.8) ^a	Very low	Retrospective	Very serious ^{b, c, f, g, h, i}	NA	Serious ^j	Serious ^k	Yes ^{d, l}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	41 (26 to 56) ^a	97 (94 to 100) ^a	76 (58 to 94) ^a	88 (83 to 92) ^a	13.9 (5.4 to 35.6) ^a	0.6 (0.5 to 0.8) ^a	Very low	Prospective	Very serious ^{b, c, g, h, i, m}	NA	Serious ⁿ	No serious	Yes ^{d, o}

NA Not applicable

NC Not calculable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice

^c It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms

^d It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study

^e Included children aged 6 months to 5 years. Fever not defined, seizures associated with fever. Undertaken in the paediatric department of a hospital in Iran

^f It is unclear whether the test used to confirm serious illness was likely to confirm the serious illness being detected

^g Not all of the children received the same test to confirm serious illness

^h It is not clear if the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious infection

ⁱ It is not clear whether the whole sample (or a random selection of the sample) were tested to confirm serious infection

^j Includes children aged from 3 months to 6 years

^k The confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%

^l Includes children aged 3 months to 6 years. Fever not defined, seizure associated with fever. Undertaken in the emergency department of two hospitals in the Netherlands.

^m It is not clear if the child's signs and symptoms formed part of the test to confirm serious illness

ⁿ Includes children aged from 1 month to 16 years

^o Includes children aged from 1 month to 16 years. Includes temperature greater than 38°C some time within the 24 hours prior to inclusion. Children had skin haemorrhages. Undertaken in five paediatric departments in hospitals in Denmark.

Table I5.29 GRADE profile for evaluation of focal seizures

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Focal seizures														
<i>For detecting meningitis</i>														
1 (Akpede, 1992)	522	41 (20 to 61) ^a	92 (90 to 94) ^a	18 (8 to 29) ^a	97 (96 to 99) ^a	5.1 (2.9 to 9.2) ^a	0.6 (0.5 to 0.9) ^a	Very low	Prospective	Very serious ^{b, c, d}	NA	Serious ^e	Serious ^f	Yes ^{g, h}
1 (Joffe, 1983)	241	38 (12 to 65) ⁱ	91 (87 to 95) ⁱ	20 (4 to 34) ⁱ	96 (94 to 99) ⁱ	4.2 (1.9 to 9.3) ^a	0.7 (0.4 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	Serious ^j	Serious ^f	Yes ^{f, k}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study.^b It is unclear whether the spectrum of children in the study is representative of those who will present to a healthcare professional in practice.^c It is not clear if the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious infection.^d It is not clear if the results of the test used to confirm serious infection were interpreted without knowledge of the child's signs and symptoms.^e Included children aged from 1 month to 6 years old.^f The confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%.^g It is unclear whether all of the data that would be available when signs and symptoms are interpreted in practice were available in the study.^h Included children aged 1 month to 6 years. Included temperatures 38°C or greater, convulsions associated with fever. Undertaken in the children's emergency room of a hospital in Nigeria.ⁱ Confidence intervals were calculated by the NCC-WCH based on results reported in the study.^j Included children from 6 months to 6 years old.^k Included children aged 6 months to 6 years. Fever not defined, seizure associated with fever. Undertaken in the emergency room of a hospital in the USA.

Table I5.30 GRADE profile for evaluation of non-blanching rash

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Rash														
<i>For detecting serious bacterial infection</i>														
1 (Nijman, 2011)	1255	3 (0 to 6) ^a	97 (96 to 98) ^a	12 (1 to 23) ^a	90 (88 to 91) ^a	1.1 (0.4 to 3.1) ^a	1.0 (1.0 to 1.0) ^a	Very serious	Prospective	Very serious ^{b, c, d, e}	NA	Serious ^f	No serious	Yes ^g
<i>For detecting pneumonia, UTI or bacteraemia</i>														
1 (Craig, 2010)	12,807	12 (10 to 14) ^a	82 (81 to 83) ^a	5 (4 to 6) ^a	92 (92 to 93) ^a	0.7 (0.6 to 0.8) ^a	1.1 (1.1 to 1.1) ^a	Low	Prospective	Very serious ^{b, c, h}	NA	No serious	No serious	Yes ^{g, i}
Purpura														
<i>For detecting bacteraemia</i>														
1 Mandl (1997)	411	83 (40 to 99)	97 (95 to 98)	31 (5 to 57)	99 (99 to 100)	28.1 (14.5 to 54.5) ^a	0.2 (0.0 to 1.0) ^a	Very low	Prospective and retrospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^k	Serious ^l	Yes ^{g, m, n, o}
Petechiae														
<i>For detecting serious disease</i>														
1 (Nademi, 2001)	141	29 (15 to 43)	98 (95 to 100)	86 (67 to 100)	77 (69 to 84)	8.9 (2.6 to 30.4) ^a	0.8 (0.6 to 0.9) ^a	Very low	Prospective	Very serious ^{b, d, e}	NA	Serious ^f	No serious	Yes ^{g, p}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting invasive disease</i>														
1 (Baker, 1989)	190	40 (15 to 65) ^a	89 (80 to 98) ^a	55 (25 to 84) ^a	82 (71 to 92) ^a	3.6 (1.3 to 10.1) ^a	0.7 (0.4 to 1.0) ^a	Very low	Prospective	Very serious ^{c, d, e, j}	NA	Serious ^f	Serious ^l	Yes ^{g, q}
<i>For detecting meningitis</i>														
1 (Offringa, 1992)	401	13 (0 to 27) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	78 (69 to 86) ^a	NC	0.9 (0.7 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^r	No serious	Yes ^{n, s}
Purpura and petechiae														
<i>For detecting serious invasive bacteraemia</i>														
1 Mandl (1997)	411	83 (54 to 100) ^a	97 (95 to 99) ^a	31 (9 to 54) ^a	100 (99 to 100) ^a	28.5 (14.4 to 56.4) ^a	0.2 (0.0 to 1.0) ^a	Very low	Prospective and retrospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^k	Serious ^l	Yes ^{g, m, n, o}
More than 20 skin haemorrhages														
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	74 (61 to 88) ^a	49 (42 to 57) ^a	25 (17 to 33) ^a	89 (83 to 96) ^a	1.5 (1.2 to 1.9) ^a	0.5 (0.3 to 0.9) ^a	Very low	Prospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^f	No serious	Yes ^{g, t}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Maximum diameter of haemorrhages greater than 1mm														
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	95 (88 to 100) ^a	78 (72 to 84) ^a	50 (39 to 61) ^a	99 (96 to 100) ^a	4.3 (3.2 to 5.8) ^a	0.1 (0.0 to 0.3) ^a	Very low	Prospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^f	No serious	Yes ^{g, t}
Maximum diameter of haemorrhages greater than 2mm														
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	74 (61 to 88) ^a	92 (88 to 96) ^a	67 (53 to 81) ^a	94 (90 to 98) ^a	9.0 (5.3 to 15.3) ^a	0.3 (0.2 to 0.5) ^a	Very low	Prospective	Very serious ^{b, c, d, e, h, j}	NA	Serious ^f	No serious	Yes ^{g, t}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children received the same test to confirm serious illness

^c It is not clear whether the test to confirm serious illness was independent of the symptoms and signs

^d It is unclear whether the symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness

^e It is unclear whether the results of the test to confirm serious illness were interpreted without knowledge of the symptoms or signs

^f Included children up to 16 years old

^g It is not clear whether the same clinical data were available as would be when the test is used in practice

^h It is not clear whether all of the children (or a random selection of the children) received a test to confirm serious illness

ⁱ Included children under 5 years of age. Included those with an axillary temperature of 38°C or higher; a parental report of a temperature of 38°C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in the emergency department of a children's hospital in Australia

^j It is unclear whether the spectrum of children included was representative of those that would be seen in practice

^k Included children up to 18 years old

^l The difference between the upper and lower confidence intervals for one, two, or three of sensitivity, specificity, positive predictive value or negative predictive value was 40% or greater

^m It is unclear whether the period of time between assessing the child's symptoms and signs and using a test to confirm serious illness was short enough

ⁿ Not enough detail regarding the test for serious illness was provided to allow another clinician to repeat the test

^o Included children aged 18 years and younger. Included those with a temperature of 38°C or higher. Undertaken in the emergency department of a paediatric hospital in the USA.

^p Included children aged up to 16 years old. Included those with a temperature of 38°C or higher. Undertaken in the paediatric assessment unit of two hospitals in the UK.

^q Included children up to 15 years old. Included those with a temperature higher than 38°C. Undertaken in a children's hospital medical centre in the USA.

^r Included children up to 6 years old

^s Included children from 3 months to 6 years old. Fever was not defined, included children had had a seizure associated with fever. Undertaken in the emergency room of a hospital in the Netherlands.

^t Included children aged 1 month to 16 years. Included those with a fever higher than 38°C. Undertaken in a hospital in Denmark.

Table I5.31 GRADE profile for evaluation of diarrhoea

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Diarrhoea														
<i>For detecting serious bacterial infection</i>														
1 (Craig, 2010)	15781	21 (19 to 24) ^a	74 (73 to 75) ^a	6 (5 to 7) ^a	92 (92 to 93) ^a	0.8 (0.7 to 0.9) ^a	1.1 (1.0 to 1.1) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e, f}
1 (Berger, 1996)	138	55 (38 to 72) ^a	20 (12 to 28) ^a	18 (10 to 25) ^a	58 (42 to 74) ^a	0.7 (0.5 to 0.9) ^a	2.3 (1.3 to 3.9) ^a	Low	Prospective	Very serious ^{b, c, g, h}	NA	No serious	No serious	Yes ^{d, e, i}
<i>For detecting urinary tract infection</i>														
1 (Morris, 2007)	98	NC ^j	NC ^j	NC ^j	NC ^j	NC ^j	NC ^j	Low	Prospective	Very serious ^{c, g, h, k, l}	NA	No serious	NA	Yes ^{d, e, m, n}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting bacterial illness</i>														
1 (Trautner, 2006)	103	NC ^o	NC ^o	NC ^o	NC ^o	NC ^o	NC ^o	Very low	Prospective	Very serious ^{c, g, h, p}	NA	Serious ^q	NA	Yes ^{d, e, m, r}
Diarrhoea and vomiting														
<i>For detecting serious bacterial infection</i>														
1 (Nijman, 2011)	1255	6 (2 to 10) ^a	91 (89 to 92) ^a	7 (2 to 12) ^a	89 (87 to 91) ^a	0.6 (0.3 to 1.3) ^a	1.0 (1.0 to 1.1) ^a	Very low	Prospective	Very serious ^{c, g, h, l}	NA	Serious ^s	No serious	Yes ^{e, t}
Mild gastrointestinal symptoms														
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	15 (4 to 25) ^a	89 (84 to 94) ^a	24 (7 to 41) ^a	81 (76 to 87) ^a	1.3 (0.6 to 3.1) ^a	1.0 (0.8 to 1.1) ^a	Low	Prospective	Very serious ^{g, h, l}	NA	No serious	No serious	Yes ^{e, u}

NC Non-calculable

^a Calculated by the NCC-WCH based on results reported in the study.^b It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness.^c It is not clear whether all of the children received the same test to confirm serious illness.^d It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough.^e It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice.^f Included children were under 5 years. Children were included if they had an axillary temperature/parental report of a temperature of 38°C or higher. The study was conducted in the emergency department of a hospital in Australia. Results are reported per illness rather than per child – some children were included more than once for different illnesses.^g It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness.^h It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

ⁱ Included children were between 2 weeks and 1 years old with a rectal temperature of 38°C or higher. The study was undertaken in the paediatric emergency room of a hospital in the Netherlands.

^j Text in the paper stated that diarrhoea is not predictive of urinary tract infection

^k The selection criteria used to recruit children into the study were not clearly described

^l It is not clear whether the test to confirm serious illness was independent of the child's symptoms and signs

^m Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician

ⁿ Included children less than 36 months. Included those with an axillary temperature higher than 37.2°C. The study was undertaken in the Children's Outpatients Department in a hospital in Papua New Guinea

^o The paper reported: OR 3.93 (95% CI 1.27 to 12.19)

^p It is not clear whether the spectrum of included participants in the study was representative of the children that would be assessed in practice

^q Included children were less than 18 years old. 84.5% were 3 -35 months and 15.5% were 36 months or younger.

^r Included children were less than 18 years old with a rectal temperature of 41.1°C or higher. The study was undertaken in the paediatric emergency department of a hospital in USA.

^s Included children aged 1 month to 16 years. Included those with a temperature of 38.5°C or higher, a recent high fever, or fever as a reason for referral. Conducted in the emergency department of a children's hospital in the Netherlands.

^t Included children up to 16 years old (83% of children were five years old or younger)

^u Included children aged less than 3 months. Included those with axillary temperature of 38°C or higher. Undertaken in an outpatients clinic in South Korea.

Table I5.32 GRADE profile for evaluation of vomiting

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Vomiting														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2007)	381	49 (40 to 59) ^a	69 (64 to 75) ^a	36 (28 to 44) ^a	80 (75 to 85) ^a	1.6 (1.2 to 2.1) ^a	0.7 (0.6 to 0.9) ^a	Low	Prospective	Very serious ^{b, c, d, e}	NA	No serious	No serious	Yes ^{f, g, h, i}
1 (Bleeker, 2001)	231	37 (30 to 44) ^a	43 (30 to 56) ^a	66 (57 to 75) ^a	19 (12 to 25) ^a	0.7 (0.5 to 0.9) ^a	1.5 (1.1 to 2.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, e}	NA	No serious	No serious	Yes ^{f, g, h, j}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting serious disease</i>														
1 (Nademi, 2001)	141	59 (43 to 73)	60 (50 to 69)	38 (25 to 49)	78 (68 to 87)	1.5 (1.0 to 2.1) ^a	0.7 (0.5 to 1.0) ^a	Very low	Prospective	Very serious ^{b, c, d, e, k, l}	NA	Serious	No serious	Yes ^{f, g, h, n}
<i>For detecting bacterial illness</i>														
1 (Trautner, 2006)	103	NR ^o	NR ^o	NR ^o	NR ^o	NR ^o	NR ^o	Very low	Prospective	Very serious ^{b, c, d, l}	NA	Serious	NA	Yes ^{f, g, q, r}
<i>For detecting urinary tract infection</i>														
1 (Morris, 2007)	98	NR ^s	NR ^s	NR ^s	NR ^s	NR ^s	NR ^s	Low	Prospective	Very serious ^{b, c, d, k, t}	NA	No serious	NA	Yes ^{f, g, q, u}
1 (Rabasa Al, 2009)	145	60 (39 to 81) ^a	60 (51 to 69) ^a	19 (10 to 29) ^a	90 (84 to 97) ^a	1.5 (1.0 to 2.3) ^a	0.7 (0.4 to 1.2) ^a	Low	Prospective	Very serious ^{b, c, d, e}	NA	No serious	Serious	Yes ^{g, q, v}
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	67 (40 to 93) ^a	100 (100 to 100) ^a	100 (100 to 100) ^a	98 (97 to 100) ^a	NC	0.3 (0.1 to 0.7) ^a	Very low	Prospective	Very serious ^{c, d, t}	NA	No serious	Serious	Yes ^{f, g, q, w}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
1 (Offringa, 1992)	92	48 (27 to 68) ^a	81 (72 to 90) ^a	46 (26 to 66) ^a	82 (73 to 91) ^a	2.5 (1.3 to 4.9) ^a	0.6 (0.4 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, l, t}	NA	Serious ^x	Serious	Yes ^{f, g, y}
<i>For detecting meningococcal disease</i>														
1 (Nielsen, 2001)	208	44 (28 to 59) ^a	60 (52 to 67) ^a	20 (12 to 29) ^a	82 (75 to 89) ^a	1.1 (0.7 to 1.6) ^a	0.9 (0.7 to 1.3) ^a	Very low	Prospective	Very serious ^{b, c, d, e, l}	NA	Serious ^z	No serious	Yes ^{g, aa}
Increased vomiting														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	15 (9 to 20) ^a	82 (80 to 84) ^a	8 (5 to 11) ^a	90 (88 to 92) ^a	0.8 (0.6 to 1.2) ^a	1.0 (1.0 to 1.1) ^a	Low	Prospective	Very serious ^{b, e, t}	NA	No serious	No serious	Yes ^{f, g, q, ab}
Diarrhoea and vomiting														
<i>For detecting serious bacterial infection</i>														
1 (Nijman, 2011)	1255	6 (2 to 10) ^a	91 (89 to 92) ^a	7 (2 to 12) ^a	89 (87 to 91) ^a	0.6 (0.3 to 1.3) ^a	1.0 (1.0 to 1.1) ^a	Very low	Prospective	Very serious ^{b, c, d, k}	NA	Serious ^{ac}	No serious	Yes ^{g, ad}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Mild gastrointestinal symptoms														
<i>For detecting serious bacterial infection</i>														
1 (Shin, 2009)	221	15 (4 to 25) ^a	89 (84 to 94) ^a	24 (7 to 41) ^a	81 (76 to 87) ^a	1.3 (0.6 to 3.1) ^a	1.0 (0.8 to 1.1) ^a	Low	Prospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{g, ae}

NR Not reported

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children received the same test to confirm serious illness

^c It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness

^d It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^e It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness

^f It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough

^g It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^h Not enough detail regarding the test to confirm serious illness was provided to allow another clinician to replicate the results

ⁱ Included children 1 to 36 months with acute fever without apparent source. The study was undertaken in two hospitals in the Netherlands.

^j Included children 1 to 36 months with acute fever without apparent source. The study was undertaken in two hospitals in the Netherlands.

^k It is not clear whether the test to confirm serious illness was independent of the child's symptoms and signs

^l It is not clear whether the spectrum of included participants in the study was representative of the children that would be assessed in practice

^m Included children from 8 days to 16 years old

ⁿ Included children 8 days to 16 years with a temperature of 38°C or higher. The study was undertaken in two hospitals in the UK.

^o The paper reported: OR 0.76 (95% CI 0.26 to 2.18)

^p Included children less than 18 years

^q Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician

^r Included children were less than 18 years old with a rectal temperature of 41.1°C or higher. The study was undertaken in the paediatric emergency department of a hospital in USA.

^s The text in the paper stated that vomiting is not predictive of urinary tract infection

^t The selection criteria used to recruit children into the study were not clearly described

^u Included children less than 36 months. Included axillary temperatures higher than 37.2°C. The study was undertaken in the Children's Outpatients Department in a hospital in Papua New Guinea.

^v Included children 1 month to 60 months (5 years) with an axillary temperature of 37.5°C or higher. The study was undertaken in the paediatric department of a hospital in Nigeria.

^w Included children 6 months to 5 years. Fever was not defined. The study was undertaken in the paediatric ward of a hospital in Iran.

^x Included children up to the age of 6

^y Included children 3 months to 6 years with first episode of seizure associated with fever (fever not defined). The study was undertaken in two hospitals in the Netherlands.

^z Included children older than 1 month and younger than 16 years old

^{aa} Included children greater than 1 month and less than 16 years with rectal temperature above 38°C. The study was undertaken in 5 paediatric departments in Denmark.

^{ab} Included children 3 months or younger with an axillary, rectal or tympanic temperatures of 38°C or higher. The study was undertaken in GP offices in USA.

^{ac} Included children up to the age of 16 (83% of children were aged 5 years or younger)

^{ad} Included children aged 1 month to 16 years. Included those with a temperature of 38.5°C or higher, or a history of fever, or fever as a reason for referral. Undertaken in the emergency department of a paediatric hospital in the Netherlands.

^{ae} Included children aged less than 3 months. Included those with axillary temperature of 38°C or higher. Undertaken in an outpatients clinic in South Korea.

Table I5.33 GRADE profile for evaluation of abdominal pain

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Abdominal pain														
<i>For detecting serious illness</i>														
1 (Nijman, 2011)	1255	5 (1 to 8) ^a	97 (95 to 98) ^a	13 (3 to 23) ^a	90 (88 to 91) ^a	1.3 (0.6 to 3.1) ^a	1.0 (1.0 to 1.0) ^a	Very low	Prospective	Very serious ^{b, c, d, e}	NA	Serious ^f	No serious	Yes ^{g, h}
<i>For detecting urinary tract infection</i>														
1 (Morris, 2007)	98	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	NR ⁱ	Low	Prospective	Very serious ^{b, c, d, e, j}	NA	No serious	NA	Yes ^{g, k, l, m}

NR Not reported

^a Calculated by the NCC-WCH based on data reported in the study

^b It is not clear whether all of the children received the same test to confirm serious illness

^c It is not clear whether the test to confirm serious illness was independent of the child's symptoms and signs

^d It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness

Feverish illness in children (appendices)

^e It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^f Included children up to the age of 16 years

^g It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^h Included children aged less than 36 months. Included axillary temperatures higher than 37.2°C. The study was undertaken in the Children's Outpatient Department of a hospital in Papua New Guinea.

ⁱ The text in the paper stated that abdominal pain is not predictive of urinary tract infection

^j The selection criteria used to recruit children into the study were not clearly described

^k It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough

^l Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician

^m Included children with a fever of 38.5°C or higher, a recent high fever, or fever as a reason for referral. Included children aged 1 month to 16 years. Undertaken in the emergency department of a children's hospital in the Netherlands.

Table I5.34 GRADE profile for evaluation of crying on micturition/dysuria

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Crying on micturition/dysuria														
<i>For detecting urinary tract infection</i>														
1 (Rabasa AI, 2009)	145	10 (0 to 23) ^a	86 (79 to 92) ^a	10 (0 to 23) ^a	86 (79 to 92) ^a	0.7 (0.2 to 2.8) ^a	1.1 (0.9 to 1.2) ^a	Low	Propose ctive	Very seriou s ^{b, c, d, e}	NA	No serious	No serious	Yes ^{f, g, h}

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness

^c It is not clear whether all of the children received the same test to confirm serious illness

^d It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness

^e It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^f Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician

^g It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^h Included children aged 1 month to 60 months (5 years) old with an axillary temperature of 37.5°C or higher. The study was undertaken in the paediatric department of a hospital in Nigeria.

Table I5.35 GRADE profile for evaluation of headache

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Headache														
<i>For detecting meningitis</i>														
1 (Ghotbi, 2009)	254	17 (0 to 38) ^a	100 (99 to 100) ^a	67 (13 to 100) ^a	96 (94 to 98) ^a	40.3 (3.9 to 414.3) ^a	0.8 (0.6 to 1.1) ^a	Very low	Prospective	Very serious ^{b, c, d}	NA	No serious	Serious ^e	Yes ^{f, g, h, i}

^a Calculated by the NCC-WCH based on results reported in the study^b The selection criteria used to recruit children into the study were not clearly described^c It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness^d It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^e The difference between the upper and lower confidence intervals is 40% or greater for 1,2, or 3 of sensitivity, specificity, PPV and NPV^f It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough^g Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician^h It is not clear whether the same clinical data were available during the study as would be available when the test is used in practiceⁱ Included children 6 months to 5 years. Fever was not defined. The study was undertaken in the paediatric ward of a hospital in Iran.

Table I5.36 GRADE profile for evaluation of conjunctivitis

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Conjunctivitis														
<i>For detecting urinary tract infection</i>														
1 (Newman, 2002)	1666	1 (1 to 2) ^a	99 (99 to 100) ^a	7 (6 to 21) ^a	90 (89 to 92) ^a	0.7 (0.1 to 5.5) ^a	1.0 (1.0 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g, h}

^a Calculated by the NCC-WCH based on results reported in the study^b The selection criteria used to recruit children into the study were not clearly described^c It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^d It is not clear whether all of the children received the same test to confirm serious illness^e It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough^f Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician^g It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice^h Included children 3 months or younger with axillary, rectal or tympanic temperatures of 38°C or higher. The study was undertaken in GP offices in USA.

Table I5.37 GRADE profile for evaluation of poor peripheral circulation

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Poor peripheral circulation														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2001)	231	11 (6 to 16) ^a	78 (69 to 88) ^a	59 (42 to 76) ^a	23 (17 to 28) ^a	0.5 (0.3 to 0.9) ^a	1.1 (1.0 to 1.3) ^a	Very low	Retro specti ve	Very serious ^{b, c, d, e}	NA	No serious	No serious	Yes ^{f, g, h, i}

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether all of the children (or a random selection of the children) received a test to confirm serious illness^c It is not clear whether all the children received the same test to confirm serious illness^d It is not clear whether the clinical symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness^e It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the clinical symptoms and signs^f It is not clear whether the period of time between assessing the symptoms and signs and performing the test to confirm serious illness was short enough^g Not enough detail was provided regarding the test to confirm serious illness to allow it to be performed by another clinician^h It is not clear whether the same clinical data that was available when the test results were interpreted would be available in practiceⁱ Included children 1 to 36 months with acute fever without apparent source. The study was undertaken in two hospitals in the Netherlands.

Table I5.38 GRADE profile for evaluation of bulging abdomen

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bulging abdomen														
<i>For detecting serious bacterial infection</i>														
1 (Bleeker, 2001)	231	6 (2 to 9) ^a	88 (80 to 96) ^a	59 (35 to 82) ^a	24 (18 to 30) ^a	0.5 (0.2 to 1.2) ^a	1.1 (1.0 to 1.2) ^a	Very low	Retrospective	Very serious ^{b, c, d, e}	NA	No serious	Serious ^f	Yes ^{g, h, i, j}

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^c It is not clear whether all of the children received the same test to confirm serious illness^d It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness^e It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^f The difference between the upper and lower confidence intervals is 40% or greater for 1,2, or 3 of sensitivity, specificity, PPV and NPV^g It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough^h Not enough detail regarding the test to confirm serious illness was provided to allow another clinician to replicate the resultsⁱ It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice^j Included children 1 to 36 months with acute fever without apparent source. The study was undertaken in two hospitals in the Netherlands.

Table I5.39 GRADE profile for evaluation of paresis or paralysis

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Paresis or paralysis														
<i>For detecting meningitis</i>														
1 (Offringa, 1992)	92	30 (12 to 49) ^a	91 (85 to 98) ^a	54 (27 to 81) ^a	80 (71 to 89) ^a	3.5 (1.3 to 9.4) ^a	0.8 (0.6 to 1.0) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, g}	NA	Serious ^h	Serious ⁱ	Yes ^{j, k, l}

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether the spectrum of included participants in the study was representative of the children that would be assessed in practice^c The selection criteria used to recruit children into the study were not clearly described^d It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^e It is not clear whether all of the children received the same test to confirm serious illness^f It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness^g It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^h Included children up to the age of 6ⁱ The difference between the upper and lower confidence intervals is 40% or greater for 1,2, or 3 of sensitivity, specificity, PPV and NPV^j It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough^k It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice^l Included children 3 months to 6 years with first episode of seizure associated with fever (fever not defined). The study was undertaken in two hospitals in the Netherlands.

Table I5.40 GRADE profile for evaluation of abnormal neurological findings

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Abnormal neurological findings														
<i>For detecting meningitis</i>														
1 (Joffe, 1983)	241	92 (78 to 100) ^a	84 (79 to 89) ^a	25 (13 to 37) ^a	99 (98 to 100) ^a	5.8 (4.2 to 8.2) ^a	0.1 (0.0 to 0.6) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f}	NA	Serious ^g	No serious	Yes ^{h, i, j}
1 (Offringa, 1992)	92	64 (44 to 84) ^a	91 (88 to 94) ^a	35 (20 to 50) ^a	97 (95 to 99) ^a	7.0 (4.3 to 11.4) ^a	0.4 (0.2 to 0.7) ^a	Very low	Retrospective	Very serious ^{b, c, d, e, f, k}	NA	Serious ^g	Serious ^l	Yes ^{h, i, m}
Neurological deficit														
<i>For detecting meningitis</i>														
1 (Batra, 2011)	199	80 (45 to 100) ^a	99 (98 to 100) ^a	80 (45 to 100) ^a	99 (98 to 100) ^a	155.2 (20.9 to 1150.8) ^a	0.2 (0.0 to 1.2) ^a	Very low	Retrospective	Very serious ^{c, d, e, f, n}	NA	No serious	Serious ^l	Yes ^{h, i, o}

^a Calculated by the NCC-WCH based on data reported in the study^b It is not clear whether the spectrum of included participants in the study was representative of the children that would be assessed in practice^c It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^d It is not clear whether all of the children received the same test to confirm serious illness^e It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness^f It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^g Included children up to the age of 6^h It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enoughⁱ It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^j Included children between 6 months and 6 years. Fever was not defined. The study was undertaken in two hospitals in the USA.

^k The selection criteria used to recruit children into the study were not clearly described

^l The difference between the highest and lowest confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and/or negative predictive value are greater than 40%

^m Included children 3 months to 6 years with first episode of seizure associated with fever (fever not defined). The study was undertaken in two hospitals in the Netherlands.

ⁿ It is not clear whether the test to confirm serious illness was independent of the child's symptoms and signs

^o Included children aged 6-18 months presenting with a first episode of seizure with fever. Fever not defined. The study was undertaken in the paediatric casualty ward of a hospital in India.

Table I5.41 GRADE profile for evaluation of impression of tone

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Impression of tone														
<i>For detecting bacteraemia</i>														
1 (Crain, 1982)	175	NR ^a	NR ^a	NR ^a	NR ^a	NR ^a	NR ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	NA	Yes ^{d, e, f}

^a Text in the paper stated that impression of tone is not significantly associated with bacteraemia

^b It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^c The selection criteria used to recruit children into the study were not clearly described

^d It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^e It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough

^f Included children 8 weeks old and younger. Included rectal temperatures of 38°C and greater. The study was undertaken in a paediatric emergency room in the USA.

Table I5.42 GRADE profile for evaluation of tenderness on examination

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Tenderness on examination														
<i>For detecting urinary tract infection</i>														
1 (Shaw, 1998)	2411	5 (0 to 10) ^a	99 (98 to 99) ^a	13 (1 to 26) ^a	97 (96 to 98) ^a	4.5 (1.6 to 12.5) ^a	1.0 (0.9 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}

^a Calculated by the NCC-WCH based on data reported in the study^b It is not clear whether the spectrum of included participants in the study was representative of the children that would be assessed in practice^c It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^d It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^e Not enough detail was provided to allow the child's symptom or sign to be assessed by a different clinician^f It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice^g Included boys younger than 1 year and girls younger than 2 years. Included children with a temperature of 38.3°C or higher. It took place in an emergency department in the USA

Table I5.43 GRADE profile for evaluation of urinary symptoms

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Urinary symptoms														
<i>For detecting serious bacterial infection</i>														
1 (Craig, 2010)	15781	5 (4 to 6) ^a	98 (98 to 98) ^a	17 (13 to 21) ^a	93 (93 to 93) ^a	2.7 (2.0 to 3.6) ^a	1.0 (1.0 to 1.0) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e, f}
1 (Nijman, 2011)	1255	8 (4 to 13) ^a	99 (98 to 99) ^a	41 (22 to 59) ^a	90 (89 to 92) ^a	5.9 (2.8 to 12.4) ^a	0.9 (0.9 to 1.0) ^a		Prospective	Very serious ^{c, g, h, i}	NA	Serious ^j	No serious	Yes ^{e, k}

^a Calculated by the NCC-WCH based on data reported in the study

^b It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness

^c It is not clear whether all of the children received the same test to confirm serious illness

^d It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough

^e It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice

^f Included children were under 5 years. Children were included if they had an axillary temperature or parental report of a temperature of 38°C or higher. The study was conducted in the emergency department of a hospital in Australia. Results are reported per illness rather than per child – some children were included more than once for different illnesses.

^g It is not clear if the test to confirm serious illness was independent of the child's symptoms and signs

^h It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the test to confirm serious illness

ⁱ It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^j Included children up to the age of 16 years old

^k Included children aged 1 month to 16 years. Included children with a temperature of 38.5°C or higher, a recent history of fever, or fever as a reason for referral. Undertaken in the emergency department of a children's hospital in the Netherlands.

Table I5.44 GRADE profile for evaluation of abnormal ear, nose and throat signs

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Abnormal ear, nose and throat signs														
<i>For detecting serious bacterial infection</i>														
1 (Craig, 2010)	15781	42 (39 to 45) ^a	45 (44 to 46) ^a	6 (5 to 6) ^a	91 (90 to 92) ^a	0.8 (0.7 to 0.8) ^a	1.3 (1.2 to 1.4) ^a	Low	Prospective	Very serious ^{b, c}	NA	No serious	No serious	Yes ^{d, e, f}
Ear problems														
<i>Serious bacterial infection</i>														
1 (Nijman, 2011)	1255	4 (1 to 7) ^a	99 (98 to 99) ^a	17 (3 to 31) ^a	94 (93 to 95) ^a	3.2 (1.2 to 8.3) ^a	1.0 (0.9 to 1.0) ^a	Very low	Prospective	Very serious ^{c, g, h, i}	NA	Serious ^j	No serious	Yes ^{e, k}

^a Calculated by the NCC-WCH based on data reported in the study^b It is not clear whether all of the children (or a random sample of the children) received the test to confirm serious illness^c It is not clear whether all of the children received the same test to confirm serious illness^d It is not clear whether the period of time between assessing the child's symptoms and signs and administering the test to confirm serious illness was short enough^e It is not clear whether the same clinical data were available during the study as would be available when the test is used in practice^f Included children were under 5 years. Children were included if they had an axillary temperature/parental report of a temperature $\geq 38^{\circ}\text{C}$. The study was conducted in the emergency department of a hospital in Australia. Results are reported per illness rather than per child – some children were included more than once for different illnesses.^g It is not clear whether the test to confirm serious illness was independent of the child's symptoms and signs^h It is not clear whether the child's symptoms and signs were interpreted without knowledge of the results of the tests to confirm serious illnessⁱ It is not clear whether the results of the tests to confirm serious illness were interpreted without knowledge of the child's symptoms and signs^j Included children aged up to 16 years^k Included children aged one month to 16 years. Included those with a temperature of 38.5°C or higher, recent high fever or fever as a reason for referral. Undertake in the emergency department of a children's hospital in the Netherlands.

Table I5.45 GRADE profile for evaluation of rigor and/or chills

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Rigors														
<i>For detecting confirmed or presumed bacterial illness</i>														
1 (Tal, 1997)	434	28 (23 to 34) ^a	83 (78 to 89) ^a	67 (78 to 95) ^a	49 (44 to 55) ^a	1.7 (1.2 to 2.5) ^a	0.9 (0.8 to 1.0) ^a	Very low	Prospective	Very serious ^{b, c, d}	NA	Serious ^e	No serious	Yes ^{f, g}

NA Not applicable

^a Calculated by the NCC-WCH based on results reported in the study^b It is not clear whether all children received the same test to confirm serious infection^c It is not clear whether the symptoms and signs were interpreted without knowledge of the results of the test for detecting serious illness^d It is not clear whether the results of the test for serious illness were interpreted without knowledge of the symptoms and signs^e Included children aged up to 16 years old^f Included children were aged 6 months to 16 years old. Children were included if they had a rectal temperature greater than or equal to 38.5°C and were admitted to hospital. The study was conducted in a hospital in Israel.^g It is not clear whether the same clinical data were available when the results of the test for serious illness were interpreted as would be available in practice

Table I5.46 GRADE profile for evaluation of Yale Observation Scale

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Score of 3 or 4														
<i>For detecting serious illness</i>														
1 (McCarthy, 1981)	312	67 (45 to 88) ^a	79 (74 to 84) ^a	19 (9 to 29) ^a	97 (95 to 99) ^a	3.2 (2.1 to 4.8) ^a	0.4 (0.2 to 0.8) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	No serious	Yes ^{e, f, g}
1 (McCarthy, 1981)	312	56 (33 to 79) ^a	89 (85 to 93) ^a	27 (13 to 41) ^a	96 (94 to 99) ^a	5.0 (2.9 to 8.7) ^a	0.5 (0.3 to 0.8) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	Serious ^h	Yes ^{e, f, g}
1 (McCarthy, 1981)	312	72 (52 to 93) ^a	79 (74 to 84) ^a	20 (10 to 30) ^a	97 (95 to 100) ^a	3.5 (2.4 to 5.0) ^a	0.4 (0.2 to 0.7) ^a	Very low	Retrospective	Very serious ^{b, c, d}	NA	No serious	Serious ^h	Yes ^{e, f, g}
Score of 4 or 5														
<i>For detecting bacteraemia</i>														
1 (Haddon, 1999)	534	6 (0 to 16) ^a	95 (92 to 97) ^a	5 (0 to 15) ^a	95 (93 to 97) ^a	1.0 (0.1 to 7.4) ^a	1.0 (0.9 to 1.1) ^a	Low	Prospective	Very serious ^{c, d}	NA	No serious	No serious	Yes ^{f, i}
Score of 5, 6, or 7														
<i>For detecting bacterial illness or pneumonia</i>														
1 (McCarthy, 1980)	219	60 (35 to 85) ^a	76 (70 to 82) ^a	16 (6 to 25) ^a	96 (93 to 99) ^a	2.5 (1.5 to 4.0) ^a	0.5 (0.3 to 1.0) ^a	Very low	Prospective	Very serious ^{b, c, d, e}	NA	No serious	Serious ^h	Yes ^{f, j}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
1 (McCarthy, 1980)	219	27 (4 to 49) ^a	94 (91 to 97) ^a	25 (4 to 46) ^a	95 (91 to 98) ^a	4.5 (1.7 to 12.4) ^a	0.8 (0.6 to 1.1) ^a	Very low	Prospective	Very serious ^{b, c, d, e}	NA	No serious	Serious ^h	Yes ^{f, j}
Score > 6														
<i>For detecting bacteraemia</i>														
1 (Teach, 1995)	6680	29 (22 to 35) ^m	83 (82 to 83) ^m	5 (3 to 6) ^m	97 (97 to 98) ^m	1.6 (1.3 to 2.1) ^a	0.9 (0.8 to 0.9) ^a	Very low	Retrospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, l}
Score > 8														
<i>For detecting bacteraemia</i>														
1 (Teach, 1995)	6680	17 (11 to 22) ^m	92 (91. to 93) ^m	6 (4 to 8) ^m	97 (97 to 98) ^m	2.0 (1.5 to 2.8) ^a	0.9 (0.9 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, l}
1 (Bang, 2009)	219	97 (79 to 99)	66 (55 to 72)	52 (43 to 62)	98 (93 to 100)	2.8 (2.2 to 3.5)	0.1 (0.0 to 0.2)	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, n}
Score > 9														
<i>For detecting serious bacterial infection</i>														
1 (Thayyil, 2005)	72	13 (0 to 35) ^a	33 (21 to 44) ^a	2 (0 to 7) ^a	75 (59 to 91) ^a	0.2 (0.0 to 1.2) ^a	2.7 (1.7 to 4.1) ^a	Low	Prospective	Very serious ^{b, d, k}	NA	No serious	No serious	Yes ^{f, o}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Score of > 10														
<i>For detecting serious illness (including aseptic meningitis)</i>														
1 (Baker, 1990)	126	46 (30 to 62) ^m	80 (71 to 88) ^m	49 (32 to 65) ^m	78 (70 to 87) ^m	2.3 (1.3 to 3.9) ^a	0.7 (0.5 to 0.9) ^a	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, p}
<i>For detecting serious bacterial infection</i>														
1 (Galletto-Lacour, 2003)	110	23 (5 to 54)	82 (67 to 92)	32 (12 to 51)	75 (66 to 84)	1.3 (0.6 to 2.9) ^m	0.9 (0.8 to 1.2) ^m	Very low	Prospective	Very serious ^{b, d, k}	NA	No serious	Serious ^h	Yes ^{f, q}
1 (Andreola, 2007)	408	38 (28 to 48) ^m	68 (63 to 73) ^m	26 (19 to 34) ^m	79 (74 to 83) ^m	1.2 (0.9 to 1.6) ^m	0.9 (0.8 to 1.1) ^m	Low	Prospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, r}
<i>For detecting bacteraemia</i>														
1 (Teach, 1995)	6680	5 (2 to 8) ^m	97 (96 to 97) ^m	5 (2 to 7) ^m	97 (97 to 98) ^m	1.6 (0.9 to 3.0) ^a	1.0 (0.9 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, l}
1 (Bang, 2009)	219	88 (71 to 93)	84 (73 to 87)	68 (56 to 78)	95 (89 to 98)	5.4 (3.7 to 7.9)	0.1 (0.1 to 0.3)	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, n}
<i>For detecting bacterial disease</i>														
1 (Baker, 1990)	126	33 (7 to 60) ^m	73 (65 to 81) ^m	11 (1 to 22) ^m	91 (85 to 97) ^m	1.2 (0.5 to 2.9) ^a	0.9 (0.6 to 1.4) ^a	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, p}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>For detecting urinary tract infection</i>														
1 (Zorc, 1995)	1025	4 (0 to 9) ^a	93 (91 to 94) ^a	6 (0 to 11) ^a	91 (89 to 93) ^a	0.6 (0.2 to 1.6) ^a	1.0 (1.0 to 1.1) ^a	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, s}
Score of 10 to 16														
<i>For detecting serious bacterial infection</i>														
1 (Andreola, 2007)	408	43 (33 to 53) ^a	74 (69 to 79) ^a	33 (24 to 41) ^a	81 (77 to 86) ^a	1.6 (1.2 to 2.2) ^a	0.8 (0.6 to 0.9) ^a	Low	Prospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, r}
Score of 11 to 15														
<i>For detecting serious illness</i>														
1 (McCarthy, 1982)	312	31 (16 to 46) ^a	84 (79 to 89) ^a	26 (13 to 39) ^a	87 (82 to 92) ^a	1.9 (1.1 to 3.4) ^a	0.8 (0.7 to 1.0) ^a	Low	Prospective	Very serious ^{b, c, d, k}	NA	No serious	No serious	Yes ^{f, j}
Score > 12														
<i>For detecting bacteraemia</i>														
1 (Teach, 1995)	6680	1 (0 to 2) ^m	99 (99 to 99) ^m	1 (0 to 4) ^m	97. (97 to 97) ^m	0.4 (0.1 to 3.2) ^a	1.0 (1.0 to 1.0) ^a	Very low	Retrospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, l}
1 (Bang, 2009)	219	48 (27 to 56)	91 (67 to 90)	68 (52 to 82)	82 (75 to 87)	5.5 (3.0 to 9.8)	0.6 (0.4 to 0.7)	Moderate	Prospective	Serious ^{d, k}	NA	No serious	No serious	Yes ^{f, n}

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Score of ≥ 16														
<i>For detecting serious illness</i>														
1 (McCarthy, 1982)	312	33 (18 to 49) ^a	99 (98 to 100) ^a	92 (78 to 100) ^a	89 (85 to 93) ^a	64.7 (8.7 to 482.0) ^a	0.7 (0.5 to 0.8) ^a	Low	Prospective	Very serious ^{b, c, d, k}	NA	No serious	No serious	Yes ^{f, j}
<i>For detecting serious bacterial infection</i>														
1 (Andreola, 2007)	408	9 (3 to 14) ^a	98 (96 to 99) ^a	53 (28 to 79) ^a	78 (74 to 82) ^a	3.8 (1.4 to 10.3) ^a	0.9 (0.9 to 1.0) ^a	Low	Prospective	Very serious ^{c, d, k}	NA	No serious	No serious	Yes ^{f, r}

NA Not applicable

^a Calculated by the NCC-WCH from results reported in the study

^b Not all children received the same test to confirm serious illness

^c It is not clear whether the test to confirm serious illness was independent of the child's signs and symptoms

^d It is not clear whether the results of the test to confirm serious illness were interpreted without knowledge of the child's symptoms and signs

^e Not enough detail was provided to allow the test to confirm serious illness to be replicated by another healthcare professional

^f It is not clear if the same data were available when interpreting the test results as would be available in practice

^g Included children aged 24 months or less. Included temperatures of 38.3°C or higher. Undertaken in an emergency room of a hospital in the USA.

^h The difference between the upper and lower confidence intervals for one, two or three of sensitivity, specificity, positive predictive value and negative predictive value is 40% or greater

ⁱ Included children aged 3 to 36 months. Included temperatures of 39°C or higher by tympanic thermometry. Undertaken in an emergency department in Australia.

^j Included children aged 24 months or younger. Included temperatures of 38.3°C or higher. Undertaken in the emergency room of a hospital in the USA.

^k It is not clear whether the child's signs and symptoms were interpreted without knowledge of the results of the test used to confirm serious illness

^l Included children aged 90 days to 36 months. Included temperatures of 39°C or higher. Undertaken at a hospital in the USA.

^m Confidence intervals calculated by the NCC-WCH from data reported in the study

ⁿ Included children aged 3 to 36 months. Included temperature greater than 38°C. Undertaken in a paediatric ward of a hospital in India.

^o Included children aged 1 to 36 months. Included temperatures higher than 39°C. Undertaken in a hospital in the UK.

^p Included children aged 29 to 56 days. Included temperatures greater than 38.2°C. Undertaken at the emergency department of a children's hospital in the USA.

^q Included children aged 7 days to 36 months. Included temperatures of 38°C or higher. Undertaken at a referral centre in Switzerland.

^r Included children aged less than 3 years. Included those with a fever, although fever was not defined. Undertaken in an emergency department in Italy.

^s Included children aged 60 days or younger. Included temperatures of 38°C or higher. Undertaken in 8 paediatric emergency departments in the USA.

Table I5.47 GRADE profile for comparison of Yale Observation Scores

Number of studies	Duration of fever		Effect	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	With SBI (Mean, SD)	Without SBI (Mean, SD)	<i>P</i> value							
Yale Observation Score										
<i>For detecting serious bacterial infection</i>										
1 (Hsiao, 2006)	9.4 (SD 4.6)	8.1 (SD 3.6)	<i>P</i> < 0.05	High	Prospective	No serious	NA	No serious	NA	Yes ^a
<i>For detecting bacteraemia</i>										
1 (Haddon, 1999)	7.0 (SD 1.5)	7.4 (SD 1.9)	<i>P</i> = 0.45	High	Prospective	No serious	NA	No serious	NA	Yes ^b

NA Not applicable

^a Includes children aged 2 to 6 months old. Includes those with a rectal temperature higher than 37.9°C. Undertaken in the emergency department of a hospital in the USA.

^b Includes children aged 90 days to 36 months. Includes those with temperatures of 39°C or higher. Undertaken at a hospital in the USA.

Chapter 5

Heart rate

Review question

The predictive value of heart rate, including:

- how heart rate changes with temperature?
- whether heart rate outside the normal range detects serious illness?
- whether heart rate and temperature outside normal range detects serious illness?

Table I5.51 Summary of study quality for change in heart rate with change in body temperature

Number of studies	Number of children	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Change in heart rate (with increasing body temperature)								
1 study (Davies 2009)	21,033 ^a	Very low	Observational study	Very serious ^{b, c}	None	Serious ^d	None	None
Change in heart rate (with increasing body temperature)^e								
1 study (Thompson 2009)	1,589 ^f	Low	Observational study	Serious ⁱ	None	Serious ^d	None	None
Change in heart rate (with increasing body temperature)								
1 study (Hanna 2004)	490 ^g	Very low	Observational study	Very serious ^{h, i}	None	None	None	None

^a The data were analysed using a quantile regression and a statistical model developed a best fit equation:

Expected parameter value = (Temperature (°C) × **a**) + (Age (months) × **b**) + (Age² (months²) × **c**) + constant

The temperature multiplier **a**, has a mean increase of 10.52 beat per minute (bpm) through the centile, resulting in a heart rate increase of approximately 10 bpm with each 1°C increment in temperature

^b Retrospective study

^c Measurement bias likely due to variation in pulse and temperature assessments

^d This study includes children older than 5 years of age

^e Centiles charts of heart rate plotted against temperature in febrile children were produced. The incremental increases of heart rate for each increment in 1 °C of temperature are showed in appendices x.x table x. Heart rate was negatively correlated with age ($r = -0.62$) and positively correlated with temperature ($r = 0.49$). This study showed that, in the study population, the heart rate increases by 9.9 to 14.1 bpm with each 1°C increment in temperature.

^f Children were not truly representative of a primary care population due to problems with recruiting. Recruitment was not systematic, the proportion of children consulting out-of-hours care was high, and the researcher set the minimum recruitment targets for each age–temperature combination.

^g Mean increase in pulse rate per 1°C increase in temperature was calculated using linear regression analysis of the relation between pulse rate and temperature. The authors report that for every 1°C rise in body temperature, the resting heart rate rose by 9.6 bpm.

^h Restricted data on the clinical status of the patients from which to determine the exclusion criteria.

ⁱ Impossible to control the baseline variation between children when evaluating the effect of temperature on pulse rate.

Table I5.53 Evidence profile for the distribution of age specific heart rate data by centile group for 1,360 children presenting at a paediatric emergency department with suspected serious bacterial infection for the detection of serious illness

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Total	Children with SBI	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Detection of serious illness using heart rate above 97 th centile											
1 study (Brent et al., 2011)	28	1	OR 1.51 (95% CI 0.19 to 12.0)	-	Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None
Detection of serious illness using heart rate above 90 th centile											
1 study (Brent et al., 2011)	91	10	OR 5.04 (95% CI 2.14 to 11.9)	-	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate above 75 th centile											
1 study (Brent et al., 2011)	199	12	OR 2.62 (95% CI 1.19 to 5.79)	-	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate above 50 th centile											
1 study (Brent et al., 2011)	324	14	OR 1.85 (95% CI 0.87 to 3.93)	-	Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Total	Children with SBI	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Detection of serious illness using heart rate below equal 50 th centile											
1 study (Brent et al., 2011)	586	14	OR 1.00 (Ref)	-	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Tachycardia											
1 study (Brent et al., 2011)	514	34	OR 2.90 (95% CI 1.60 to 5.26)	-	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None

OR odds ratios; SBI serious bacterial infection.

^a No definition of SBI

^b This study includes children older than 5 years of age

^c 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both no effect and appreciable harm

Table I5.54 Evidence profile for the Sensitivity, specificity, positive and negative likelihood ratios for significant bacterial infection of cut-offs defined by pulse centiles in 1,360 children presenting at a paediatric emergency department with suspected serious bacterial infection for the detection of serious illness

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Detection of serious illness using heart rate above 97th centile												
1 (Brent 2011)	1360	2.0 (0.04 to 10.4)	97.7 (96.7 to 98.5)	2.7 (2.2 to 3.4)	0.96 (0.76 to 1.2)	Low	Observational cohort study (Retrospective)	Serious ^a	NA	Serious ^b	None	None

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Detection of serious illness using heart rate above 90th centile												
1 (Brent 2011)	1360	21.6 (11.3 to 35.3)	90.8 (89.0 to 92.4)	2.4 (1.6 to 3.7)	0.86 (0.57 to 1.3)	Low	Observational cohort study (Retrospective)	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate above 75th centile												
1 (Brent 2011)	1360	45.1 (31.1 to 59.7)	75.7 (73.1 to 78.1)	1.7 (0.84 to 3.3)	0.78 (0.40 to 1.5)	Low	Observational cohort study (Retrospective)	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate above 50th centile												
1 (Brent 2011)	1360	72.5 (58.3 to 84.1)	48.6 (45.7 to 51.5)	1.3 (0.58 to 3.1)	0.64 (0.28 to 1.5)	Low	Observational cohort study (Retrospective)	Serious ^a	NA	Serious ^b	None	None
Tachycardia												
1 study (Brent et al., 2011)	1360	66.7 (52.1 to 79.2)	59.2 (56.3 to 62.0)	1.5 (0.67 to 3.4)	0.65 (0.29 to 1.46)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None

^a Lack of clear definition of SBI^b This study includes children older than 5 years of age

Table I5.55 Evidence profile for the sensitivity of cut-offs defined by heart rate centiles for detecting children with meningococcal septicaemia of various degrees of severity in 325 children presenting to hospital with meningitis

Number of studies	Total number of children	Sensitivity (95% confidence interval)		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
		All children with meningococcal septicaemia	Children with severe disease on admission							
Detection of serious illness using heart rate above 97 th centile										
1 study (Brent et al., 2011)	325	11.0 (7.7 to 15.1)	17.9 (10.2 to 28.3)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart above 90 th centile										
1 study (Brent et al., 2011)	325	27.8 (22.8 to 33.2)	38.5 (27.7 to 50.2)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate above 75 th centile										
1 study (Brent et al., 2011)	325	49. (43.4 to 55.0)	61.5 (49.8 to 72.3)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate above 50 th centile										
1 study (Brent et al., 2011)	325	73.9 (68.5 to 78.8)	84.6 (74.7 to 91.8)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate below 50 th centile										
1 study (Brent et al., 2011)	325	26.1 (21.2 to 31.5)	15.4 (8.2 to 25.3)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None

^a The study includes only children with meningococcal disease. Therefore, the researchers were unable to assess the specificity of centile cut-offs in identifying children presenting with meningococcal disease.

^b This study includes children older than 5 years of age

Table I5.56 GRADE findings for evaluation of elevated heart rate

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Total	Children with SBI	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Tachycardia											
Thompson, 2009	691	191 of 307 compared to 160 of 384	2.3 (1.7 to 3.1)	-	Low	Prospective	Serious ^a	NA	Serious ^b	None	No

^a All the children did not have the same tests^b Study included children aged up to 16 years.**Table I5.57** GRADE findings for evaluation of elevated heart rate

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Elevated heart rate^h														
<i>For detecting pneumonia, urinary tract infection, or bacteraemia</i>														
1 (Craig, 2010)	12,807	58 (55 to 61)	58 (57 to 59)	10 (9 to 10)	95 (94 to 95)	1.4 (1.3 to 1.5)	0.7 (0.7 to 0.8)	Low	Prospective	Serious ^{b, c, d}	NA	Serious ^f	None	Yes ^{e, g}
Thompson, 2009	691	62 (57 to 68)	58 (53 to 63)	NR	NR	1.5 (1.3 to 1.7)	0.7 (0.6 to 0.8)	Low	Prospective	Serious ^c	NA	Serious ^f	None	No

NA Not applicable, NR Not reported

^a Calculated by the NCC-WCH based on results reported in the study

^b It is not clear whether all of the children or a random sample of the children were given a test to confirm serious illness

^c It is not clear whether all children received the same test to confirm serious illness

^d It is not clear whether the test to confirm serious illness was independent of the clinical signs and symptoms

^e It is not clear whether the clinical data available when the test results were interpreted are what would be available when the test is used in practice

^f Included children aged under 5 years. Included those with one or more of the following elements: a measured auxiliary temperature of 38C or higher; parental report of a temperature of 38C or higher measured at home within the previous 24 hours; a parental report that the child 'felt hot' in the previous 24 hours; or a presenting problem related to fever as determined by a triage nurse. Undertaken in a children's emergency department of a hospital in Australia.

^g Not enough detail was provided regarding the measurement of the sign or symptom to allow another healthcare professional to make the same diagnosis

^h Based on figures: Age (years) and recommended upper limit of normal for FEVER study (source): 0 = 160 (WHO); 1 = 150 (WHO); 2 = 150 (WHO); 3 = 140 (WHO); 4 = 130 (Wallis); 5 = 120 (Wallis). From: 1) Wallis et al, Arch. Dis. Child. 2005;90;1117-1121. 2) WHO. Pocket Book of Hospital Care for Children: Guidelines for the management of common illnesses with limited resources. 2005, page 232

Table I5.59 Evidence profile for the distribution of age specific heart rate temperature data by centile group for 1,360 children presenting at a paediatric emergency department with suspected serious bacterial infection for the detection of serious illness

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Total	Children with SBI	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Detection of serious illness using heart rate and temperature above 97 th centile											
1 study (Brent et al., 2011)	135	7	OR 1.84 (95% CI 0.72 to 4.71)	-	Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None
Detection of serious illness using heart rate and temperature above 90 th centile											
1 study (Brent et al., 2011)	110	4	OR 1.19 (95% CI 0.38 to 3.73)	-	Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None
Detection of serious illness using heart rate and temperature above 75 th centile											
1 study (Brent et al., 2011)	227	11	OR 1.67 (95% CI 0.73 to 3.79)	-	Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Total	Children with SBI	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Detection of serious illness using heart rate and temperature above 50 th centile											
1 study (Brent et al., 2011)	316	16	OR 1.75 (95% CI 0.83 to 3.69)		Very low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	Serious ^c	None
Detection of serious illness using heart rate and temperature below equal 50 th centile											
1 study (Brent et al., 2011)	439	13	OR 1.00 (NR)		Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None

OR odds ratios; NR not reported; SBI serious bacterial infection.

^a No definition of SBI

^b This study includes children older than 5 years of age

^c 95% confidence interval (or alternative estimate of precision) around the pooled or best estimate of effect includes both no effect and appreciable harm

Table I5.60 Evidence profile reporting the sensitivity, specificity, positive and negative likelihood ratio for significant bacterial infection of cut-offs defined by heart rate and body temperature for 1,360 children presenting at a paediatric emergency department with suspected serious bacterial infection

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Detection of serious illness using heart rate and temperature above 97th centile												
1 study (Brent et al., 2011)	1360	13.7 (5.7 to 26.3)	89.4 (87.5 to 91.1)	1.4 (0.69 to 2.7)	0.96 (0.48 to 1.9)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Detection of serious illness using heart rate and temperature above 90th centile												
1 study (Brent et al., 2011)	1360	21.6 (11.3 to 35.3)	80.0 (77.6 to 82.3)	1.2 (0.76 to 1.8)	0.96 (0.63 to 1.5)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate and temperature above 75th centile												
1 study (Brent et al., 2011)	1360	43.1 (29.3 to 57.8)	61.7 (58.8 to 64.5)	1.2 (0.58 to 2.3)	0.90 (0.45 to 1.8)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Detection of serious illness using heart rate and temperature above 50th centile												
1 study (Brent et al., 2011)	1360	74.5 (60.4 to 85.7)	36.2 (33.4 to 39.0)	1 (0.50 to 2.6)	0.75 (0.33 to 1.7)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None
Tachycardia												
1 study (Brent et al., 2011)	1360	66.7 (52.1 to 79.2)	59.2 (56.3 to 62.0)	1.5 (0.67 to 3.4)	0.65 (0.29 to 1.46)	Low	Cross-sectional prospective study	Serious ^a	NA	Serious ^b	None	None

^a No definition of SBI^b This study includes children older than 5 years of age

Table I5.61 Evidence profile for the sensitivity of cut-offs defined by heart rate and body temperature centiles and tachycardia for detecting children with meningococcal septicaemia of various degrees of severity in 325 children presenting to hospital with meningitis

Number of studies	Total number of children	Sensitivity (95% confidence interval)		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
		All children with meningococcal septicaemia	Children with severe disease on admission							
Detection of serious illness using heart rate and temperature above 97 th centile										
1 study (Brent et al., 2011)	325	23.6 (18.5 to 29.3)	33.3 (22.9 to 45.2)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate and temperature above 90 th centile										
1 study (Brent et al., 2011)	325	37.8 (31.8 to 44.1)	50.7 (38.9 to 62.4)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate and temperature above 75 th centile										
1 study (Brent et al., 2011)	325	55.5 (49.2 to 61.7)	62.7 (50.7 to 73.6)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate and temperature above 50 th centile										
1 study (Brent et al., 2011)	325	70.1 (64.0 to 75.6)	74.7 (63.3 to 84.0)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None
Detection of serious illness using heart rate and temperature below 50 th centile										
1 study (Brent et al., 2011)	325	29.9 (24.4 to 36.0)	25.3 (16.0 to 36.7)	Low	Cross-sectional prospective study	None	NA	Very serious ^{a, b}	None	None

^a The study includes only children with meningococcal disease. Therefore, the researchers were unable to assess the specificity of centile cut-offs in identifying children presenting with meningococcal disease.

^b This study includes children older than 5 years of age

Chapter 8

Children 3 months and older

Review question

What is the predictive value of procalcitonin compared to C-reactive protein for detecting serious illness in fever without apparent source in children under 5?

Table I8.1 GRADE findings for comparison of different procalcitonin thresholds

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia, pyelonephritis, pneumonia, meningitis, sepsis, bone infections. Prevalence = 23%														
<i>0.5 ng/ml</i>														
1 (Andreola et al, 2007)	N = 408	73.4 (63 to 82)	76 (71 to 81)	48 (40 to 56) ^a	91 (87, 94) ^a	3.1 (2.5, 3.9) ^b	0.4 (0.2, 0.5) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e
<i>1 ng/ml</i>														
1 (Andreola et al, 2007)	N = 408	64 (53 to 74)	90 (86 to 93)	65 (55 to 75) ^a	89 (85, 93) ^a	6.2 (4.4, 9.0) ^b	0.4 (0.3, 0.5) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e
<i>2 ng/ml</i>														
1 (Andreola et al, 2007)	N = 408	48 (38 to 58)	97 (94 to 98)	80 (70 to 91) ^a	86 (82 to 90) ^a	13.6 (7.4 to 25.3) ^b	0.5 (0.4 to 0.7) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Fever < 8hours														
<i>1 ng/ml</i>														
1 (Andreola et al, 2007)	N = 45	86 (Not reported)	100 (Not reported)	Not reported	Not reported	Not reported	Not reported	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e
Bacteraemia, pyelonephritis, lobar pulmonary condensation. Prevalence = 22.6%														
<i>0.9 ng/ml</i>														
1 (Lacour et al, 2001)	N = 124	93 (77 to 99)	78 (69 to 86)	55 (41 to 70) ^a	97 (94 to 101) ^a	4.2 (2.9 to 6.3) ^b	0.1 (0.0 to 0.3) ^b	Low	Prospective Observational	Serious ^f	-	None	None	Yes ^g
<i>< 12 months of age</i>														
1 (Lacour et al, 2001)	N = 80	94 (Not reported)	87 (Not reported)	68 (Not reported)	98 (Not reported)	Not reported	Not reported	Very low	Prospective Observational	Very serious ^h	-	-	None	Yes ^g
<i>➤ 12 months of age</i>														
1 (Lacour et al, 2001)	N = 44	90 (Not reported)	62 (Not reported)	41 (Not reported)	96 (Not reported)	Not reported	Not reported	Very low	Prospective Observational	Very serious ^h	-	-	None	Yes ^g

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia, pyelonephritis, pneumonia, mastoiditis and retropharyngeal abscess. Prevalence = 29%														
<i>0.5 ng/ml</i>														
1 (Galetto-Lacour et al, 2003)	N = 99	93 (77 to 99)	74 (62 to 84)	60 (46, 74) ^a	96 (91, 101) ^a	3.6 (2.4, 5.5) ^a	0.1 (0.0 to 0.4)	Low	Prospective Observational	Serious ⁱ	-	None	None	Yes ^j
Bacteremia, meningitis, sepsis, UTI, pneumonia, gastroenteritis, cellulitis. Prevalence = 23.6%														
<i>≥0.5 ng/ml</i>														
1 (Olaciregui et al, 2009)	N = 347	63 (52 to 74)	87 (83 to 91)	59 (48 to 70)	89 (85 to 93)	4.8 (3.5 to 7.0) ^b	0.4 (0.3 to 0.5) ^b	Low	Retrospective Observational	Serious ^k	-	None	None	Yes ^l
Bacteremia, UTI and bacteremia/UTI . Prevalence = 13%														
<i>0.13 ng/ml</i>														
1 (Maniaci et al, 2008)	N = 234	97 (81 to 100)	30 (24 to 38)	17 (11 to 23)	98 (90 to 100)	1.4 (1.2 to 1.6)	0.1 (0.0 to 0.8)	Low	Prospective cohort	Serious ^m	-	None	None	No
Bacteremia, UTI, bacteremia/UTI, bacterial pneumonia. Prevalence = 18%														
<i>0.12 ng/ml</i>														
1 (Maniaci et al, 2008)	N = 234	95 (83 to 99)	26 (20 to 32)	22 (16 to 28)	96 (85 to 99)	1.3 (1.1 to 1.4)	0.2 (0.1 to 0.7)	Low	Prospective cohort	Serious ^m	-	None	None	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia, UTI, pneumonia and meningitis. Prevalence = 16%														
<i>> 0.2 ng/ml</i>														
1 (Manzano et al, 2011)	N = 328	85 (74 to 92)	70 (68 to 71)	36 (31 to 39)	96 (93 to 98)	2.8 (2.3 to 3.2)	0.2 (0.1 to 0.4)	Low	Prospective observational	Serious ⁿ	-	None	None	Yes ^o
Children with normal urine analysis only														
<i>> 0.2 ng/ml</i>														
1 (Manzano et al, 2011)	N = 262	88 (54 to 98)	71 (69 to 71)	9 (5 to 10)	99 (98 to 100)	3.0 (1.8 to 3.3)	0.2 (0.0 to 0.7)	Low	Prospective observational	Serious ⁿ	-	None	None	Yes ^o
Bacterial pneumonia, meningitis, septicaemia and pyelonephritis. Prevalence = 1.1%														
<i>> 500 ng/ml (> 0.5 ng/l)</i>														
1 (Thayyil et al, 2005)	N = 72	88 (65 to 110) ^b	50 (38 to 62) ^b	18 (6 to 30) ²	97 (91 to 103) ^b	1.8 (1.2 to 2.5) ^b	0.3 (0.0 to 1.6) ^b	Very Low	Prospective Observational	Very serious ^p	-	None	Serious ^q	Yes ^r
<i>> 2000 ng/ml (> 2 ng/l)</i>														
1 (Thayyil et al, 2005)	N = 72	50 (15 to 85) ^b	86 (77 to 94) ^b	31 (6 to 56) ^b	93 (87 to 100) ^b	3.6 (1.4 to 8.9) ^b	0.6 (0.3 to 1.2) ^b	Very Low	Prospective Observational	Very serious ^p	-	None	Serious ^q	Yes ^r

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia/sepsis. Prevalence = 0.6%														
<i>> 0.5 ng/ml</i>														
1 (Olacregui et al, 2009)	N = 347	86 (58 to 100)	93 (90 to 96)	35 (19 to 51)	99 (98 to 100)	12.3 (Not reported)	0.2 (Not reported)	Low	Retrospective Observational	Serious ^k	-	None	None	Yes ^l
Bacteremia. Prevalence = 3.2%														
<i>≥ 2 ng/ml (± IC 95%)</i>														
1 (Guenet al, 2007)	N = 215	57.1 ± 0.37	86.4 ± 0.05	13.8 ± 0.26	98.1 ± 0.06	4.19	0.49	Low	Prospective observational	Serious ^s	-	None	None	No
Invasive bacterial infections: Bacterial meningitis, Occult bacteremia & Sepsis. Prevalence = 1.7%														
<i>≥ 0.5 ng/mL</i>														
1 (Luaces-Cubells et al, 2012)	N = 868	0.87 (0.60 to 0.98)	0.83 (0.81 to 0.86)	0.09 (0.05 to 0.14) ^a	1.00 (0.99 to 1.00) ^a	5.15 (4.04 to 6.66) ^a	0.16 (0.04 to 0.58) ^a	Low	Prospective observational	Serious ^t	-	Serious ^u	None	No
<i>≥ 0.9 ng/mL</i>														
1 (Luaces-Cubells et al, 2012)	N = 868	0.87 (0.60 to 0.98)	0.91 (0.88 to 0.92)	0.14 (0.08 to 0.23) ^a	1.00 (0.99 to 1.00) ^a	9.13 (6.84 to 12.18) ^a	0.15 (0.04 to 0.54) ^a	Low	Prospective observational	Serious ^t	-	Serious ^u	None	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
≥ 1 ng/mL														
1 (Luaces-Cubells et al, 2012)	N = 868	0.73 (0.45 to 0.92)	0.92 (0.89 to 0.93)	0.14 (0.07 to 0.23) ^a	0.99 (0.99 to 1.00) ^a	8.72 (5.97 to 12.73) ^a	0.29 (0.13 to 0.67) ^a	Low	Prospective observational	Serious ^t	-	Serious ^u	None	No
≥ 2 ng/mL														
1 (Luaces-Cubells et al, 2012)	N = 868	0.60 (0.32 to 0.84)	0.95 (0.94 to 0.97)	0.19 (0.09 to 0.33) ^a	0.99 (0.98 to 1.00) ^a	12.80 (7.65 to 21.41) ^a	0.42 (0.23 to 0.78) ^a	Low	Prospective observational	Serious ^t	-	Serious ^u	None	No
Serious bacterial infections: Bacterial meningitis, Occult bacteremia & UTI. Prevalence = 8.3%														
≥ 0.2 ng/mL														
1 (Woelker et al, 2012)	N = 155	1.0 (0.72 to 1.0)	0.41 (0.33 to 0.49)	0.13 (0.08 to 0.22) ^a	1.0 (0.92 to 1.0) ^a	1.69 (1.47 to 1.94) ^a	NC	Very low	Prospective observational	Very serious ^v	-	Serious ^w	None	No
≥ 0.26 ng/mL														
1 (Woelker et al, 2012)	N = 155	0.92 (0.62 to 1.0)	0.64 (0.55 to 0.72)	0.19 (0.11 to 0.31) ^a	0.99 (0.93 to 1.0) ^a	2.57 (1.96 to 3.37) ^a	0.12 (0.02 to 0.80)	Very low	Prospective observational	Very serious ^v	-	Serious ^w	None	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
≥ 0.3 ng/mL														
1 (Woelker et al, 2012)	N = 155	0.85 (0.54 to 0.97)	0.64 (0.55 to 0.72)	0.19 (0.10 to 0.32) ^a	0.98 (0.92 to 1.0) ^a	2.56 (1.84 to 3.55) ^a	0.23 (0.06 to 0.83) ^a	Very low	Prospective observational	Very serious ^v	-	Serious ^w	None	No

^a Estimates and confidence intervals were calculated by the NCC-WCH technical team.

^b Confidence intervals were calculated by the NCC-WCH technical team.

^c All participants did not receive the same reference standard; Toxic appearing children were given a full sepsis work up while well appearing children were given tests if they fulfilled certain criteria. Apart from the chest X-ray, it is not clear whether any other test (reference or index) was interpreted in a blinded manner.

^d Indirectness of population: Toxic appearing children were included in the study.

^e There was no significant difference when the AUC data for PCT and CRP were compared ($P = 0.75$). A subgroup analysis by age and duration of evolution of fever also showed no difference when PCT and CRP were compared. The authors concluded that PCT and CRP are both valuable markers for prediction of SBI but PCT seems to be a more accurate at the beginning of an infection whereas CRP if properly employed may be a better test in emergency settings because of its overall better sensitivity and feasibility. (Andreola 2007)

^f It is not clear whether there was blinding in interpreting all reference (except the chest x-ray) and/or index tests.

^g About 7% of children with SBI had PCT concentration below the cut off level (0.9 ng/ml). The authors concluded that PCT offers only a modest advantage over CRP.

^h It is not clear whether there was blinding in interpreting all reference (except the chest x-ray) and/or index tests. Confidence intervals were not reported and not calculable by the NCC technical team (Lacour 2001)

ⁱ Participants did not receive the same reference tests; non-toxic appearing children received individualised tests according to certain clinical/laboratory criteria.

^j The authors concluded that PCT seems to have a slight advantage over CRP because of its earlier increase after stimulation and a better negative predictive value. (Lacour 2003)

^k Retrospective study design

^l The reference tests were not performed in a small percentage of the infants included in the study (Olaciregui)

^m Participants received tests depending on what condition was suggested by physical examination or clinical history. (Maniaci)

ⁿ Not all markers were available in every patient as some were missing in 15% (56/384) of the children included in the RCT.

^o The authors concluded that CRP, PCT, WBC and ANC had similar diagnostic properties to detect an SBI in the study population (Manzano)

^p The execution of the reference standard was not described in sufficient detail. It is not clear whether the index test results were interpreted without knowledge of the results of the index test. Blood cultures (gold standard) in the study population was done only when other markers of infection were positive which could have introduced bias into the analysis (Thayyil)

^q Wide confidence interval ($\geq 20\%$ around the point estimate).

^r The authors conclude that while the elevation of all the inflammatory markers makes SBI very likely in fever without localising signs, normal procalcitonin does not exclude SBI in this population (Thayyil)

^s It is not clear whether there was blinding in interpreting any of the reference and/or index tests (Guen)

[†] Children with UTI included as possible invasive illness, but unclear how they were included in the analysis.

^u Only included children who appeared non-toxic. All children seen in emergency department

^v Potential selection bias due to number of eligible children 'missed', only 19% of eligible children recruited. Did not compare CRP and PCT..

^w Only included children who appeared well. All children seen in an emergency department.

Table I8.2 GRADE findings for comparison of different C-Reactive Protein thresholds

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia, pyelonephritis, pneumonia, meningitis, bone infections, sepsis. Prevalence = 23%														
<i>20 mg/l</i>														
1 (Andreola et al, 2007)	N = 408	88 (80 to 94)	61 (55 to 66)	40 (34 to 47) ^a	95 (91 to 98) ^a	2.3 (1.9 to 2.6) ^b	0.2 (0.1 to 0.3) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e
<i>40 mg/l</i>														
1 (Andreola et al, 2007)	N = 408	71 (61 to 80)	81 (76 to 85)	53 (44 to 66) ^a	90 (87 to 94) ^a	3.8 (2.9 to 4.9) ^b	0.4 (0.3 to 0.5) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e
<i>80 mg/l</i>														
1 (Andreola et al, 2007)	N = 408	46 (36 to 57)	95 (92 to 97)	72 (60 to 83) ^a	85 (82 to 89) ^a	8.7 (5.1 to 14.1) ^b	0.6 (0.5 to 0.7) ^b	Very Low	Prospective Observational	Very serious ^c	-	Serious ^d	None	Yes ^e

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteraemia, pyelonephritis, lobar pulmonary condensation. Prevalence = 22.6%														
<i>40 mg/l</i>														
1 (Lacour et al, 2001)	N = 124	89 (72 to 98)	75 (65 to 83)	96 (92 to 100) ^a	51 (37 to 65) ^a	3.6 (2.5 to 5.2) ^b	0.1 (0.0 to 0.4) ^b	Low	Prospective Observational	Serious ^f	-	None	None	Yes ^g
<i>< 12 months of age</i>														
1 (Lacour et al, 2001)	N = 80	94 (Not reported)	84 (Not reported)	63 (Not reported)	98 (Not reported)	Not reported	Not reported	Very low	Prospective Observational	Very serious ^h	-	None	None	Yes
<i>> 12 months of age</i>														
1 (Lacour et al, 2001)	N = 80	80 (Not reported)	59 (Not reported)	91 (Not reported)	36 (Not reported)	Not reported	Not reported	Very low	Prospective Observational	Very serious ^h	-	None	None	Yes
Bacteremia, pyelonephritis, pneumonia, meningitis and deep abscess. Prevalence = 29%														
<i>40 mg/l</i>														
1 (Galetto-Lacour et al, 2003)	N = 99	79 (65 to 94)	79 (69 to 88)	61 (45 to 76) ^d	90 (83 to 98) ^d	3.7 (2.3 to 6.0) ^e	0.3 (0.1 to 0.5) ^e	Low	Prospective Observational	Serious ⁱ	-	None	None	Yes ^j

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteremia, meningitis, sepsis, UTI, pneumonia, gastroenteritis, cellulitis. Prevalence = 23.6%														
<i>≥ 20mg/l</i>														
1 (Olaciregui et al, 2009)	N = 347	64 (54 to 74)	84 (80 to 88)	55 (45 to 65)	88 (84 to 92)	4.0 (2.9 to 5.5) ^b	0.4 (0.3 to 0.6) ^b	Low	Retrospective Observational	Serious ^k	-	None	None	Yes ^l
<i>≥ 30mg/l</i>														
1 (Olaciregui et al, 2009)	N = 347	59 (48 to 70)	89 (85 to 93)	63 (52 to 74)	83 (87 to 91)	5.4 (3.6 to 7.9) ^b	0.5 (0.4 to 0.6) ^b	Low	Retrospective Observational	Serious ^k	-	None	None	Yes ^l
Bacteremia, UTI, pneumonia and meningitis. Prevalence = 16%														
<i>> 17.7mg/l</i>														
1 (Manzano et al, 2011)	N = 328	94 (96 to 98)	69 (67 to 69)	37 (34 to 39)	98 (96 to 100)	3.0 (2.6 to 3.2)	0.1 (0.0 to 0.2)	Low	Prospective observational	Serious ^m	-	None	None	Yes ⁿ
Children with normal urine analysis only														
<i>> 17.7mg/l</i>														
1 (Manzano et al, 2011)	N = 262	88 (54 to 98)	70 (69 to 70)	8 (5 to 9)	99 (98 to 100)	2.9 (2.4 to 3.5)	0.2 (0.1 to 0.4)	Low	Prospective observational	Serious ^m	-	None	None	Yes ⁿ

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacterial pneumonia, meningitis, septicaemia and pyelonephritis. Prevalence = 11.1%														
<i>> 50 mg/l</i>														
1 (Thayyil et al, 2005)	N = 72	75 (45 to 105) ^b	69 (57 to 80) ^b	23 (7 to 39) ^b	96 (90 to 102) ^b	2.4 (1.4 to 4.1) ^b	0.4 (0.1 to 1.2) ^b	Very Low	Prospective Observational	Very serious ^o	-	None	Serious ^p	Yes ^q
Bacteremia/sepsis. Prevalence = 0.6%														
<i>> 30 mg/l</i>														
1 (Olaciregui et al, 2009)	N = 347	56 (32 to 80)*	74 (69 to 79)	10 (4 to 16)	95 (97 to 99)	2.2 (Not reported)	0.6 (Not reported)	Very Low	Retrospective Observational	Serious ^k	-	None	Serious ^p	Yes ^l
Bacteremia. Prevalence = 3.2%														
<i>≥ 40 mg/l (± IC 95%)</i>														
1 (Guen et al, 2007)	N = 215	42.8±0.37	64.8±0.07	3.8±0.22	97.2±0.06	1.21	0.88	Low	Prospective observational	Serious ^r	-	None	None	No
Bacteraemia, urinary tract infection. Prevalence = 10.3%														
<i>> 2 mg/l</i>														
1 (Hsiao et al, 2006)	N = 387	100 (89 to 100)	29 (24 to 34)	74 (69 to 79)	26 (22 to 31)	1.4 (1.3 to 1.5)	-	Very Low	Prospective observational	Very serious ^{s, t}	-	Serious ^u	None	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>> 5.2 mg/l</i>														
1 (Hsiaio et al, 2006)	N = 387	84 (70 to 94)	54 (49 to 60)	50 (45 to 55)	50 (45 to 55)	1.9 (1.6 to 2.3)	0.27 (0.13 to 0.57)	Very Low	Prospective observational	Very serious ^{s, t}	-	Serious ^u	None	No
<i>> 9.8 mg/l</i>														
1 (Hsiaio et al, 2006)	N = 387	51 (31 to 67)	80 (76 to 84)	23 (16 to 34)	77 (72 to 81)	2.6 (1.8 to 3.8)	0.6 (0.4 to 0.8)	Very Low	Prospective observational	Very serious ^{s, t}	-	Serious ^u	None	No
Pneumonia, urinary tract infection, bacteraemia, meningitis, cellulitis, septic arthritis, osteomyelitis, otitis media, bacterial gastroenteritis. Prevalence= 23.9%														
<i>> 20 mg/l</i>														
1 (Berger et al, 1996)	N = 138	83.3 (70.0-96.7)	67.0 (57.7-76.4)	43.9 (31.0-56.7)	92.9 (86.8-98.9)	2.53 (1.82-3.50)	0.25 (0.11-0.56)	Moderate	Prospective observational	None	-	None	None	No
Occult bacteremia, bacterial meningitis, UTI. Prevalence = 0.9%														
<i>20 g/l</i>														
1 (Gomez et al, 2010)	N = 1018	73.9 (53.5 to 87.5)	74.8 (72 to 77.5)	3 (1 to 5)	100 (99 to 100)	3.1 (2.1 to 4.5)	0.3 (0.1 to 1.0)	Very low	Retrospective observational	Serious ^v	-	Serious ^w	Serious ^x	No

Feverish illness in children (appendices)

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>70 g/l</i>														
1 (Gomez et al, 2010)	N = 1018	69.6 (49.1 to 89.4)	93.8 (92.1 to 95.1)	9 (2 to 15)	99.3 (98.5 to 99.6)	10.7 (6.3 to 18.0)	0.4 (0.1 to 0.9)	Very low	Retrospective observational	Serious ^v	-	Serious ^w	Serious ^x	No
Occult bacteremia, UTI, Pneumonia. Prevalence = 14.3%														
<i>3 mg/dl</i>														
1 (Pratt et al, 2007)	N = 119	88 (62 to 98)	68 (58 to 76)	0.31 (19 to 46)	97 (89 to 100)	2.7 91.96 to 3.80)	0.17 (0.05 to 0.64)	Very Low	Prospective observational	Serious ^y	-	Serious ^z	Very serious ^{aa}	Yes ^{af}
<i>5 mg/dl</i>														
1 (Pratt et al, 2007)	N = 119	71 (44 to 89)	84 (75 to 100)	43 (25 to 63)	94 (87 to 98)	4.5 (2.6 to 7.8)	0.35 (0.17 to 0.73)	Very Low	Prospective observational	Serious ^y	-	Serious ^z	Very serious ^{aa}	Yes ^{af}
<i>7 mg/dl</i>														
1 (Pratt et al, 2007)	N = 119	59 (33 to 81)	87 (79 to 93)	43 (24 to 65)	93 (85 to 97)	4.6 (2.4 to 8.8)	0.47 (0.27 to 0.83)	Very Low	Prospective observational	Serious ^y	-	Serious ^z	Very serious ^{aa}	Yes ^{af}

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>3 mg/dl < 12 hours</i>														
1 (Pratt et al, 2007)	N = 45	67 (24 to 94)	74 (58 to 86)	28 (5 to 52)	94 (85 to 102)	2.6 (1 to 5.2)	0.4 (0.1 to 1.4)	Very Low	Prospective observational	Serious ^Y	-	Serious ^z	Very serious ^{aa}	No
<i>5 mg/dl</i>														
1 (Pratt et al, 2007)	N = 45	50 (14 to 86)	92 (78 to 98)	50 (10 to 90)	92 (84 to 101)	6.5 (1.7 to 22.3)	0.5 (0.2 to 1.2)	Very Low	Prospective observational	Serious ^Y	-	Serious ^z	Very serious ^{aa}	No
<i>7 mg/dl</i>														
1 (Pratt et al, 2007)	N = 45	33 (6 to 76)	97 (85 to 100)	67 (13 to 120)	90 (82 to 99)	13 (1.8 to 88.4)	0.7 (0.4 to 1.2)	Very Low	Prospective observational	Serious ^Y	-	Serious ^z	Very serious ^{aa}	No
<i>3 mg/dl > 12 hours</i>														
1 (Pratt et al, 2007)	N = 74	100 (72 to 100)	63 (50 to 75)	32 (17 to 48)	100 (98 to 101)	2.7 (1.7 to 3.8)	0.0 (0.0 to 6.8)	Very Low	Prospective observational	Serious ^Y	-	Serious ^z	Serious ^{ab}	No
<i>5 mg/dl</i>														
1 (Pratt et al, 2007)	N = 74	82 (48 to 97)	79 (67 to 88)	41 (20 to 61)	96 (91 to 101)	4 (2.1 to 6.9)	0.2 (0.1 to 0.8)	Very Low	Prospective observational	Serious ^Y	-	Serious ^z	Serious ^{ab}	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
<i>7 mg/dl</i>														
1 (Pratt et al, 2007)	N = 74	73 (40 to 93)	81 (69 to 89)	40 (19 to 61)	94 (88 to 101)	3.8 (1.9 to 7)	0.3 (0.1 to 0.9)	Very Low	Prospective observational	Serious ^y	-	Serious ^z	Serious ^{ab}	No
Occult bacteremia, UTI, Pneumonia. Prevalence = 11.3%														
<i>4.4 mg/dl</i>														
1 (Isaacman et al, 2002)	N = 256	63 (43 to 82)	81 (76 to 87)	30 (18 to 43)	94 (91 to 98)	3.3 (2.2 to 4.8)	0.5 (0.3 to 0.7)	Low	Prospective observational	Serious ^{ac}	-	None	Serious ^{ad}	No
Occult bacteremia, UTI, Pneumonia. Prevalence = 18%														
<i>7 mg/dl</i>														
1 (Pulliam et al, 2001)	N = 77	79 (49 to 94.2)	91 (79.8 to 96)	65 (38.3 to 85.8)	95 (86.1 to 99)	8.3 (3.8 to 27.3)	0.2 (0.1 to 0.6)	Moderate	Prospective observational	None	-	None	Serious ^{ae}	No
Invasive bacterial infections: Bacterial meningitis, occult bacteremia & sepsis. Prevalence = 1.7%														
<i>≥ 20 mg/L</i>														
1 (Luaces-Cubells et al, 2012)	N = 868	0.80 (0.52 to 0.96)	0.66 (0.63 to 0.69)	0.04 (0.02 to 0.07) ^a	0.99 (0.98 to 1.00) ^a	2.36 (1.80 to 3.09) ^a	0.30 (0.11 to 0.83) ^a	Low	Prospective observational	Serious ^{ag}	None	Serious ^{ah}	None	No

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
≥ 40 mg/L														
1 (Luaces-Cubells et al, 2012)	N = 868	0.47 (0.21 to 0.73)	0.83 (0.80 to 0.85)	0.05 (0.02 to 0.10) ^a	0.99 (0.98 to 0.99) ^a	2.72 (1.55 to 4.76) ^a	0.64 (0.40 to 1.03) ^a	Low	Prospective observational	Serious ^{ag}	None	Serious ^{ah}	None	No
≥ 80 mg/L														
1 (Luaces-Cubells et al, 2012)	N = 868	0.33 (0.12 to 0.62)	0.95 (0.93 to 0.96)	0.10 (0.04 to 0.23) ^a	0.99 (0.98 to 0.99) ^a	6.45 (2.98 to 13.97) ^a	0.70 (0.49 to 1.01) ^a	Low	Prospective observational	Serious ^{ag}	None	Serious ^{ah}	None	No
≥ 91 mg/L														
1 (Luaces-Cubells et al, 2012)	N = 868	0.33 (0.12 to 0.62)	0.96 (0.94 to 0.97)	0.13 (0.05 to 0.28) ^a	0.99 (0.98 to 0.99) ^a	8.16 (3.71 to 17.93) ^a	0.70 (0.49 to 0.99) ^a	Low	Prospective observational	Serious ^{ag}	None	Serious ^{ah}	None	No

^a Estimates and confidence intervals were calculated by the NCC-WCH technical team.

^b Confidence intervals were calculated by the NCC-WCH technical team.

^c All participants did not receive the same reference standard; Toxic appearing children were given a full sepsis work up while well appearing children were given tests if they fulfilled certain criteria. Apart from the chest X-ray, it is not clear whether any other test (reference or index) was interpreted in a blinded manner.

^d Indirectness of population: Toxic appearing children were included in the study.

^e There was no significant difference when the AUC data for PCT and CRP were compared ($P = 0.75$). A subgroup analysis by age and duration of evolution of fever also showed no difference when PCT and CRP were compared. The authors concluded that PCT and CRP are both valuable markers for prediction of SBI but PCT seems to be a more accurate at the beginning of an infection whereas CRP if properly employed may be a better test in emergency settings because of its overall better sensitivity and feasibility. (Andreola 2007)

^f It is not clear whether there was blinding in interpreting all reference (except the chest x-ray) and/or index tests.

^g About 7% of children with SBI had PCT concentration below the cut off level (0.9 ng/ml). The authors concluded that PCT offers only a modest advantage over CRP.

^h It is not clear whether there was blinding in interpreting all reference (except the chest x-ray) and/or index tests. Confidence intervals were not reported and not calculable by the NCC technical team (Lacour 2001)

ⁱ Participants did not receive the same reference tests; non-toxic appearing children received individualised tests according to certain clinical/laboratory criteria.

^j The authors concluded that PCT seems to have a slight advantage over CRP because of its earlier increase after stimulation and a better negative predictive value. (Lacour 2003)

^k Retrospective study design

^l The reference tests were not performed in a small percentage of the infants included in the study (Olaciregui)

^m Not all markers were available in every patient as some were missing in 15% (56/384) of the children included in the RCT.

ⁿ The authors concluded that CRP, PCT, WBC and ANC had similar diagnostic properties to detect an SBI in the study population (Manzano)

^o The execution of the reference standard was not described in sufficient detail. It is not clear whether the index test results were interpreted without knowledge of the results of the index test. Blood cultures (gold standard) in the study population was done only when other markers of infection were positive which could have introduced bias into the analysis (Thayyil)

^p Wide confidence interval ($\geq 20\%$ around the point estimate).

^q The authors conclude that while the elevation of all the inflammatory markers makes SBI very likely in fever without localising signs, normal procalcitonin does not exclude SBI in this population (Thayyil)

^r It is not clear whether there was blinding in interpreting any of the reference and/or index tests (Guen)

^s Subjects did not all receive tests

^t Gold standards not described in detail

^u Children with symptoms of specific conditions included

^v Retrospective study design is liable to bias

^w Low prevalence is unlikely to be representative of clinical situations in which use of CRP is considered

^x Imprecision of 40% across two of four outcomes

^y Not all subjects had reference tests

^z Study examining sub-groups of children presenting <12 hours or >12 hours after becoming febrile.

^{aa} Imprecision greater than 40% across all outcomes (Pratt < 12 hours)

^{ab} Imprecision of 40% across two of four outcomes (Pratt > 12 hours)

^{ac} Blinding of assessment of specified

^{ad} Imprecision greater than 40% across all outcomes

^{ae} Imprecision greater than 40% across all outcomes

^{af} Reviewer calculated from sub-groups (Pratt)

^{ag} Children with UTI included as possible invasive illness, but unclear how they were included in the analysis.

^{ah} Only included children who appeared non-toxic. All children seen in emergency department

Table I8.3 GRADE findings for combined PCT and CRP tests

Number of studies	Number of children	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)	Positive predictive value (95% confidence interval)	Negative predictive value (95% confidence interval)	Positive likelihood ratio (95% confidence interval)	Negative likelihood ratio (95% confidence interval)	Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
Bacteraemia, pyelonephritis, lobar pulmonary condensation. Prevalence = 22.6%														
<i>PCT 0.9 ng/ml or CRP 40 mg/l</i>														
1 (Lacour et al, 2001)	N = 124	96 (82 to 100)	67 (56 to 76)	46 (33 to 58) ^a	98 (95 to 101) ^a	2.9 (2.2 to 3.9) ^b	0.1 (0.0 to 0.4) ^b	Low	Prospective Observational	Seriou ^c	-	None	None	Yes ^d
Bacteremia. Prevalence = 3.2%														
<i>PCT ≥ 2ng/ml and/or CRP ≥ 40mg/l</i>														
1 (Guen et al, 2007)	N = 215	71.4 ±0.33	61.4±0.07	6.5 ±0.37	98.2 ±0.06	1.85	0.46	Low	Prospective observational	Seriou ^e	-	None	None	No

^a Estimates and confidence intervals were calculated by the NCC-WCH technical team.^b Confidence intervals were calculated by the NCC-WCH technical team.^c It is not clear whether there was blinding in interpreting all reference (except the chest x-ray) and/or index tests.^d About 7% of children with SBI had PCT concentration below the cut off level (0.9 ng/ml). The authors concluded that PCT offers only a modest advantage over CRP (Lacour)^e It is not clear whether there was blinding in interpreting any of the reference and/or index tests (Guen)

Response to antipyretic medication

Review question

What is the predictive value of the clinical response to paracetamol or NSAIDs?

Table 18.7 GRADE findings of response to antipyretics by children with bacterial or non-bacterial illnesses.

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Serious disease (Δ °C, (SD), n)	Not serious disease (Δ °C, (SD), n)	Relative (95% confidence interval (CL)) (MD and Standardise MD) (95% confidence interval)	Absolute mean difference							
Final symptoms score – Yale Observation Score											
Baker et al, 1989	7.5, (± 1.4), n = 15	7.7, (± 2.2), n = 135	0.2 (NS)	-	Very low	Prospective cohort	Serious ^{a,b}	-	Serious ^c	None	None
Change in symptoms – Yale Observation Score											
Baker et al, 1989	-3.8 (± 3.2), n = 15	-1.6 (± 2.5), n = 135	2.2 (<i>P</i> < 0.001)	-	Very low	Prospective cohort	Very serious ^{a, b, ,}	-	Serious ^c	None	None ^c
Change in temperature°C between serious and non-serious disease											
Torrey et al, 1984	-1.32, -, n = 16	-1.05, -, n = 239	0.27 (<i>P</i> = 0.14)	-	Very low	Prospective cohort	Very serious ^{a, b ,d}	-	None	None	Some ^{e, f, g}
Baker et al, 1989	-1.7, (± 0.8), n = 15	-1.6, (± 0.6), n = 135	SMD -0.16 (-0.69, to +0.37)	-	Very low	Prospective cohort	Very serious ^{a,b}	-	Serious ^c	None	Some ^f
Yamamoto et al, 1987	-1.606 (± 0.722), n = 17	-1.639 (± 0.705), N = 216	SMD 0.05 (-0.45 to +0.54)	-	Very low	Prospective cohort	Very serious ^{a, d, h, i}	-	None	None	Some ^f

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Serious disease (Δ °C, (SD), n)	Not serious disease (Δ °C, (SD), n)	Relative (95% confidence interval (CL)) (MD and Standardise MD) (95% confidence interval)	Absolute mean difference							
Mazur et al, 1989	-1.0 (\pm 0.6), N = 34	-1.5 (\pm 0.5), N = 68	SMD 0.92 (0.49 to 1.36)	-	Very low	Retrospective	Very serious _{a, j}	-	None	None	Some _{f, k}
Weisse et al, 1987	1.48°F, -, n = 17	1.16°F, -, 1n = 6	0.32°F (p = 0.37) ^o	-	Very low	Prospective cohort	Serious _l	-	Very serious _{m, c}	None	Some _{e, f}
Baker et al, 1987	1.3 (\pm 0.8), n = 62	1.0 (\pm 0.6), n = 234	SMD -0.46 (-0.75 to -0.18) <i>P</i> < 0.01 against all groups ^o	-	Very low	Prospective cohort	Very serious _{l, n, o}	-	Very Serious _{m, c}	None	Some _{e, f}
Mazur et al, 1994	-1.0, (\pm 0.6, n = 34	-1.2, (\pm 0.6), n = 450	SMD -0.33 (-0.68 to +0.02)	-	Very low	Retrospective	Very serious _{a, j}	-	None	None	Some _{f, k}
Bonadio et al, 1993	-1.40, -, n = 59	-1.44, -, n = 59	0.04 (NS) ^o	-	Very low	Retrospective	Very serious _{a, j}	-	Serious ^c	None	Some _{e, f}
Final temperature (°C) between serious and non-serious disease											
Torrey et al, 1984	38.8, -, n = 16	38.8, -, n = 239	(<i>P</i> = 0.46) ^o	-	Very low	Prospective cohort	Very serious _{a b d}	-	None	None	Some _{e, f, g}
Baker et al, 1989	38.5 (SD \pm 0.6), n = 15	38.4 (SD \pm 0.6), n = 135	(NS) ^o SMD 0.17 (-0.37 to +0.70)	-	Very low	Prospective cohort	Very serious _{a b}	-	Serious ^c	None	Some _f

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Serious disease (Δ °C, (SD), n)	Not serious disease (Δ °C, (SD), n)	Relative (95% confidence interval (CL)) (MD and Standardise MD) (95% confidence interval)	Absolute mean difference							
Change in febrile state											
Yamamoto et al, 1987	15 of 17	180 of 216	RR 1.06 (0.88 to 1.27)	-	Very low	Prospective cohort	Very serious a, d, h, i	-	None	None	Some f
Mazur et al, 1989	18 of 34	62 of 68	Univariate OR = 9.2 (95% CI 2.7 to 32.0) ^o Multivariate OR = 9.4 (95% CI 2.6 to 34.2) ^o	-	Very low	Retrospective	Very serious a, j	-	None	None	Some f, k
Weisse et al, 1987	4 of 35	10 of 65	RR 0.74 (0.25 to 2.20)	-	Very low	Prospective cohort	Serious l	-	Very Serious m, c	None	Some e, f
Mazur et al, 1994	18 of 34	335 of 450	RR 0.71 (0.52, 0.98) Univariate OR = 2.6 (95% CI 1.3 to 5.2) ^o Multivariate OR = 3.4 (95% CI 1.6 to 7.3) ^o	-	Very low	Retrospective	Very serious a, j	-	None	None	Some f, k

NS, OR, RR, SD SMD

^a No blinding^b Different measurement times between patients^c Other groups defined in study but not included in table. Baker 1989 – meningitis (-1.3 (SD \pm 0.8) Weisse, 1987 - symptoms of viral illness or bacterial illness Baker, 1987 - Group A B-hemolytic streptococcus pharyngitis, non-cultured gastroenteritis, Pneumonia, Otitis media, Viral syndrome. Bonadio, 1993 - Bacterial meningitis (mean -1.06°C)^d Different antipyretics given (paracetamol or aspirin)^e Poor reporting of results. Data not reported for calculation.^f Different definitions of fever – Torrey >38.9°C, Baker 1989 >39.4°C, Yamamoto, 1987 \geq 40°C, Mazur, 1989 \geq 38.9°C, Weisse, 1987 \geq 39.8°C, Baker, 1987 Rectal temperature > 38.4°C, Mazur, 1994 \geq 38.9°C, Bonadio, 1993 \geq 39.0°C rectal temperature.

^g Different conditions being compared. – Torrey Occult bacteremia vs non-bacterial illness, Baker 1989 + bacteremia vs – bacteremia culture, Yamamoto, 1987 + bacteremia vs – bacteremia culture, Mazur, 1989 + bacteremia vs – bacteremia culture, Weisse, 1987 + bacteremia vs + viral culture, Baker, 1987 Bacterial vs. non-bacterial, Mazur, 1994 + bacteremia vs – bacteremia culture, Bonadio, 1993 Isolated bacteremia vs non-bacterial illness.

^h Timing of 2nd temperature measurement not defined

ⁱ Sample size calculation not reported

^j Retrospective design

^k Same cases used but control populations different.

^l Not all children had reference tests. Diagnosis were not based on single ‘gold’ standard reference test.

^m Included children outside specified age range

ⁿ Reference tests not described in enough detail to repeat

^o Subjects were not required to stay for completion of study.

Chapter 9 Antipyretic interventions

9.1 Effects of body temperature reduction

Review question

Whether reducing fever with paracetamol or non-steroidal anti-inflammatory drugs (NSAIDs) affects the course of the disease?

Table I9.1 GRADE findings for outcome of disease in children after antipyretics.

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Antipyretic	No treatment	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Cases of complicated pneumonia vs. uncomplicated pneumonia using ibuprofen											
1 (Byington et al., 2002)	Ibuprofen	No treatment	Adjusted OR 4.0 (2.5 to 6.5), $P < 0.001^a$	-	Very low	Retrospective observational	None	-	Serious ^b	None	Yes ^c
1 (Francois et al., 2010)	Ibuprofen	No treatment	Adjusted OR 2.57 (1.51 to 4.35), $P < 0.001^a$	-	Very low	Retrospective observational	None	-	Serious ^b	None	Yes ^c
Primary varicella with skin or soft tissue complications using paracetamol											
1 (Mikaelof f et al., 2007)	Paracetamol	No treatment	Adjusted RR 4.9 (2.1 to 11.4) ^a	-	Very low	Prospective observational	None	-	Serious ^b	None	Yes ^c
1 (Mikaelof f et al., 2007)	Paracetamol	No treatment	Adjusted RR 1.5 (1.0 to 2.2) ^a	-	Very low	Prospective observational	None	-	Serious ^b	None	Yes ^c

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Antipyretic	No treatment	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Dubos et al., 2008)	Paracetamol	No treatment	Adjusted OR 4.8 (1.6 to 14.4), $P = 0.005^a$	-	Very low	Prospective observational	None	-	Serious ^b	None	Yes ^c
Risk of any invasive group A streptococcal infection using ibuprofen or paracetamol											
1 (Lesko et al., 2001)	Any Ibuprofen during illness	No ibuprofen	OR 3.9, (1.3 to 12) ^a	-	Very low	Prospective observational	None	-	Serious ^b	None	Yes ^d
1 (Lesko et al., 2001)	Any Acetaminophen during illness	No acetaminophen	OR 1.2, (0.50 to 3.0) ^a	-	Very low	Prospective observational	None	-	Serious ^b	Serious ^e	Yes ^d
1 (Lesko et al., 2001)	Ibuprofen only	No medication	Matched OR 1.5 (0.58 to 11) ^a	-	Very low	Prospective observational	None	-	Serious ^b	Serious ^e	Yes ^d
1 (Lesko et al., 2001)	Acetaminophen only	No medication	Matched OR 0.98 (0.43 to 2.2) ^a , Adjusted OR 0.94 (0.34 to 2.6) ^a	-	Very low	Prospective observational	None	-	Serious ^b	Serious ^e	Yes ^d
1 (Lesko et al., 2001)	Acetaminophen and ibuprofen	Neither	Matched OR 5.0 (1.6 to 16) ^a Adjusted OR 5.6 (1.2 to 25) ^a	-	Very low	Prospective observational	None	-	Serious ^b	Serious ^e	Yes ^d

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Antipyretic	No treatment	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Time to total scabbing using paracetamol											
1 (Doran et al., 1988)	6.7 days (SD 2.3)	5.6 days (SD 2.5)	$P < 0.05^a$	-	Very low	RCT	Serious ^g	-	Serious ^b	Serious ^f	No
Time to last new vesicle using paracetamol											
1 (Doran et al., 1988)	3.9 days (SD 1.4)	4.1 days (SD 1.2)	$P = 0.64^a$	-	Very low	RCT	Serious ^g	-	Serious ^b	Serious ^f	No
Time to total healing using paracetamol											
1 (Doran et al., 1988)	16.1 (SD 5.6)	16.2 (SD 5.8)	$P = 0.45^a$	-	Very low	RCT	Serious ^g	-	Serious ^b	Serious ^f	No
Number of paracetamol doses used by parents											
1 (Sugimura et al., 1994)	Complicated pneumonia 2.52 (SD 0.80)	Pneumonia 1.37 (SD 0.72)	$P < 0.001^a$	-	Very low	Prospective observational	None	-	Serious ^b	None	Yes ^c

Note: Observational studies are set at low quality unless they have design aspects that increase this.

^a As reported by authors

^b Included children aged over 5 (Sugimura- Aged 6 to 15; Byington up to 19; Francois up to age of 15; Mikaeloff – all ages; Dubos – aged up to 16; Doran aged 1 to 12; Lesko age up to 19)

^c Causal pathway is unclear – not established that antipyretics caused or were an effect of illness.

^d Casual relationship examined by restricting cases to those who received antipyretics in 7 days before emergence of GAS infection.

^e Crosses 0 and ± 0.25

^f Small sample size ($n < 100$) so results sensitive to change.

^g Investigators were not blinded and method of allocation is unclear.

9.3 Physical and drug interventions

Review question

Effect on fever and associated symptoms of treatment with:

- Paracetamol alone or NSAIDs alone, compared with placebo and with one another
- Alternating paracetamol and NSAIDs, compared with placebo, either drug alone, and taking both at the same time
- Paracetamol and NSAIDs taken at the same time, compared with placebo, and either drug alone and either drug alone.

Table I9.2 GRADE findings for paracetamol vs. placebo

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
Quality of Life at 1 to 2 hours											
No data											
Quality of Life at > 2 to 5 hours											
At 4 hours											
Comfort 1 (Gupta et al, 2007)	19 of 103 ^a	9 of 107 ^b	RR 2.19 (1.04, 4.62)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
Activity 1 (Gupta et al, 2007)	29 of 103 ^a	4 of 107 ^b	RR 7.53 (2.74, 20.67)	-	Low	RCT	Very serious ^c	-	None ^d	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
<i>Alertness</i> 1 (Gupta et al, 2007)	22 of 103 ^a	4 of 107 ^b	RR 5.71 (2.04, 16.01)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
<i>Mood</i> 1 (Gupta et al, 2007)	1 of 103 ^a	3 of 107 ^b	RR 3.81 (1.09, 13.26)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
<i>Appetite</i> 1 (Gupta et al, 2007)	7 of 103 ^a	1 of 107 ^b	RR 7.27 (0.91, 58.08)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
Quality of life at > 5 to 24 hours											
<i>At 6 hours</i>											
<i>Comfort</i> 1 (Gupta et al, 2007)	38 of 103 ^a	8 of 107 ^b	RR 4.93 (2.42 to 10.06)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
<i>Activity</i> 1 (Gupta et al, 2007)	62 of 103 ^a	17 of 107 ^b	RR 3.79 (2.38 to 6.02)	-	Low	RCT	Very serious ^c	-	None ^d	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
<i>Alertness</i> 1 (Gupta et al, 2007)	60 of 103 ^a	22 of 107 ^b	RR 2.83 (1.89, 4.26)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
<i>Mood</i> 1 (Gupta et al, 2007)	37 of 103 ^a	13 of 107 ^b	RR 2.96 (1.67 to 5.23)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
<i>Appetite</i> (Gupta et al, 2007)	21 of 103 ^a	1 of 103 ^b	RR 21.00 (2.88 to 153.23)	-	Low	RCT	Very serious ^c	-	None ^d	None	None
Discomfort > 24 hours											
No data											
Mean temperature at 1 to 2 hours											
<i>1 hour</i>											
1 (Walson et al., 1989a)	101.2°F (SD 0.9), n = 31 ^e	102.1°F (SD 0.9), n = 33 ^b	SMD -0.99 (-1.51 to -0.47)	-	Low	RCT	None ^{f, g, h}	-	Serious ^d	None	None
1 (Gupta et al., 2007)	38.4°C (SD 1.0), n = 101 ^a	38.7°C (SD 0.9), n = 102 ^b	SMD -0.31 (-0.59 to -0.04)	-	Low	RCT	None	-	None ^d	Very Serious ⁱ	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
1 (Kauffman et al., 1992)	38.2°C (SD 0.5657), n = 8 ^e	38.8°C (SD 0.6), n = 9 ^b	SMD -0.97 (-2.00 to +0.05)	-	Very Low	RCT	None _g	-	Serious _d	Very Serious _i	None
<i>2 hours</i>											
1 (Walson et al., 1989a)	100.3°F (SD 0.9), n = 31 ^e	101.8°F (SD 1.3), n = 33 ^b	SMD -1.32 (-1.86 to -0.77)	-	Low	RCT	Serious _{f, g, h}	-	Serious _d	None	None
1 (Gupta et al., 2007)	38.0°C (SD 0.8), n = 101 ^a	38.6°C (SD 0.9), n = 102 ^b	SMD -0.70 (-0.99 to -0.42)	-	Low	RCT	None	-	None _d	Very Serious _i	None
1 (Kauffman et al., 1992)	37.7°C (SD 0.6), n = 8 ^e	39.0°C (SD 0.56), n = 9 ^b	SMD -2.13 (-3.39 to -0.88)	-	Very Low	RCT	None _g	-	Serious _d	Very Serious _i	None
Mean in temperature at > 2 to 5 hours											
<i>3 hours</i>											
1 (Walson et al., 1989a)	100.1°F (SD 1.0), n = 31 ^e	101.7°F (SD 1.4), n = 33 ^b	SMD -1.29 (-1.83, -0.75)	-	Very Low	RCT	None _{f, g, h}	-	Serious _d	None	None
1 (Gupta et al., 2007)	37.8°C (SD 0.8), n = 101 ^a	38.55°C (SD 1.0), n = 102 ^b	SMD -0.82 (-1.11 to -0.54)	-	Low	RCT	None	-	None _d	Very serious _i	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
1 (Kauffman, et al, 1992)	37.7°C (SD 0.8485), n = 8 ^e	39.2 °C (SD 0.9), n = 9 ^b	SMD -1.62 (-2.76 to -0.49)	-	Very Low	RCT	None _g	-	Serious _d	Very Serious _i	None
<i>4 hours</i>											
1 (Walson et al, 1989a)	100.3°F (SD 1.3), n = 31 ^e	101.6°F (SD 1.5), n = 33 ^b	SMD -0.91 (-1.43 to -0.40)	-	Low	RCT	Serious _{f, g, h}	-	Serious _d	None	None
1 (Gupta et al, 2007)	37.6°C (SD 0.8), n = 101 ^a	38.5°C (SD 1.0), n = 102 ^b	SMD -0.99 (-1.28 to -0.70)	-	Low	RCT	None	-	None ^d	Very Serious _i	None
1 (Kauffman, et al, 1992)	37.8°C (SD 0.8485), n = 8 ^e	39.4 °C (SD 0.6), n = 9 ^b	SMD -2.09 (-3.33 to -0.85)	-	Very Low	RCT	None _{e f}	-	Serious _b	Very Serious _i	None
<i>5 hours</i>											
1 (Walson et al, 1989a)	100.5°F (SD 1.3), n = 31 ^e	101.3°F (SD 1.6), n = 33 ^b	SMD -0.54 (-1.04 to -0.04)	-	Low	RCT	Serious _{f, g, h}	-	Serious _d	None	None
1 (Gupta et al, 2007)	37.6°C (SD 0.7), n = 101 ^a	38.4°C (SD 0.9), n = 102 ^b	SMD -0.99 (-1.28 to -0.70)	-	Low	RCT	None	-	None ^d	Very Serious _i	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
1 (Kauffman, et al, 1992)	38.1°C (SD 0.5657), n = 8 ^e	39.4°C (SD 0.9), n = 9 ^b	SMD -1.62 (-2.76 to -0.48)	-	Very Low	RCT	None _g	-	Serious _d	Very Serious _i	None
Mean in temperature at > 5 to 24 hours											
<i>6 hours</i>											
1 (Walson et al, 1989a)	100.8°F (SD 1.9), n = 31 ^e	101.2°F (SD 1.5), n = 33 ^b	SMD -0.23 (-0.72 to 0.26)	-	Low	RCT	None _{f, g}	-	Serious _d	Serious _j	None
1 (Gupta et al, 2007)	37.7°C (SD 0.7), n = 101 ^a	38.3°C (SD 1.0), n = 102 ^b	SMD -0.69 (-0.98 to -0.41)	-	Low	RCT	None	-	None ^d	Very Serious _i	None
1 (Kauffman, et al, 1992)	38.5°C (SD 1.1314), n = 8 ^e	39.3°C (SD 0.6), n = 9 ^b	SMD -0.85 (-1.86 to +0.15)	-	Very Low	RCT	None _{e f}	-	Serious _d	Very Serious _i	None
<i>8 hours</i>											
1 (Walson et al, 1989a)	101.6°F (SD 1.8), n = 31 ^e	101.2°F (SD 1.7), n = 33 ^b	SMD 0.23 (-0.27 to +0.72)	-	Very Low	RCT	Very serious _{f, g, h}	-	Serious _d	Serious _j	None
1 (Kauffman, et al, 1992)	38.8°C (SD 0.8485), n = 8 ^e	39.2°C (SD 0.6), n = 9 ^b	SMD -0.52 (-1.50 to +0.45)	-	Very Low	RCT	None _g	-	Serious _d	Very Serious _i	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)								
Mean in temperature at > 24 hours												
No data												
Mean change temperature at 1 to 2 hours												
2 hours												
1 (Gupta et al, 2007)	70.3% (SD 24.8), n = 101 ^a	30.7% (SD 26.1), n = 102 ^b	SMD 1.55 (+1.24 to +1.86)	-	High	RCT	None	-	None ^d	None	None	
Mean change temperature at > 2 to 5 hours												
4 hours												
1 (Gupta et al, 2007)	85.4% (SD 22.4), n = 101 ^a	45.5% (SD 34.1), n = 102 ^b	SMD 1.38 (+1.68 to +1.07)	-	High	RCT	None	-	None ^d	None	None	
Mean change temperature at > 5 to 24 hours												
6 hours												
1 (Gupta et al, 2007)	87.6% (SD 18.6), n = 101 ^a	51.0% (SD 33.3), n = 102 ^b	SMD 1.35 (+1.66 to +1.04)	-	High	RCT	None	-	None ^d	None	None	
Mean change temperature at > 24 hours												
No data												
Afebrile at 1 to 2 hours												
No data												

Number of studies	Number of children		Effect [*]		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 2 to 5 hours											
No data											
Afebrile at > 5 to 24 hours											
No data											
Afebrile at > 24 hours											
No data											
Temperature Area Under the Curve											
0 to 8 hours											
1 (Kauffman et al, 1992)	328 (-356 to 686) ^e	- 67 (-629 to 120) ^b	<i>P</i> < 0.01	-	Low	RCT	Serious ^{g, h}	-	Serious _d	- ^k	Yes ^l
1 (Walson, et al, 1989)	365.0 ^e	166.5 ^b	<i>P</i> < 0.05	-	Low	RCT	Serious ^{f, g, h}	-	Serious _d	- ^k	Yes ^m
0 to 6 hours											
1 (Wilson, et al, 1991)	6.72 (± 0.58) ⁿ	11.70 (0.83) ^b	-	-	Low	RCT	Very serious ^{h, o}	-	Serious _d	- ^k	Yes ^l

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
Adverse events											
5 (Southey et al., 2009; Brewer et al., 1968; Gupta et al., 2007; Kauffman et al., 1992; and Walson et al., 1989)	23 of 385	12 of 371	RR 1.81 (0.94 to 3.50)	-	Very low	Meta-analyses of RCTs	Serious ^p	None	Serious ^d	Serious ^j	None
Long-term effects of paracetamol – Asthma											
1 (Beasley et al., 2008)	NR	NR	RR 1.46 (1.36 to 1.56)	-	Very low	Observational	Very Serious ^{q,r,s}	-	None ^d	None	None
Long-term effects of paracetamol – Rhinoconjunctivitis											
1 (Beasley et al., 2008)	NR	NR	RR 1.48 (1.38 to 1.60)	-	Very low	Observational	Very Serious ^{q,r,s}	-	None ^d	None	None

Number of studies	Number of children		Effect [*]		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Paracetamol	Placebo	Relative risk (95% confidence interval)	Absolute (95% confidence interval)							
Long-term effects of paracetamol – Eczema											
1 (Beasley et al., 2008)	NR	NR	RR 1.35 (1.26 to 1.45)	-	Very low	Observational	Very Serious ^{q,r,s}	-	None ^d	None	None

NR Not reported

^a15 mg/kg paracetamol repeated at 6 hours

^b Placebo

^c Outcome measure was not based on a validated questionnaire and was the subjective assessment of the clinician.

^d Children aged more than 5 years included in study (Gupta – up to 6; Walson – up to 11; Kauffman – up to 12; Brewer – up to 14; Wilson up to 12)

^e 10mg/kg paracetamol single dose

^f Children recruited from three sources, including newspaper advert.

^g Method of randomisation and allocation not described in detail

^h Small sample size (<100)

ⁱ Figures taken from graph, so likely to have measurement error.

^j Wide confidence intervals (CI > 0.5 around SMD)

^k Imprecision could not be calculated

^l AUC of percentage decrease of temperature (from baseline to normal 37°C) vs. time

^m AUC of percentage decrease of temperature (from baseline to 98.6°F) vs. time

ⁿ 120 mgm/ 5ml

^o Study not blinded

^p Different definitions of treatment regimens used

^q Observational study design starts at low

^r Causal pathway and confounding of underlying conditions

^s Treatment regimen unknown.

^{*} Relative and absolute differences are calculated by the NCC technical team based on the data presented in the papers. When this data is unavailable the authors reported figures may be used.

Table I9.3 GRADE findings for ibuprofen vs. placebo

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort at 1 to 2 hours											
No data											
Discomfort at > 2 to 5 hours											
No data											
Discomfort at > 5 to 24 hours											
No data											
Discomfort > 24 hours											
No data											
Mean change temperature at 1 to 2 hours											
No data											
Mean change in temperature at > 2 to 5 hours											
No data											
Mean change in temperature at > 5 to 24 hours											
No data											
Mean change in temperature at > 24 hours											
No data											

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean temperature at 1 to 2 hours												
1 hour												
1 (Walson et al., 1989)	100.9°F (SD 1.0), n = 29 ^b	102.1°F (SD 0.9), n = 33 ^c	SMD -1.25 (-1.80 to -0.70)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	None	
1 (Walson et al., 1989)	100.8°F (SD 0.9), n = 25 ^h	102.1°F (SD 0.9), n = 33 ^c	SMD -1.43 (-2.01 to -0.84)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	
2 hours												
1 (Walson et al., 1989)	99.8°F (SD 1.1), n = 29 ^b	101.8°F (SD 1.3), n = 33 ^c	SMD -1.63 (-2.21 to -1.05)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	
1 (Walson et al., 1989)	99.5°F (SD 0.7), n = 25 ^g	101.8°F (SD 1.3), n = 33 ^c	SMD -2.09 (-2.75 to -1.44)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	
Mean temperature at > 2 to 5 hours												
3 hours												
1 (Walson et al., 1989)	99.5°F (SD 1.3), n = 29 ^b	101.7°F (SD 1.4), n = 33 ^c	SMD -1.60 (-2.18 to -1.03)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Walson et al., 1989)	99.3°F (SD 0.7), n = 25 ^h	101.7°F (SD 1.4), n = 33 ^c	SMD -2.05 (-2.70 to -1.41)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No
<i>4 hours</i>											
1 (Walson et al., 1989)	99.5°F (SD 1.6) n = 29 ^b	101.6°F (SD 1.5) n = 33 ^c	SMD -1.34 (-1.90 to -0.78)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No
1 (Walson et al., 1989)	99.2°F (SD 1.2) n = 25 ^g	101.6°F (SD 1.5) n = 33 ^c	SMD -1.72 (-2.33 to -1.10)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No
<i>5 hours</i>											
1 (Walson et al., 1989)	99.8°F (SD 1.9) n = 29 ^b	101.3°F (SD 1.6) n = 33 ^c	SMD -0.85 (-1.37 to -0.33)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No
1 (Walson et al., 1989)	99.3°F (SD 1.7) n = 25 ^g	101.3°F (SD 1.6) n = 33 ^c	SMD -1.20 (-1.77 to -0.63)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean temperature at > 5 to 24 hours												
6 hours												
1 (Walson et al, 1989)	100.2°F (SD 2.2) n = 29 ^b	101.2°F (SD 1.5) n = 33 ^c	SMD -0.53 (-1.04 to -0.02)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	
1 (Walson et al., 1989)	99.7°F (SD 1.9) n = 25 ^h	101.2°F (SD 1.5) n = 33 ^c	SMD -0.88 (-1.42 to -0.33)	-	Moderate	RCT	Serious ^{d, e, f}	-	Serious ^g	None	No	
7 hours												
1 (Walson et al., 1989)	101.2°F (SD 2.0) n = 29 ^b	101.2°F (SD 1.7) n = 33 ^c	SMD 0.00 (-0.50 to +0.50)	-	Low	RCT	Serious ^{d, e, f}	-	Serious ^g	Serious ⁱ	No	
1 (Walson et al., 1989)	100.6°F (SD 2.2) n = 25 ^h	101.2°F (SD 1.7) n = 33 ^c	SMD -0.31 (-0.83 to +0.22)	-	Low	RCT	Serious ^{d, e, f}	-	Serious ^g	Serious ⁱ	No	
Mean temperature at > 24 hours												
No data												
Afebrile at 1 to 2 hours												
No data												

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 2 to 5 hours											
No data											
Afebrile at > 5 to 24 hours											
No data											
Afebrile at > 24 hours											
No data											
Temperature Area Under the Curve											
0 to 8 hours											
1 (Kauffman et al., 1992)	730 (576 to 839) ^j	-67 (-629 to 120) ^c	<i>P</i> < 0.01	-	Low	RCT	Serious ^{e,f}	-	Serious _g	- ^k	Yes ^l
1 (Kauffman et al., 1992)	590 (160 to 875) ^h	-67 (-629 to 120) ^c	<i>P</i> < 0.01	-	Low	RCT	Serious ^{e,f}	-	Serious _g	- ^k	Yes ^l
1 (Walson et al., 1989)	460.9 ^b	139.0 ^c	<i>P</i> < 0.05	-	Low	RCT	None _{d, e, f}	-	Serious _g	- ^k	Yes ^m
1 (Walson et al., 1989)	510.8 ^h	139.0 ^c	<i>P</i> < 0.05	-	Low	RCT	Serious ^{d, e, f}	-	Serious _g	- ^k	Yes ^m

Feverish illness in children (appendices)

Number of studies	Number of children		Effect ^a		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
0 to 6 hours – Change in temperature											
1 (Wilson et al., 1991)	7.09 (0.58) ^b	11.70 (0.83) ^c		-	Low	RCT	Serious ^f	-	Serious ^g	- ^k	Yes ^l
1 (Wilson et al., 1991)	4.91 (0.47) ^h	11.70 (0.83) ^c		-	Low	RCT	Serious ^f	-	Serious ^g	- ^k	Yes ^l
Adverse events											
4 (Southey et al., 2009; Kauffman et al., 1992; Walson et al., 1989a; and Wilson et al., 1991)	55 of 357	27 of 294	RR 1.67 (1.12, 2.48)	-	Low	Meta-analyses	Serious ⁿ	None	Serious ^g	None	None

NR Not reported

^a Relative and absolute differences are calculated by the NCC technical team based on the data presented in the papers. When this data is unavailable the authors reported figures may be used.

^b Dose of 5 mg/kg

^c Placebo

^d Children recruited from three sources, including newspaper advert

^e Method of randomisation and allocation not explained in detail

^f Small sample size (< 100 in total)

^g Children aged more than 5 years included in study (Gupta – up to 6; Walson – up to 11; Kauffman – up to 12; Wilson up to 12)

^h Dose of 10 mg/kg ibuprofen

ⁱ Wide confidence intervals (CI > 0.5 around SMD)

^j 7.5 mg/kg ibuprofen

^k Imprecision could not be calculated

^l AUC of percentage decrease of temperature (from baseline to normal 37°C) vs. time

^m AUC of percentage decrease of temperature (from baseline to 98.6°F) vs. time

ⁿ Different definitions of treatment regimens used

Table I9.4 GRADE findings for paracetamol vs. ibuprofen

Number of studies	Number of children		Effect [*]		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort at 1 to 2 hours											
No data											
Discomfort at > 2 to 5 hours											
4 hours											
GBC-score 1 (Autret et al., 1997)	0.8 (SD 1), n = 116 ^a	0.6 (SD 0.9), n = 113 ^b	NS ^c	-	Low	RCT	Very serious _{d,e,f,g}	-	None	None	None
GBC-VAS 1 (Autret et al., 1997)	27.8 (SD 29.5), n = 114 ^a	18.3 (SD 26.5), n = 108 ^b	SMD 0.34 (0.07, 0.60)	-	Low	RCT	Very serious _{d,e,f,g}	-	None	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
<i>CHEOPs discomfort</i> 1 (Autret et al., 1997)	2.2 (SD 0.9), n = 114 ^a	2.5 (1.0), n = 108 ^b	NS ^c	-	Low	RCT	Very serious _{d,e,f,g}	-	None	None	None
<i>Overall efficacy</i> 1 (Figueras Nadal et al., 2002)	64 of 94 ^h	61 of 93 ⁱ	RR 1.04 (0.85 to 1.27)	-	Very low	RCT	Very serious _{d,j,k}	-	Serious _l	Serious _m	None
Discomfort at > 5 to 24 hours											
<i>6 hours</i>											
<i>GBC-score</i> 1 (Autret et al., 1997)	0.8 (SD 1.0), n = 114 ^a	0.5 (SD 1.0), n = 112 ^b	NS ^c	-	Low	RCT	Very serious _{d,e,f,g}	-	None	None	None
<i>GBC-VAS</i> 1 (Autret et al., 1997)	26.7 (SD 30.6), n = 112 ^a	15.9 (SD 31.1), n = 107 ^b	SMD 0.35 (+0.08 to +0.62)	-	Low	RCT	Very serious _{d,e,f,g}	-	None	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
<i>CHEOPS discomfort</i> 1 (Autret et al., 1997)	2.3 (SD 0.9), n = 112 ^a	2.5 (SD 1), n = 107 ^b	NS ^c	-	Low	RCT	Very serious ^{d,e,f,g}	-	None	None	None
Discomfort > 24 hours											
<i>Day 1</i>											
<i>NCCPC stress test</i> 1 (Sarrell et al., 2006)	11.48 (SD 2.58), n = 155 ⁿ	11.77 (SD 2.64), n = 154 ^o	SMD -0.11 (-0.33 to +0.11)	-	High	RCT	None _p	-	None	None	Yes ^q
<i>Day 2</i>											
<i>NCCPC stress test</i> 1 (Sarrell et al., 2006)	8.83 (SD 2.67) n = 155 ⁿ	8.87 (SD 2.54) n = 154 ^o	SMD 0.02 (-0.24 to +0.21)	-	High	RCT	None _p	-	None	None	Yes ^q

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Day 3											
NCCPC stress test 1 (Sarrell et al., 2006)	7.96 (SD 2.71), n = 155 ⁿ	7.66 (SD 2.96) n = 154 ^o	SMD 0.11 (-0.12 to +0.33)	-	High	RCT	None _p	-	None	None	Yes ^q
Mean change temperature at 1 to 2 hours											
1 hour											
1 (Autret et al., 1997)	-0.97°C (SD 0.58) n = 114 ^a	-0.90°C (SD 0.56) n = 114 ^b	SMD -0.12 (-0.38 to +0.14)	-	Low	RCT	Very serious _{d,e,f}	-	None	None	None
1 (Wong et al., 2001)	-1.00°C (SD 0.65), n = 185 ^r	-1.05°C (SD 0.70), n = 191 ^s	SMD 0.07 (-0.13 to +0.28)	-	Moderate	RCT	Serious _{d,k}		None ^l	None	None
1 (Erlewyn-Lajeunesse et al., 2006)	-0.92°C (95% CI 0.70 to 1.14), n = 35 ⁿ	-0.95°C (95% CI 0.72 to 1.17), n = 37 ^t	SMD 0.04 (-0.42 to +0.51)	-	Low	RCT	Serious _{d,e,u}	-	Serious ^l	None	None
1 (Wilson et al., 1991)	-0.8°C (SD 0.3279), n = 43 ⁿ	-0.8°C (SD 0.3606), n = 52 ^o	SMD 0.04 (-0.42 to +0.51)	-	Very low	RCT	None _{d,u}	-	Serious ^l	Very serious ^v	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Wilson et al., 1991)	-0.8°C (SD 0.3428), n = 47 ^w	-0.8°C (SD 0.3606), n = 52 ^o	SMD 0.00 (-0.40 to +0.40)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
<i>1.5 hours</i>											
1 (Wong et al., 2001)	-1.33°C (SD 0.66), n = 185 ^r	-1.33°C (SD 0.68), n = 191 ^s	SMD 0.00 (-0.20 to +0.20)	-	Moderate	RCT	Serious _{d, k}	-	None _l	None	None
<i>2 hours</i>											
1 (Wong et al., 2001)	-1.56°C (SD 0.72), n = 185 ^r	-1.55°C (SD 0.68), n = 191 ^s	SMD: -0.01 (-0.22 to +0.19)	-	Moderate	RCT	Serious _{d, k}	-	None _l	None	None
1 (Wilson et al., 1991)	-1.2°C (SD 0.6557), n = 43 ⁿ	-1.2°C (SD 0.7211), n = 52 ^o	SMD 0.00 (-0.40 to +0.40)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
1 (Wilson et al., 1991)	-1.2°C (SD 0.6856), n = 47 ^w	-1.2°C (SD 0.7211), n = 52 ^o	SMD 0.00 (-0.39 to +0.39)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
Mean change in temperature at > 2 to 5 hours											
<i>3 hours</i>											
1 (Wong et al., 2001)	-1.58°C (SD 0.81), n = 185 ^r	-1.52°C (SD 0.79), n = 191 ^s	SMD -0.07 (-0.28 to +0.13)	-	Moderate	RCT	Serious _{d, k}	-	None _l	None	None
1 (Wilson et al., 1991)	-1.5°C (SD 0.6856), n = 47 ⁿ	-1.4°C (SD 0.7211), n = 52 ^o	-0.14 (-0.54 to +0.25)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Wilson et al., 1991)	-1.4°C (SD 0.6557), n = 43 ^w	-1.4°C (SD 0.7211), n = 52 ^o	0.00 (-0.40 to +0.40)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
4 hours											
1 (Autret et al., 1997)	-1.42°C (SD 0.85), n = 112 ^a	-1.04°C (SD 0.85), n = 110 ^b	SMD -0.45 (-0.71 to -0.18)	-	Very low	RCT	Very serious _{d,e,f}	-	None	None	None
1 (Wilson et al., 1991)	-1.6°C (SD 0.6856), n = 47 ⁿ	-1.3°C (SD 1.4422), n = 52 ^o	SMD -0.26 (-0.66 to +0.14)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
1 (Wilson et al., 1991)	-1.2°C (SD 0.6557), n = 43 ^w	-1.3°C (SD 1.4422), n = 52 ^o	SMD 0.09 (-0.32 to +0.49)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _v	None
1 (Ulukol et al., 1999)	-1.86°C (SD 0.74), n = 30 ^w	-1.29°C (SD 0.71), n = 30 ^b	SMD 0.78 (+0.25 to +1.30)	-	Low	RCT	Serious _{d,e,f, u}	-	Serious _l	None	None
1 (Autret et al., 1994)	-1.32°C (SD 1.00), n = 77 ^a	-1.02°C (SD 1.05), n = 74 ^b	SMD -0.29 (-0.61 to +0.03)	-	Low	RCT	Serious _{d,e}	-	None	Serious _m	None
1 (McIntyre et al., 1996)	-1.80°C (SD -), n = 76 ^x	-1.6°C (SD -), n = 74 ^y	P = 0.39	-	Moderate	RCT	Serious _{d, e}	-	Serious _l	- ^z	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Nadal et al., 2002)	-1.30°C (SD 1.1), n = 94 ^{aa}	-1.20°C (SD 0.96), n = 93 ^{ab}	SMD -0.10 (-0.38 to +0.19)	-	Very low	RCT	Very serious ^{d,h,k}	-	Serious ⁱ	None	None
1 (Wong, 2001)	-1.44°C (SD 0.98), n = 185 ^r	-1.47°C (SD 0.91), n = 191 ^s	SMD 0.03 (-0.17 to +0.23)	-	Moderate	RCT	Serious ^{d,k}	-	None ⁱ	None	None
<i>5 hours</i>											
1 (Wong et al., 2001)	-1.35°C (SD 1.06), n = 185 ^r	-1.34°C (SD 1.05) ^j , n = 191 ^s	SMD -0.01 (-0.21 to +0.19)	-	Moderate	RCT	Serious ^{d,k}	-	None ⁱⁱ	None	None
1 (Wilson et al., 1991)	-1.4°C (SD 0.6856), n = 47 ⁿ	-1.0°C (SD 1.4422), n = 52 ^o	SMD -0.35 (-0.74 to +0.05)	-	Very low	RCT	None ^{d,u}	-	Very serious ⁱ	Serious ^v	None
1 (Wilson et al., 1991)	-1.1 °C (SD 0.6557), n = 43 ^w	-1.0°C (SD 1.4422), n = 52 ^o	SMD -0.09 (-0.49 to +0.32)	-	Very low	RCT	None ^{d,u}	-	Very serious ⁱ	Serious ^v	None
Mean change in temperature at > 5 to 24 hours											
<i>6 hours</i>											
1 (Autret et al., 1997)	-1.19°C (SD 0.94), n = 108 ^a	-0.88°C (SD 0.85), n = 108 ^b	SMD -0.34 (-0.61 to -0.08)	-	Low	RCT	Very serious ^{d,e,f}	-	None	None	None
1 (Wong et al., 2001)	-1.24°C (SD 1.08), n = 185 ^r	-1.20°C (SD 1.09), n = 191 ^s	SMD -0.04 (-0.24 to +0.17)	-	Moderate	RCT	Serious ^{d,k}	-	None	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Wilson et al., 1991)	-1.1°C (SD 0.6557), n = 43 ⁿ	-0.9°C (SD 1.4422), n = 52 ^o	SMD -0.17 (-0.58 to +0.23)	-	Very low	RCT	None _{d, u}	-	Very serious ^l	Serious ^v	None
1 (Wilson et al., 1991)	-1.2°C (SD 0.6856), n = 47 ^w	-0.9°C (SD 1.4422), n = 52 ^o	SMD -0.26 (-0.66 to +0.14)	-	Very low	RCT	None _{d, u}	-	Very serious ^l	Serious ^v	None
Mean change in temperature at > 24 hours											
No studies found											
Mean temperature at 1 to 2 hours											
<i>1 hour</i>											
1 (Kauffman et al., 1992)	38.0°C (SD 0.6928), n = 12 ^a	38.2°C (SD 0.5657), n = 8 ^b	SMD -0.30 (-1.20 to +0.60)	-	Very low	RCT	None _{d, u}	-	Serious ^l	Very serious ^{v, ac}	None
1 (Kauffman et al., 1992)	37.9°C (SD 0.4243), n = 8 ^w	38.2°C (SD 0.5657), n = 8 ^b	SMD -0.57 (-1.57 to +0.44)	-	Very low	RCT	None _{d, u}	-	Serious ^l	Very serious ^{v, ac}	None
1 (Vauzelle - Kervrodan et al., 1997)	38.4°C (SD 0.6), n = 60 ^a	38.3°C (SD 0.6), n = 56 ^b	SMD: 0.17 (-0.20 to +0.53)	-	Low	RCT	Serious ^d	-	Serious ^l	Serious ^m	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Erlewyn-Lajeunesse et al., 2006)	37.81°C (SD 0.69), n = 35 ⁿ	37.98°C (SD 0.47), n = 37 ^t	SMD: -0.29 (-0.75 to +0.18)	-	Low	RCT	Serious ^{d, e, u}	-	Serious _l	Serious _m	None
1 (Walson et al., 1989)	100.9°F (SD 1), n = 29 ⁿ	102.1°F (SD 0.9), n = 31 ^b	SMD -0.31 (-0.82 to +0.20)	-	Low	RCT	None _{d, ad, u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Walson et al., 1989)	100.8°F (SD 0.9), n = 25 ^w	102.1°F (SD 0.9), n = 31 ^b	SMD -0.44 (-0.97 to +0.10)	-	Low	RCT	None _{d, ad, u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Nadal et al., 2002)	37.93°C (SD 0.72), n = 100 ^{aa}	38.06°C (SD 0.72), n = 99 ^{ab}	SMD -0.18 (-0.46 to +0.10)	-	Very low	RCT	Very serious _{s, d, h, k}	-	Serious _l	None	None
<i>1.5 hours</i>											
1 (Nadal et al., 2002) 1.5 hr	37.61°C (SD 0.73), n = 100 ^{aa}	37.78°C (SD 0.70), n = 99 ^{ab}	SMD -0.24 (-0.52 to +0.04)	-	Very low	RCT	Very serious _{s, d, h, k}	-	Serious _l	Serious _m	None
<i>2 hours</i>											
1 (Nadal et al., 2002)	37.50°C (SD 0.74), n = 100 ^{aa}	37.67°C (SD 0.78), n = 99 ^{ab}	SMD -0.22 (-0.50 to +0.06)	-	Very low	RCT	Very serious _{s, d, h, k}	-	Serious _l	Serious _m	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Van Esch et al., 1995)	37.60°C (SD 0.6025), n = 30 ⁿ	37.96°C (SD 0.9155), n = 29 ^b	SMD -0.46 (-0.98 to +0.06)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
1 (Vauzelle - Kervroda n et al., 1997)	37.9°C (SD 0.7), n = 58 ^w	37.9°C (SD 0.7), n = 55 ^b	SMD 0.00 (-0.37 to +0.37)	-	Low	RCT	Serious _d	-	Serious _l	Serious _m	None
1 (Walson et al., 1989)	99.8°F (SD 1.1), n = 29 ⁿ	101.8°F (SD 0.9), n = 31 ^b	SMD -0.49 (-1.01 to +0.02)	-	Low	RCT	None _{d, ad, u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Walson et al., 1989)	99.5°F (SD 0.7), n = 25 ^w	101.8°F (SD 0.9), n = 31 ^b	SMD -0.97 (-1.52 to -0.41)	-	Moderate	RCT	None _{d, ad, u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Kauffman, et al., 1992)	37.3°C (SD 0.5196), n = 12 ^a	37.7 °C (SD 0.6), n = 8 ^b	SMD -0.69 (-1.62 to +0.23)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	None
1 (Kauffman et al., 1992)	37.2°C (SD 0.2828), n = 8 ^w	37.7 °C (SD 0.6), n = 8 ^b	SMD -1.01 (-2.07 to +0.05)	-	Low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Autret-Leca et al., 2007	37.4 °C (SD 0.75), n = 151 ^w	37.4°C (SD 0.8), n = 150 ^{ah}	SMD 0.00 (-0.23 to +0.23)	-	Very low	RCT	None ^d		Serious ^l	Very serious ^v	None
Mean temperature at > 2 to 5 hours											
<i>3 hours</i>											
1 (Walson et al., 1989)	99.5°F (SD 1.0), n = 29 ⁿ	101.7°F (SD 1.0), n = 31 ^b	SMD -0.51 (-1.03 to 0.00)	-	Low	RCT	None ^{d, ad, u}	-	Serious ^l	Serious ^m	Yes ^{ae}
1 (Walson et al., 1989)	99.3°F (0.7), n = 25 ^w	101.7 °F (SD 1.0), n = 31 ^b	SMD -0.90 (-1.45 to -0.34)	-	Moderate	RCT	None ^{d, ad, u}	-	Serious ^l	Serious ^m	Yes ^{ae}
1 (Vauzelle - Kervrodan et al., 1997)	37.6°C (SD 0.7), n = 58 ^w	37.8°C (SD 0.7), n = 56 ^b	SMD -0.28 (-0.65 to +0.09)	-	Very Low	RCT	Serious ^d	-	Serious ^l	Serious ^m	None
1 (Nadal et al., 2002)	37.57°C (SD 0.92), n = 100 ^{aa}	37.78°C (SD 0.92), n = 99 ^{ab}	SMD -0.23 (-0.51 to +0.05)	-	Very low	RCT	Very serious ^{d, h, k}	-	Serious ^l	Serious ^m	None
1 (Kauffman et al., 1992)	36.9°C (SD 0.6928), n = 12 ^a	37.7°C (SD 0.8485), n = 8 ^b	SMD -1.01 (-1.97 to -0.05)	-	Very low	RCT	None ^{d, u}	-	Serious ^l	Very serious ^{v, ac}	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Kauffman et al., 1992)	36.7°C (SD 0.2828), n = 8 ^w	37.7°C (SD 0.8485), n = 8 ^b	SMD -1.49 (-2.64 to -0.35)	-	Very low	RCT	None _{d, u}	-	Serious _i	Very serious _{v, ac}	None
Autret-Leca et al., 2007	37.3°C (SD 0.75), n = 151 ^w	37.3°C (SD 0.75), n = 150 ^{ah}	SMD 0.00 (-0.23 to +0.23)	-	Very low	RCT	None _d	-	Serious _i	Very serious _v	None
<i>4 hours</i>											
1 (Van Esch et al., 1995)	37.38°C (SD 1.0022), n = 31 ⁿ	37.95°C (SD 1.2806), n = 31 ^b	SMD -0.49 (-1.00 to +0.02)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
1 (Vauzelle - Kervroda et al., 1997)	37.6°C (SD 0.8), n = 58 ^w	37.8°C (SD 0.8), n = 55 ^b	SMD -0.25 (-0.62 to +0.12)	-	Very Low	RCT	Serious _d	-	Serious _i	Serious _m	None
1 (Nadal et al, 2002)	37.82°C (SD 1.05), n = 100 ^{aa}	37.97°C (SD 1.02), n = 99 ^{ab}	SMD -0.14 (-0.42 to +0.13)	-	Very low	RCT	Very serious _{s^{d, h, k}}	-	Serious _i	None	None
1 (Walson et al., 1989)	99.5°F (SD 1.6), n = 29 ⁿ	101.6°F (SD 1.3), n = 31 ^b	SMD -0.54 (-1.06 to -0.03)	-	Moderate	RCT	None _{d, ad, u}	-	Serious _i	Serious _m	Yes ^{ae}

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Walson et al., 1989)	99.2°F (SD 1.2), n = 25 ^w	101.6°F (SD 1.3), n = 31 ^b	SMD -0.86 (-1.42 to -0.31)	-	Moderate	RCT	None d, ad, u	-	Serious l	Serious m	Yes ^{ae}
1 (Kauffman et al., 1992)	36.9°C (SD 0.6928), n = 12 ^a	37.8°C (SD 0.8485), n = 8 ^b	SMD -1.14 (-2.12 to -0.16)	-	Very low	RCT	None d, u		Serious l	Very serious v, ac	None
1 (Kauffman et al., 1992)	36.7°C (SD 0.2828), n = 8 ^a	37.8°C (SD 0.8485), n = 8 ^w	SMD -1.64 (-2.82 to -0.47)	-	Very low	RCT	None d, u	-	Serious l	Very serious v, ac	None
1. (Autret-Leca et al., 2007)	37.4°C (SD 0.9), n = 151 ^w	37.4°C (SD 1.0), n = 150 ^{ag}	SMD 0.00 (-0.23 to +0.23)		Very low	RCT	None d		Serious l	Very serious v	None
<i>5 hours</i>											
1 (Walson et al., 1989)	99.8°F (SD 1.9), n = 29 ⁿ	101.3°F (SD 1.3), n = 31 ^b	SMD -0.43 (-0.94 to +0.09)	-	Moderate	RCT	None d, ad, u	-	Serious l	Serious m	Yes ^{ae}
1 (Walson et al., 1989)	99.3°F (SD 1.7) n = 25 ^w	101.3°F (SD 1.3) n = 31 ^b	SMD -0.79 (-1.34 to -0.25)	-	Moderate	RCT	None d, ad, u	-	Serious l	Serious m	Yes ^{ae}

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Nadallet al., 2002)	37.88°C (SD 1.07), n = 100 ^{aa}	37.85°C (SD 0.87), n = 99 ^{ab}	SMD 0.03 (-0.25 to +0.31)	-	Very low	RCT	Very serious ^{d, h, k}	-	Serious _l	None	None
1 (Kauffman et al., 1992)	37.0°C (SD 0.6928), n = 12 ^a	38.1°C (SD 0.5657), n = 8 ^b	SMD -1.63 (-2.69 to -0.57)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	None
1 (Kauffman et al., 1992)	36.9°C (SD 0.5657), n = 8 ^w	38.1°C (SD 0.5657), n = 8 ^b	SMD -2.01 (-3.27 to -0.74)	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	None
Autret-Leca et al., 2007	37.4°C (SD 0.9), n = 151 ^w	37.6°C (SD 1.0), n = 150 ^{ag}	SMD -0.21 (-0.44 to +0.02)	-	Very low	RCT	None _d	-	Serious _l	Very serious _v	None
<i>6 hours</i>											
1 (Vauzelle-Kervrodan et al., 1997)	38°C (SD 0.8), n = 56 ^w	38°C (SD 0.8), n = 55 ^b	SMD 0.00 (-0.37 to +0.37)	-	Low	RCT	Serious _d	-	Serious _l	Serious _m	None
1 (Van Esch et al., 1995)	37.82°C (SD 1.2828), n = 34 ⁿ	38.23°C (SD 1.3015), n = 35 ^b	SMD -0.31 (-0.79 to +0.16)	-	Very low	RCT	None _{d, v}	-	Very serious _{af}	Serious _m	Yes ^{ag}

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Nadal et al., 2002)	37.87°C (SD 0.96), n = 100 ^{aa}	38.10°C (SD 0.97), n = 99 ^{ab}	SMD -0.24 (-0.52 to +0.04)	-	Very low	RCT	Very serious _{d,h,k}	-	Serious _l	Serious _m	None
1 (Walson et al., 1989)	100.2°F (SD 2.2), n = 29 ⁿ	101.2°F (SD 1.9), n = 31 ^b	SMD -0.29 (-0.80 to +0.22)	-	Low	RCT	None _{d,ad,u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Walson et al., 1989)	99.7°F (SD 1.9), n = 25 ^w	101.2°F (SD 1.9), n = 31 ^b	SMD -0.57 (-1.11 to -0.03)	-	Low	RCT	None _{d,ad,u}	-	Serious _l	Serious _m	Yes ^{ae}
1 (Kauffman et al., 1992)	37.3°C (SD 0.6928), n = 12 ^a	38.5°C (SD 1.1314), n = 8 ^b	SMD -1.29 (-2.29 to -0.29)	-	Very low	RCT	None _{d,u}	-	Serious _l	Very serious _{v,ac}	None
1 (Kauffman et al., 1992)	37.2°C (SD 0.5657), n = 8 ^w	38.5°C (SD 1.1314), n = 8 ^b	SMD -1.37 (-2.50 to -0.25)	-	Very low	RCT	None _{d,u}	-	Serious _l	Very serious _{v,ac}	None
Autret-Leca et al., 2007	37.5°C (SD 0.9), n = 151 ^w	37.7°C (SD 1.0), n = 150 ^{ah}	SMD -0.21 (-0.44 to +0.02)	-	Very low	RCT	None _d	-	Serious _l	Very serious _v	None
<i>8 hours</i>											
1 (Nadal et al., 2002)	38.00°C (SD 1.33), n = 100 ^{aa}	38.20°C (SD 0.84), n = 99 ^{ab}	SMD -0.18 (-0.46 to +0.10)	-	Very low	RCT	Very serious _{d,h,k}	-	Serious _l	None	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Walson et al., 1989)	101.2°F (SD 2.0), n = 29 ⁿ	101.2°F (SD 1.8), n = 31 ^b	SMD -0.21 (-0.72 to +0.30)	-	Low	RCT	None d, ad, u	-	Serious l	Serious m	Yes ^{ae}
1 (Walson et al., 1989)	100.6°F (SD 2.2) n = 25 ^w	101.2°F (SD 1.8), n = 31 ^b	SMD -0.50 (-1.03 to +0.04)	-	Low	RCT	None d, ad, u	-	Serious l	Serious m	Yes ^{ae}
1 (Kauffman et al., 1992)	37.7°C (SD 0.8485), n = 8 ^a	38.8°C (SD 0.8485), n = 8 ^b	SMD -1.23 (-2.32 to -0.13)	-	Very low	RCT	None d, u	-	Serious l	Very serious v, ac	None
1 (Kauffman et al., 1992)	37.9°C (SD 1.3856), n = 12 ^w	38.8°C (SD 0.8485), n = 8 ^b	SMD -0.72 (-1.64 to +0.21)	-	Very low	RCT	None d, u	-	Serious l	Very serious v, ac	None
Autret-Leca et al, 2007	37.6°C (SD 0.9), n = 151 ^w	37.6°C (SD 0.95), n = 150 ^{ah}	SMD 0.00 (-0.23 to +0.23)	-	Very low	RCT	None d	-	Serious l	Very serious v	None
<i>12 hours</i>											
1 (Van Esch et al., 1995) 12 hr	37.87°C (SD 1.3576), n = 32 ⁿ	37.88°C (SD 1.1241), n = 35 ^b	SMD -0.01 (-0.49 to +0.47) ^b	-	Low	RCT	None d, u	-	Very serious af	Serious m	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
24 hours											
1 (Van Esch et al., 1995)	37.92°C (SD 1.1432), n = 27 ⁿ	38.18°C (SD 1.2638), n = 33 ^b	SMD -0.21 (-0.72 to +0.30)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
1 (Sarrell et al., 2006)	40.60°C (SD 1.46)n = 155 ⁿ	40.55°C (SD 1.31), n = 154 ^o	SMD 0.04 (-0.19 to +0.26)	-	High	RCT	None _p	-	None	None	Yes ^q
Mean temperature at > 24 hours											
Day 2											
1 (Sarrell et al., 2006)	39.66°C (SD 1.48), n = 155 ⁿ	39.74°C (SD 1.37), n = 154 ^o	SMD -0.06 (-0.28 to +0.17)	-	High	RCT	None _p	-	None	None	Yes ^q
Day 3											
1 (Sarrell et al., 2006)	39.64°C (SD 1.46), n = 155 ⁿ	39.34°C (SD 1.19), n = 154 ^o	SMD 0.22 (0.00 to +0.45)	-	High	RCT	None _p	-	None	None	Yes ^q
Afebrile at 1 to 2 hours											
1 hour											
1 (Autret et al., 1997)	33 of 116 ^a	25 of 113 ^b	RR 1.29 (0.82, 2.02)	-	Low	RCT	Very serious _{d,e,f}	-	None	None	None
2 hours											
1 (Wong et al., 2001)	145 of 185 ^f	130 of 191 ^s	RR 1.15 (1.02, 1.30)	-	Moderate	RCT	Serious _{d, k}	-	None ^t	None	Yes ^{ah}

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Van Esch et al, 1995)	27 of 30 ⁿ	22 of 29 ^b	RR 1.19 (0.94, 1.50) ^b	-	Very low	RCT	None _{d, v}	-	Very serious _{af}	Serious _m	None
Afebrile at > 2 to 5 hours											
<i>4 hours</i>											
1 (Autret et al., 1997)	69 of 116 ^a	45 of 113 ^b	RR 1.49 (1.14, 1.96)	-	Low	RCT	Very serious _{d,e,f}	-	None	None	None
1 (Van Esch et al., 1995)	26 of 30 ⁿ	22 of 29 ^b	RR 1.18 (0.90, 1.55)	-	Very low	RCT	None _{d, v}	-	Very serious _{af}	Serious _m	None
1 (Vauzelle - Kervroed an et al., 1997)	56 of 58 ^w	53 of 55 ^b	RR 1.00 (0.93, 1.08)	-	Moderate	RCT	Serious _d	-	Serious _l	Serious _m	Yes ^{ai}
Afebrile at > 5 to 24 hours											
<i>6 hours</i>											
1 (Autret et al., 1997)	43 of 116 ^a	40 of 113 ^b	RR 1.05 (0.74, 1.48)	-	Low	RCT	Very serious _{d,e,f}	-	None	None	None

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Van Esch et al., 1995)	20 of 34 ⁿ	18 of 35 ^b	RR 1.14 (0.75, 1.75)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
<i>12 hours</i>											
1 (Van Esch et al., 1995)	21 of 34 ⁿ	24 of 35 ^b	RR 0.96 (0.68, 1.34)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
<i>24 hours</i>											
1 (Van Esch et al., 1995)	20 of 34 ⁿ	20 of 35 ^b	RR 1.22 (0.86, 1.74)	-	Very low	RCT	None _{d, u}	-	Very serious _{af}	Serious _m	None
Afebrile at > 24 hours											
No data											
Temperature AUC											
<i>0 to 8 hours</i>											
1 (Kauffman et al., 1992)	730 (576 to 839) ^a	328 (-356 to 686) ^b	$P = 0.05$	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	Yes ^{aj}
1 (Kauffman et al., 1992)	590 (160 to 875) ^w	328 (-356 to 686) ^b	$P = 0.05$	-	Very low	RCT	None _{d, u}	-	Serious _l	Very serious _{v, ac}	Yes ^{aj}

Feverish illness in children (appendices)

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
0 to 6 hours											
1 (Wilson et al., 1991)	7.09 (SEM 0.58), n = 43 ⁿ	6.72 (SEM 0.58), n = 51 ^o	NS	-	Very Low	RCT	None _{d, u}	-	Very serious ^l	Serious ^v	Yes ^{aj}
1 (Wilson et al., 1991)	4.91 (SEM 0.47), n = 47 ^w	6.72 (SEM 0.58), n = 51 ^o	NS	-	Very low	RCT	None _{d, u}	-	Very serious ^l	Serious ^v	Yes ^{aj}
0 to 8 hours											
1 (Walson et al., 1989)	460.9 ⁿ	365.0 ^b	NS	-	Low	RCT	None _{d, ad, u}	-	Serious ^l	None	Yes ^{ae, al}
1 (Walson et al., 1989)	510.9 ^w	365.0 ^b	<i>P</i> < 0.05	-	Low	RCT	None _{d, ad, u}	-	Serious ^l	None	Yes ^{ae, al}
0 to 6 hours – total temperature change per hour											
1 (Walson et al., 1992)	297 ⁿ	377 ^b	NS	-	Moderate	RCT	None _{d, ad, u}	-	Serious ^l	None	Yes ^{ae, al}
1 (Walson et al., 1992)	385 ^w	377 ^b	NS	-	Moderate	RCT	None _{d, ad, u}	-	Serious ^l	None	Yes ^{ae, am}

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
0 to 12 hours – total temperature change per hour											
1 (Walson et al., 1992)	689 ⁿ	938 ^y	P < 0.05	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , al
1 (Walson et al., 1992)	929 ^w	938 ^b	NS	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , al
0 to 24 hours – total temperature change per hour											
1 (Walson et al., 1992)	1572 ⁿ	2100 ^b	P < 0.05	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , al
1 (Walson et al., 1992)	1995 ^w	2100 ^b	NS	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , am
0 to 48 hours – total temperature change per hour											
1 (Walson et al, 1992)	3286 ⁿ	4400 ^b	NS	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , al
1 (Walson et al, 1992)	3933 ^w	4400 ^b	NS	-	Moderate	RCT	None d, ad, u	-	Serious l	None	Yes ^{ae} , al

Number of studies	Number of children		Effect*		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Ibuprofen	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Adverse events											
5 (Southey et al., 2009; Pierce et al, 2010; Kauffman et al., 1992; Sarrell et al., 2006; Walson et al., 1989)	2962 of 21,843	1469 of 11,678	RR 1.04 (0.98 to 1.10)	-	Very low	Meta-analyses + additional RCTs	Serious ^{am}	Serious ^{ak}	Serious ^l	None	None
Discontinuation of treatment											
1 (Southey et al., 2009)	5 of 257	5 of 226	RR 0.54 (0.17 to 1.71)	-	Very low	Meta-analyses of RCTs	Serious ^{am}	Serious ^{an}	Serious ^l	Very serious ^{ac}	None

NR Not reported

NC Non-calculable

NS Not significant at $p < 0.05$

* Relative and absolute differences are calculated by the NCC technical team based on the data presented in the papers. When this data is unavailable the authors reported figures may be used.

^a Ibuprofen at 7.5 mg/kg^b Paracetamol at 10 mg/kg^c Not presented in correct format for analysis of categorical data^d Method of randomisation and/or blinding not described in detail

^e Blinding of allocation not used

^f Unclear whether groups were comparable for missing data

^g Study used a non-validated scoring system

^h 6.67 mg/kg of Ibuprofen

ⁱ 10.65 mg/kg of paracetamol

^j Investigators not blinded to allocation

^k High dropout rate: Nadal 140 of 187 patients did not complete study; Wong 25% withdrawal rate

^l Included children aged more than 5 (Nadal = 12 ; Wong Included children up to 6 years; Ulukol up to 14 years; McIntyre up to aged 12; Kaufmann up to 12; Vauzelle up to 12; Erlewyn; Autret-Leca 12)

^m Confidence intervals cross 0 and ± 0.25 effect size

ⁿ 5 mg/kg of Ibuprofen

^o 12.5 mg/kg of paracetamol

^p Allocation could be determined by different regimens

^q Daily temperature was recorded by parents instead of trained clinicians

^r At 5mg/kg for initial temp $<39.2^{\circ}\text{C}$ and 10mg/kg for initial temp $\geq 39.2^{\circ}\text{C}$

^s 12 mg/kg of paracetamol. The dose of paracetamol was adjusted according to each patient's age following package insert instructions and averaged 12mg/kg

^t 15.3 mg/kg paracetamol

^u Small sample size ($n < 100$)

^v Data measured from graph so measurement error.

^w 10 mg/kg Ibuprofen

^x At 20mg/kg in 24 hours

^y At 50mg/kg in 24 hours

^z Not calculated

^{aa} 6.67 mg/kg of Ibuprofen

^{ab} 10.65 mg/kg of paracetamol

^{ac} RR includes 0 and both ± 0.25 ; SMD crosses both ± 0.5

^{ad} Recruited children via newspaper advert

^{ae} Commercially funded

^{af} Children with febrile seizures

^{ag} A crossover analysis comparing the study drugs was performed on 22 children with a second episode of fever.

^{ah} 1.96h paracetamol; 2.16h ibuprofen

^{ai} 3.84h paracetamol; 3.79h ibuprofen

^{aj} AUC of percentage decrease of temperature (from baseline to normal 37°C) vs. time

^{ak} Studies had different treatment regimens, including multidose.

^{al} AUC of percentage decrease of temperature (from baseline to 98.6°F) vs time

^{am} Data from two meta-analysis combined. Methodological issues with underlying RCTs, especially in relation to blinding and allocation concealment.

^{an} Included studies had methodological issues, especially relating to blinding and allocation concealment.

Table I9.5 GRADE findings for paracetamol vs. paracetamol and ibuprofen combined

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort at 1 to 2 hours											
No data											
Discomfort at > 2 to 5 hours											
No data											
Discomfort at > 5 to 24 hours											
24 hours											
Discomfort 1 (Hay et al., 2009)	29 of 50 ^a	22 of 52 ^b	RR 1.37 (0.92 to 2.04)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e	None
Activity 1 (Hay et al., 2009)	23 of 48 ^a	20 of 50 ^b	RR 1.20 (0.76 to 1.88)	-	Very low	RCT	Serious ^c	-	None ^d	Serious ^e	None
Appetite 1 (Hay et al., 2009)	14 of 48 ^a	10 of 48 ^b	RR 1.40 (0.69 to 2.84)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f	None
Sleep 1 (Hay et al., 2009)	20 of 52 ^a	17 of 46 ^b	RR 1.04 (0.62 to 1.73)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Discomfort > 24 hours												
48 hours												
Discomfort 1 (Hay et al., 2009)	36 of 52 ^a	34 of 52 ^b	RR 1.06 (0.81 to 1.38)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e		
Activity 1 (Hay et al., 2009)	28 of 52 ^a	31 of 52 ^b	RR 0.90 (0.65 to 1.26)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f		
Appetite 1 (Hay et al., 2009)	21 of 51 ^a	21 of 51 ^b	RR 1.00 (0.63 to 1.59)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f		
Sleep 1 (Hay et al., 2009)	25 of 52 ^a	27 of 52 ^b	RR 0.93 (0.63 to 1.36)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f		
Day 5												
Discomfort 1 (Hay et al., 2009)	38 of 50 ^a	43 of 49 ^b	RR 0.87 (0.72 to 1.04)	-	Mode rate	RCT	Serious ^c	-	None ^d	None		
Activity 1 (Hay et al., 2009)	37 of 51 ^a	44 of 49 ^b	RR 0.81 (0.67 to 0.98)	-	Mode rate	RCT	Serious ^c	-	None ^d	None		

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
<i>Appetite</i> 1 (Hay et al., 2009)	32 of 52 ^a	29 of 50 ^b	RR 1.06 (0.77 to 1.46)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e	
<i>Sleep</i> 1 (Hay et al., 2009)	27 of 51 ^a	31 of 50 ^b	RR 0.85 (0.61 to 1.20)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e	
Mean change temperature at 1 to 2 hours											
<i>1 hour</i>											
1 (Erlewyn-Lajeunesse, 2006)	-1.22 (0.95 to 1.50), n = 36 ^g	-0.95 (0.72 to 1.17), n = 37 ^h	RR 0.36 (-0.10 to 0.82)	-	Modest	RCT	Serious ^{i,j}	-	Serious ^d	Serious ^e	None
Mean change in temperature at > 2 to 5 hours											
No data											
Mean change in temperature at > 5 to 24 hours											
No data											
Mean change in temperature at > 24 hours											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean temperature at 1 to 2 hours												
1 hour												
1 (Erlewyn-Lajeunesse, et al., 2006)	37.59°C (SD 0.61), n = 36 ^g	37.98°C (SD 0.47), n = 37 ^h	RR -0.71 (-1.18 to -0.24) Adjusted 0.35C (0.10 to 0.6), P = 0.028.	-	Mode rate	RCT	Serious ^{ij}	-	Serious ^d	None	None	
Mean temperature at > 2 to 5 hours												
No data												
Mean temperature at > 5 to 24 hours												
1 (Hay et al., 2009)	36.6°C (SD 1.01), n = 52 ^a	36.4°C (SD 0.89), n = 52 ^b	SMD 0.21 (-0.18 to +0.59)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e		
Mean temperature at > 24 hours												
1 (Hay et al., 2009)	36.0°C (SD 0.66), n = 52 ^a	36.2°C (SD 0.93), n = 52 ^b	SMD -0.25 (-0.63 to +0.14)	-	Low	RCT	Serious ^c	-	None ^d	Serious ^e		
Afebrile at 1 to 2 hours												
1 (Hay et al., 2009)	47 of 52 ^a	33 of 52 ^b	RR 1.42 (1.14 to 1.78)	-	Mode rate	RCT	Serious ^c	-	None ^d	None	Yes ^k	
Afebrile at > 2 to 5 hours												
1 (Hay et al., 2009)	51 of 52 ^a	37 of 52 ^b	RR 1.38 (1.15 to 1.65)	-	Mode rate	RCT	Serious ^c	-	None ^d	None	Yes ^k	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 5 to 24 hours											
6 hours											
1 (Hay et al., 2009)	47 of 52 ^a	39 of 52 ^b	RR 1.21 (1.01 to 1.44)	-	Mode rate	RCT	Serious ^c	-	None ^d	None	Yes ^k
8 hours											
1 (Hay et al., 2009)	45 of 52 ^a	42 of 52 ^b	RR 1.07 (0.90 to 1.27)	-	Mode rate	RCT	Serious ^c	-	None ^d	Serious ^e	Yes ^k
12 hours											
1 (Hay et al., 2009)	49 of 52 ^a	39 of 52 ^b	RR 1.26 (1.06 to 1.49)	-	Mode rate	RCT	Serious ^c	-	None ^d	None	Yes ^k
Afebrile at > 24 hours											
1 (Hay et al., 2009)	47 of 52 ^a	46 of 52 ^b	RR 1.02 (0.90 to 1.17)	-	Mode rate	RCT	Serious ^c	-	None ^d	None	Yes ^k
Time without fever											
0 to 4 hours											
1 (Hay et al., 2009)	116.2 (SD 65.0) ^a	171.1 (SD 40.8) ^b	Adjusted mean difference 55.3 (33.1 to 77.5), <i>P</i> < 0.001	-	Mode rate	RCT	Serious ^c	-	None ^d	None	None
24 hours											
1 (Hay et al., 2009)	1217.4 (SD 237.6) ^a	940.3 (SD 362.9) ^b	Adjusted mean difference 4.4 (2.4 to 6.3), <i>P</i> < 0.001	-	Mode rate	RCT	Serious ^c	-	None ^d	None	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Adverse events											
Diarrhoea											
1 (Hay et al., 2009)	12 of 52 ^a	10 of 52 ^b	RR 1.20 (0.57 to 2.53)	-	Low	RCT	Serious ^c	-	None ^d	Very Serious ^e	None
Vomiting											
1 (Hay et al., 2009)	2 of 52 ^a	6 of 52 ^b	RR 0.33 (0.07 to 1.58)	-	Low	RCT	Serious ^c	-	None ^d	Very Serious ^e	None

NR Not reported

NC Non-calculable

^a Hay - 15mg/kg paracetamol + 10mg/kg ibuprofen^b 15 mg/kg paracetamol^c Required sample size not achieved and blinding may not have been achieved^d Children aged more than 5 included in the study (Hay up to 6)^e RR includes 0 and ± 0.25 ^f RR includes 0 and both ± 0.25 ^g 15mg/kg + 5 mg/kg^h 15mg/kg paracetamolⁱ Allocation of treatment not blinded^j Small sample size ($n < 100$)^k Afebrile ≤ 37.2

Table I9.6 GRADE findings for paracetamol vs. paracetamol and ibuprofen alternating

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Alternating	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort at 1 to 2 hours											
No data											
Discomfort at > 2 to 5 hours											
No data											
Discomfort at > 5 to 24 hours											
Day 1											
1 (Sarrell, et al., 2006)	9.26 (SD 2.49), n = 155 ^a	11.77 (SD 2.64), n = 154 ^b	SMD -0.98 (-1.21 to -0.74)	-	High	RCT	None ^c	None	None	None	Yes ^d
Discomfort > 24 hours											
Day 2											
1 (Sarrell et al., 2006)	5.09 (SD 2.78), n = 155 ^a	8.87 (SD 2.54), n = 154 ^b	SMD -1.42 (-1.67 to -1.17)	-	High	RCT	None ^c	None	None	None	Yes ^d
Day 3											
1 (Sarrell et al., 2006)	4.18 (SD 2.74), n = 155 ^a	7.66 (SD 2.96), n = 154 ^b	SMD -1.22 (-1.46 to -0.97)	-	High	RCT	None ^c	None	None	None	Yes ^d
Mean change temperature at 1 to 2 hours											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Alternating	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean change in temperature at > 2 to 5 hours												
No data												
Mean change in temperature at > 5 to 24 hours												
No data												
Mean change in temperature at > 24 hours												
No data												
Mean temperature at 1 to 2 hours												
1 (Pashapour et al., 2009) 2 hours	38.8°C (SD 0.59), n = 35 ^e	38.8°C (SD 0.47), n = 35 ^f	SMD 0.00 (-0.47 to +0.47)	-	Low	RCT	Very serious ^{g, h, i, j, k}	None	None	None	None	
Mean temperature at > 2 to 5 hours												
3 hours												
1 (Kramer et al., 2008) 3 hours	37.7°C (SD 0.6224), n = 19 ^l	37.7°C (SD 0.415), n = 19 ^f	SMD 0.00 (-0.64 to +0.64)	-	Very low	RCT	Serious ^k	None	None ^m	Very serious ⁿ	None	
4 hours												
1 (Pashapour et al., 2009)	38.4°C (SD 0.34), n = 35 ^e	38.5°C (SD 0.3), n = 35 ^f	SMD -0.31 (-0.78 to +0.16)	-	Very low	RCT	Very serious ^{g, h, i, j, k}	None	None	Serious ^o	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Alternating	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
1 (Kramer et al., 2008)	37.4°C (SD 0.8299), n = 19 ^l	38.0°C (SD 1.0374), n = 19 ^f	SMD -0.63 (-1.28 to +0.03)	-	Very low	RCT	Serious ^k	None	None ^m	Serious ^o	None
<i>5 hours</i>											
1 (Pashapour et al., 2009)	38.0°C (SD 0.47), n = 35 ^e	38.2°C (SD 0.38), n = 35 ^f	SMD -0.46 (-0.94 to +0.01)	-	Very low	RCT	Very serious ^{g, h, i, j, k}	None	None	Serious ^l	None
1 (Kramer et al., 2008)	37.1°C (SD 0.6224), n = 19 ^l	37.9°C (SD 0.8299), n = 19 ^f	SMD -1.07 (-1.75 to -0.38)	-	Very low	RCT	Serious ^k	None	None ^m	None	None
Mean temperature at > 5 to 24 hours											
<i>6 hours</i>											
1 (Kramer et al., 2008)	37.4°C (SD 0.8299), n = 19 ^l	37.5°C (SD 0.8299), n = 19 ^f	SMD -0.12 (-0.75 to +0.52)	-		RCT	Serious ^k	None	None ^m	Very serious ⁿ	None
<i>7 hours</i>											
1 (Pashapour et al., 2009)	38.0°C (SD 0.48), n = 35 ^e	38.2°C (SD 0.57), n = 35 ^f	SMD -0.38 (-0.85 to +0.10)	-	Modest	RCT	Very serious ^{g, h, i, j, k}	None	None	Serious ^o	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Alternating	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
8 hours											
1 (Pashapour et al., 2009)	37.7°C (SD 0.46), n = 35 ^e	38.0°C (SD 0.52), n = 35 ^f	SMD -0.60 (-1.08 to -0.12)	-	Moderate	RCT	Very serious ^{g, h, i, j, k}	None	None	None	None
Mean temperature at > 24 hours											
Day 1											
1 (Sarrell et al., 2006)	39.64°C (SD 1.17), n = 155 ^a	40.55°C (SD 1.31), n = 155 ^b	SMD -0.73 (-0.96 to -0.50)	-	High	RCT	None ^c	None	None	None	Yes ^d
Day 2											
1 (Sarrell et al., 2006)	38.78°C (SD 0.87), n = 155 ^a	39.74°C (SD 1.37), n = 155 ^b	SMD -0.83 (-1.07 to -0.60)	-	High	RCT	None ^c	None	None	None	Yes ^d
Day 3											
1 (Sarrell et al., 2006)	38.54°C (SD 0.74), n = 155 ^a	39.34°C (SD 1.19), n = 155 ^b	SMD -0.81 (-1.04 to -0.57)	-	High	RCT	None ^c	None	None	None	Yes ^d
Afebrile at 1 to 2 hours											
No data											
Afebrile at > 2 to 5 hours											
No data											
Afebrile at > 5 to 24 hours											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Alternating	Paracetamol	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 24 hours											
No data											
Temperature AUC											
No data											
Adverse events											
No reported											

NR Not reported

^a Alternating acetaminophen (12.5 mg/kg) with ibuprofen (5 mg/kg) every 4 hours

^b Acetaminophen (12.5 mg/kg) every 6 hours

^c Allocation could be determined by different regimens

^d Daily temperature was recorded by parents instead of trained clinicians

^e Alternating ibuprofen (10 mg/kg) with acetaminophen (15 mg/kg) every 4 hours

^f Acetaminophen (15 mg/kg) every 4 hours

^g Allocation not blinded

^h Methodology not explained in detail

ⁱ Reporting schedule unclear – why 2, 4, 5, 7, and 8 hours; are 1, 3, & 6 unreported?

^j Missing data not reported

^k Small sample size (n<100)

^l Alternating acetaminophen (15 mg/kg) with ibuprofen (10 mg/kg) with every 3 hours

^m Included children aged more than 5

ⁿ RR includes 0 and both ± 0.25 ; SMD crosses both ± 0.5

^o RR includes 0 and ± 0.25 ; SMD ± 0.5

Table I9.7 GRADE findings for ibuprofen vs. paracetamol and ibuprofen combined

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Discomfort at 1 to 2 hours												
No data												
Discomfort at > 2 to 5 hours												
No data												
Discomfort at > 5 to 24 hours												
24 hours												
Discomfort 1 (Hay et al., 2009)	29 of 50 ^a	36 of 52 ^b	RR 0.84 (0.62 to 1.13)	-	Low	RCT	Serious ^c	None	None ^d	None	None	
Activity 1 (Hay et al., 2009)	23 of 48 ^a	20 of 34 ^b	RR 0.81 (0.54 to 1.22)	-	Very low	RCT	Serious ^{c,e}	None	None ^d	None	None	
Appetite 1 (Hay et al., 2009)	14 of 48 ^a	14 of 52 ^b	RR 1.08 (0.58 to 2.03)	-	Very low	RCT	Serious ^c	None	None ^d	Very serious ^f	None	
Sleep 1 (Hay et al., 2009)	20 of 52 ^a	13 of 26 ^b	RR 0.77 (0.46 to 1.29)	-	Very low	RCT	Serious ^{c,e}	None	None ^d	Very serious ^f	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort > 24 hours											
48 hours											
Comfort 1 (Hay et al., 2009)	36 of 52 ^a	37 of 52 ^b	RR 0.97 (0.76 to 1.25) Adjusted OR 0.89 (0.32 to 2.43)	-	Moderate	RCT	Serious ^c	None	None ^d	Serious ^g	None
Activity 1 (Hay et al., 2009)	28 of 52 ^a	37 of 51 ^b	RR 0.74 (0.55 to 1.00)	-	Moderate	RCT	Serious ^c	None	None ^d	Serious ^g	None
Appetite 1 (Hay et al., 2009)	21 of 51 ^a	22 of 50 ^b	RR 0.94 (0.59 to 1.47)	-	Very low	RCT	Serious ^c	None	None ^d	Very serious ^f	None
Sleep 1 (Hay et al., 2009)	25 of 52 ^a	31 of 51 ^b	RR 0.79 (0.55 to 1.13)	-	Low	RCT	Serious ^c	None	None ^d	Serious ^g	None
Day 5											
Comfort 1 (Hay et al., 2009)	38 of 50 ^a	38 of 47 ^b	RR 0.94 (0.76 to 1.16)	-	Moderate	RCT	Serious ^c	None	None ^d	None	None
Activity 1 (Hay et al., 2009)	37 of 51 ^a	39 of 46 ^b	RR 0.86 (0.69 to 1.05)	-	Low	RCT	Serious ^c	None	None ^d	Serious ^g	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
<i>Appetite</i> 1 (Hay et al., 2009)	32 of 52 ^a	29 of 49 ^b	RR 1.04 (0.76 to 1.43)	-	Low	RCT	Serious ^c	None	None ^d	Serious ^g	None
<i>Sleep</i> 1 (Hay et al., 2009)	27 of 51 ^a	25 of 50 ^b	RR 1.06 (0.72 to 1.55)	-	Low	RCT	Serious ^c	None	None ^d	Very serious ^f	None
Mean change temperature at 1 to 2 hours											
<i>1 hour</i>											
1 (Erlewyn-Lajeunesse et al., 2006)	-1.22 (0.95 to 1.50) n = 36 ^h	-0.92 (0.70 to 1.14), n = 35 ⁱ	SMD -0.33 (-0.80 to +0.13)	-	Moderate	RCT	Serious ^{j, k}	None	Serious ^d	Very serious ^f	None
Mean change in temperature at > 2 to 5 hours											
No data											
Mean change in temperature at > 5 to 24 hours											
No data											
Mean change in temperature at > 24 hours											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean temperature at 1 to 2 hours												
1 hour												
1 (Erlewyn-Lajeunesse et al., 2006)	37.59°C (SD 0.61) ^h	37.81°C (SD 0.69) ⁱ	SMD -0.33 (-0.80 to +0.13) Adjusted MD = 0.25C (-0.01 to 0.50), p = 0.166	-	Moderate	RCT	Serious ^{j, k,}	None	Serious ^d	Serious ^g	None	
1 (Paul et al., 2010)	37.4°C (SD 0.5), n = 20 ^l	37.6°C (SD 0.5), n = 20 ^m	SMD -0.39 (-1.02 to +0.23)	-		RCT	Very serious ^{k, n, o}	None	None ^d	Serious ^g	None	
2 hours												
1 (Paul et al., 2010)	37.0°C (SD 0.5), n = 20 ^l	37.1°C (SD 0.4), n = 20 ^m	SMD -0.22 (-0.84 to +0.41)	-		RCT	Very serious ^{k, n, o}	None	None ^d	Serious ^g	None	
Mean temperature at > 2 to 5 hours												
3 hours												
1 (Paul et al., 2010)	36.9°C (SD 0.4), n = 20 ^l	37.2°C (SD 0.6), n = 20 ^m	SMD -0.58 (-1.21 to +0.06)	-		RCT	Very serious ^{k, n, o}	None	None ^d	Serious ^g	None	
4 hours												
1 (Paul et al., 2010)	36.9°C (SD 0.3), n = 20 ^l	37.5°C (SD 1.1), n = 20 ^m	SMD -0.73 (-1.37 to -0.09)	-		RCT	Very serious ^{k, n, o}	None	None ^d	None	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)								
5 hours												
1 (Paul et al., 2010)	36.9°C (SD 0.5), n = 20 ^l	38.0°C (SD 1.1), n = 20 ^m	SMD -1.26 (-1.95 to -0.58)	-		RCT	Very serious ^{s_{k,n,o}}	None	None ^d	None	None	
Mean temperature at > 5 to 24 hours												
6 hours												
1 (Paul et al., 2010)	37.2°C (SD 0.6), n = 20 ^l	38.5°C (SD 1.5), n = 20 ^m	SMD -1.12 (-1.79 to -0.44)	-		RCT	Very serious ^{s_{k,n,o}}	-	None ^d	None	None	
24 hours												
1 (Hay et al., 2009)	36.6°C (SD 1.01), n = 52 ^a	36.4°C (SD 0.85), n = 52 ^b	SMD 0.21 (-0.17 to +0.60)	-	Moderate	RCT	Serious ^c	-	None ^d	Serious ^g	None	
Mean temperature at > 24 hours												
1 (Hay et al., 2009)	36.0°C (SD 0.66), n = 52 ^a	36.1°C (SD 0.78), n = 52 ^b	SMD -0.14 (-0.52 to +0.25)	-	Moderate	RCT	Serious ^c	-	None ^d	Serious ^g	None	
Afebrile at 1 to 2 hours												
1 hour												
1 (Paul et al., 2010)	18 of 20 ^l	16 of 20 ^m	RR 1.13 (0.86 to 1.46)	-	Very low	RCT	Very serious ^{s_{k,n,o}}	-	None ^d	Serious ^g	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
2 hours											
1 (Hay et al., 2009)	47 of 52 ^a	44 of 52 ^b	SMD 1.07 (+0.92 to +1.24)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
1 (Paul et al., 2010)	20 of 20 ^l	19 of 20 ^m	RR 1.05 (0.92 to 1.20)	-	Low	RCT	Very serious ^{k,n,o}	-	None ^d	None	None
Afebrile at > 2 to 5 hours											
3 hours											
1 (Paul et al., 2010)	20 of 20 ^l	18 of 20 ^m	RR 1.11 (0.93 to 1.31)	-	Very low	RCT	Very serious ^{k,n,o}	-	None ^d	Serious ^g	None
4 hours											
1 (Hay et al., 2009)	51 of 52 ^l	44 of 52 ^m	RR 1.16 (1.03 to 1.31)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
1 (Paul et al., 2010)	20 of 20 ^l	14 of 20 ^m	RR 1.41 (1.05 to 1.90)	-	Low	RCT	Very serious ^{k,n,o}	-	None ^d	None	None
5 hours											
1 (Paul et al., 2010)	20 of 20 ^l	12 of 20 ^m	RR 1.64 (1.15 to 2.35)	-	Low	RCT	Very serious ^{k,n,o}	-	None ^d	None	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 5 to 24 hours											
6 hours											
1 (Hay et al., 2009)	47 of 52 ^a	37 of 52 ^b	RR 1.27 (1.05 to 1.54)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
1 (Paul et al., 2010)	19 of 20 ^l	10 of 20 ^m	RR 1.90 (1.21 to 2.98)	-	Low	RCT	Very serious ^{k,n,o}	-	None ^d	None	None
8 hours											
1 (Hay et al., 2009) 8 hours	45 of 52 ^a	46 of 52 ^b	RR 0.98 (0.85 to 1.13)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
12 hours											
1 (Hay et al., 2009)	49 of 52	47 of 52	RR 1.04 (0.93 to 1.17)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
Afebrile at > 24 hours											
24 hours											
1 (Hay et al., 2009)	47 of 52 ^a	45 of 52 ^b	RR 1.04 (0.91 to 1.20)	-	Moderate	RCT	Serious ^c	-	None ^d	None	None
Time without fever											
4 hours											
1 (Hay et al., 2009)	171.1 (40.8)	156.0 (57.6)	adjusted mean difference 16.2 (-7.0 to 39.4), p = 0.2	-	Moderate	RCT	Serious ^c	-	None ^d	-	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Combined	Mono	Relative (95% confidence interval)	Absolute (95% confidence interval)							
24 hours											
1 (Hay et al., 2009)	1217.4 (237.6)	1055.2 (329.7)	adjusted mean difference 2.5 (0.6 to 4.4), p = 0.008	-	Moderate	RCT	Serious ^c	-	None ^d	-	None
Adverse events											
Diarrhoea											
1 (Hay et al., 2009)	12 of 52	9 of 52	RR 0.75 (0.35 to 1.63)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f	
Vomiting											
1 (Hay et al., 2009)	2 of 52	3 of 52	RR 1.50 (0.26 to 8.61)	-	Very low	RCT	Serious ^c	-	None ^d	Very serious ^f	

NR Not reported

NC Non-calculable

^a Hay - 15mg/kg paracetamol + 10mg/kg ibuprofen^b 10 mg/kg ibuprofen^c Required sample size not achieved and blinding may not have been achieved^d Children aged more than 5 included in the study (Hay up to 6; Erlewyn up to 10; Paul up to 8)^e High level of missing data for ibuprofen group^f RR includes 0 and both ± 0.25 ; SMD crosses both ± 0.5 ^g RR includes 0 and ± 0.25 ; SMD crosses ± 0.5 ^h 15mg/kg + 5 mg/kgⁱ 5 mg/kg ibuprofen^j Allocation of treatment not blinded^k Small sample size (n < 100)^l 10 mg/kg Ibuprofen and 15 mg/kg acetaminophen single dose^m 10 mg/kg Ibuprofen single doseⁿ Blinding of allocation not used^o Children included in the study more than once

Table 9.8 GRADE findings for ibuprofen vs. paracetamol and ibuprofen alternating

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Discomfort at 1 to 2 hours												
No data												
Discomfort at > 2 to 5 hours												
No data												
Discomfort at > 5 to 24 hours												
Day 1												
NCCPC score 1 (Sarrell et al., 2006)	9.26 (SD 2.49), n = 155 ^a	11.48 (SD 2.58), n = 155 ^b	SMD -0.87 (-1.11 to -0.64)	-		RCT	None ^c	-	None	None	Yes ^d	
Discomfort > 24 hours												
Day 2												
NCCPC score 1 (Sarrell et al., 2006)	5.09 (SD 2.78), n = 155 ^a	8.83 (SD 2.67), n = 155 ^b	SMD -1.37 (-1.62 to -1.12)	-	High	RCT	None ^c	-	None	None	Yes ^d	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Day 3											
NCCPC score 1 (Sarrell et al., 2006)	4.18 (SD 2.74), n = 155 ^a	7.96 (SD 2.71), n = 155 ^b	SMD -1.38 (-1.63 to -1.14)	-	High	RCT	None ^c	-	None	None	Yes ^d
Mean change temperature at 1 to 2 hours											
No data											
Mean change in temperature at > 2 to 5 hours											
No data											
Mean change in temperature at > 5 to 24 hours											
No data											
Mean change in temperature at > 24 hours											
No data											
Mean temperature at 1 to 2 hours											
1 hour											
1 (Paul et al., 2010)	37.6°C (SD 0.4), n = 20 ^e	37.6°C (SD 0.5), n = 20 ^f	SMD 0.00 (-0.62 to +0.62)	-	Very low	RCT	Serious ^{g,h,i}	-	None	Very serious ^j	None
2 hours											
1 (Paul et al.,2010)	37.2°C (SD 0.3), n = 20 ^e	37.1°C (SD 0.4), n = 20 ^f	SMD 0.28 (-0.35 to +0.90)	-	Very low	RCT	Serious ^{g,h,i}	-	None	Serious ^k	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean temperature at > 2 to 5 hours												
3 hours												
1 (Paul et al.,2010)	36.9°C (SD 0.4), n = 20 ^e	37.2°C (SD 0.6), n = 20 ^f	SMD -0.58 (-1.21 to +0.06)	-	Low	RCT	Serious ^{g,h,i}	-	None	Serious _k	None	
4 hours												
1 (Nabulsi et al., 2006)	37.5°C (SD 0.7), n = 37 ^l	37.7°C (SD 0.9), n = 33 ^m	SMD -0.25 (-0.72 to +0.22)	-	Very low	RCT	Serious ^g	-	Serious _n	Serious _k	None	
1 (Paul et al.,2010)	36.9°C (SD 0.3), n = 20 ^e	37.5°C (SD 1.1), n = 20 ^f	SMD -0.73 (-1.37 to -0.09)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None	
5 hours												
1 (Paul et al.,2010)	36.8°C (SD 0.3), n = 20 ^e	38.0°C (SD 1.1), n = 20 ^f	SMD -1.46 (-2.16 to -0.75)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None	
Mean temperature at > 5 to 24 hours												
6 hours												
1 (Paul et al.,2010)	36.9°C (SD 0.3), n = 20 ^e	38.5°C (SD 1.5), n = 20 ^f	SMD -1.45 (-2.15 to -0.75)	-	Low	RCT	Serious ^{g,h,i}	-	None	Serious _k	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Mean temperature at > 24 hours											
Day 1											
1 (Sarrell et al., 2006)	39.64°C (SD 1.17), n = 155 ^a	40.6°C (SD 1.46), n = 155 ^b	SMD -0.72 (-0.95 to -0.49)	-	High	RCT	None ^c	-	None	None	Yes ^d
Day 2											
1 (Sarrell et al., 2006)	38.78°C (SD 0.87), n = 155 ^a	39.66°C (SD 1.48), n = 155 ^b	SMD -0.72 (-0.95 to -0.49)	-	High	RCT	None ^c	-	None	None	Yes ^d
Day 3											
1 (Sarrell et al., 2006)	38.54°C (SD 0.74), n = 155 ^a	39.64°C (SD 1.46), n = 155 ^b	SMD -0.95 (-1.18 to -0.71)	-	High	RCT	None ^c	-	None	None	Yes ^d
Afebrile at 1 to 2 hours											
1 hour											
1 (Paul et al., 2010)	16 of 20 ^e	16 of 20 ^f	RR 1.00 (0.73, to1.36)	-	Very low	RCT	Serious ^{g,h,i}	-	None	Very serious ^j	None
2 hours											
1 (Paul et al., 2010)	20 of 20 ^e	19 of 20 ^f	RR 1.05 (0.92 to 1.20)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 2 to 5 hours											
3 hours											
1 (Paul et al., 2010)	20 of 20 ^e	18 of 20 ^f	RR 1.11 (0.93 to 1.31)	-	Low	RCT	Serious ^{g,h,i}	-	None	Serious _k	None
4 hours											
1 (Paul et al., 2010)	20 of 20 ^e	14 of 20 ^f	RR 1.41 (1.05 to 1.90)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None
5 hours											
1 (Paul 2010)	20 of 20 ^e	12 of 20 ^f	RR 1.64 (1.15 to 2.35)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None
Afebrile at > 5 to 24 hours											
6 hours											
1 (Paul et al., 2010)	20 of 36 ^e	10 of 33 ^f	RR 1.95 (1.27 to 3.01)	-	Moderate	RCT	Serious ^{g,h,i}	-	None	None	None
1 (Nabulsi et al., 2006)	30 of 36 ^l	19 of 33 ^m	RR 1.62 (1.25 to 2.11)	-	Low	RCT	Serious ^g	-	Serious _l	None	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
7 hours											
1 (Nabulsi et al., 2006)	31 of 36 ^l	14 of 33 ^m	RR 2.03 (1.34 to 3.08)	-	Low	RCT	Serious ^g	-	Serious ⁱ	None	None
8 hours											
1 (Nabulsi et al., 2006)	29 of 36 ^l	11 of 33 ^m	RR 2.42 (1.45 to 4.02)	-	Low	RCT	Serious ^g	-	Serious ⁱ	None	None
Afebrile at > 24 hours											
No data											
Temperature AUC											
No data											
Adverse events											
Diarrhoea											
1 Nabulsi et al., 2006	5 of 37 ^l	6 of 37 ^m	RR 0.83 (0.28 to 2.49)	-	Very low	RCT	Serious ^g	-	Serious ⁱ	Very Serious ^j	None

NR Not reported

^a Alternating acetaminophen (12.5 mg/kg) with ibuprofen (5 mg/kg) every 4 hours

^b Ibuprofen (5 mg/kg) every 6 hours

^c Allocation could be determined by different regimens

^d Daily temperature was recorded by parents instead of trained clinicians

^e 10 mg/kg Ibuprofen and 15 mg/kg acetaminophen single dose

^f 10 mg/kg Ibuprofen single dose

^g Small sample size ($n < 100$)

^h Blinding of allocation not used

ⁱ Children included in the study more than once

^j RR includes 0 and both ± 0.25 ; SMD crosses both ± 0.5

^k RR includes 0 and ± 0.25 ; SMD crosses ± 0.5

^l Ibuprofen 10mg/kg, followed by acetaminophen 15mg/kg at 4h

^m Ibuprofen 10mg/kg, followed by placebo at 4h

ⁿ Includes children age more than 5 (Nabulsi – up to 14 years)

Table I9.9 – GRADE findings for paracetamol and ibuprofen combined vs. paracetamol and ibuprofen alternating

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Discomfort at 1 to 2 hours											
No data											
Discomfort at > 2 to 5 hours											
No data											
Discomfort at > 5 to 24 hours											
No data											
Discomfort > 24 hours											
No data											
Mean change temperature at 1 to 2 hours											
No data											
Mean change in temperature at > 2 to 5 hours											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration	
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)								
Mean change in temperature at > 5 to 24 hours												
No data												
Mean change in temperature at > 24 hours												
No data												
Mean temperature at 1 to 2 hours												
1 hour												
1 (Paul et al., 2010)	37.4°C (SD 0.5), n = 20 ^a	37.6°C (SD 0.4), n = 20 ^b	SMD -0.43 (-1.06 to +0.19)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^f	None	
2 hours												
1 (Paul et al., 2010)	37.0°C (SD 0.5), n = 20 ^a	37.2°C (SD 0.3), n = 20 ^b	SMD -0.48 (-1.10 to +0.15)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^f	None	
Mean temperature at > 2 to 5 hours												
3 hours												
1 (Paul et al., 2010)	36.9°C (SD 0.4), n = 20 ^a	36.9°C (SD 0.4), n = 20 ^b	SMD 0.00 (-0.62 to +0.62)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^g	None	
4 hours												
1 (Paul et al., 2010)	36.9°C (SD 0.3), n = 20 ^a	36.9°C (SD 0.3), n = 20 ^b	SMD 0.00 (-0.62 to +0.62)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^g	None	

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
5 hours											
1 (Paul et al., 2010)	36.9°C (SD 0.5), n = 20 ^a	36.8°C (SD 0.3), n = 20 ^b	SMD 0.24 (-0.38 to +0.86)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^g	None
Mean temperature at > 5 to 24 hours											
6 hours											
1 (Paul et al., 2010)	37.2°C (SD 0.6), n = 20 ^a	36.9°C (SD 0.3), n = 20 ^b	SMD 0.62 (-0.02 to +1.26)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^g	None
Mean temperature at > 24 hours											
No data											
Afebrile at 1 to 2 hours											
1 hour											
1 (Paul et al., 2010)	18 of 20 ^a	16 of 20 ^b	RR 1.13 (0.86 to 1.46)	-	Low	RCT	Serious ^{c,d,e}	-	None	Serious ^g	None
2 hours											
1 (Paul et al., 2010)	20 of 20 ^a	20 of 20 ^b	RR 1.00 (0.91 to 1.10)	-	Moderate	RCT	Serious ^{c,d,e}	-	None	None	None

Feverish illness in children (appendices)

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Afebrile at > 2 to 5 hours											
3 hours											
1 (Paul et al., 2010)	20 of 20 ^a	20 of 20 ^b	RR 1.00 (0.91 to 1.10)	-	Moderate	RCT	Serious ^{c,d,e}	-	None	None	None
4 hours											
1 (Paul et al., 2010)	20 of 20 ^a	20 of 20 ^b	RR 1.00 (0.91 to 1.10)	-	Moderate	RCT	Serious ^{c,d,e}	-	None	None	None
5 hours											
1 (Paul et al., 2010)	20 of 20 ^a	20 of 20 ^b	RR 1.00 (0.91 to 1.10)	-	Moderate	RCT	Serious ^{c,d,e}	-	None	None	None
Afebrile at > 5 to 24 hours											
6 hours											
1 (Paul et al., 2010)	19 of 20 ^a	20 of 20 ^b	RR 0.95 (0.83 to 1.09)	-	Moderate	RCT	Serious ^{c,d,e}	-	None	None	None
Afebrile at > 24 hours											
No data											
Temperature AUC											
No data											

Number of studies	Number of children		Effect		Quality	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other consideration
	Intervention	Control	Relative (95% confidence interval)	Absolute (95% confidence interval)							
Adverse events											
No data											

NR Not reported

^a 10 mg/kg Ibuprofen and 15 mg/kg acetaminophen single dose

^b 10 mg/kg Ibuprofen single dose

^c Small sample size (n < 100)

^d Blinding of allocation not used

^e Children included in the study more than once

^f RR includes 0 and ± 0.25 ; SMD crosses ± 0.5

^g RR includes 0 and both ± 0.25 ; SMD crosses both ± 0.5

Appendix J Deleted material from 2007 version

Priorities in the clinical assessment of feverish illness in children

- 4. make appropriate management decisions based upon the results of the assessment.

Traffic light system

The GDG decided to highlight graphically the non-specific features of illness severity and the specific symptoms and signs of serious illnesses in a 'traffic light' table. The 'red' features are the most worrying, followed by the 'amber' features, and the 'green' features are the most reassuring.

The traffic light table has been developed from many different sources. To ensure the recommendations follow in a logical sequence, the table is provided here *before* the evidence and translations. These are provided in Sections 5.5 and 5.6 of this chapter and the reader is advised to refer back to the table whenever it is mentioned.

Table 5.2 Traffic light system for identifying risk of serious illness. Children with fever and any of the symptoms or signs in the 'red' column should be recognised as being at high risk. Similarly, children with fever and any of the symptoms or signs in the 'amber' column and none in the 'red' column should be recognised as being at intermediate risk. Children with symptoms and signs in the 'green' column and none in the 'amber' or 'red' columns are at low risk. The management of children with fever should be directed by the level of risk

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour	<ul style="list-style-type: none"> • Normal colour of skin, lips and tongue 	<ul style="list-style-type: none"> • Pallor reported by parent/carer 	<ul style="list-style-type: none"> • Pale/mottled/ashen/blue
Activity	<ul style="list-style-type: none"> • Responds normally to social cues • Content/smiles • Stays awake or awakens quickly • Strong normal cry/not crying 	<ul style="list-style-type: none"> • Not responding normally to social cues • Wakes only with prolonged stimulation • Decreased activity • No smile 	<ul style="list-style-type: none"> • No response to social cues • Appears ill to a healthcare professional • Does not wake or if roused does not stay awake • Weak, high-pitched or continuous cry
Respiratory	<ul style="list-style-type: none"> • 	<ul style="list-style-type: none"> • Nasal flaring • Tachypnoea: RR > 50 breaths/minute, age 6–12 months RR > 40 breaths/minutes, age > 12 months • Oxygen saturation ≤ 95% in air • Crackles 	<ul style="list-style-type: none"> • Grunting • Tachypnoea: RR > 60 breaths/minute • Moderate or severe chest indrawing

	Green – low risk	Amber – intermediate risk	Red – high risk
Hydration	<ul style="list-style-type: none"> • Normal skin and eyes • Moist mucous membranes 	<ul style="list-style-type: none"> • Dry mucous membranes • Poor feeding in infants • CRT \geq 3 seconds • Reduced urine output 	<ul style="list-style-type: none"> • Reduced skin turgor
Other	<ul style="list-style-type: none"> • None of the amber or red symptoms or signs 	<ul style="list-style-type: none"> • Fever for \geq 5 days 	<ul style="list-style-type: none"> • Age 0–3 months, temperature \geq 38°C • Age 3–6 months, temperature \geq 39°C
		<ul style="list-style-type: none"> • Swelling of a limb or joint • Non-weight bearing/not using an extremity 	<ul style="list-style-type: none"> • Non-blanching rash • Bulging fontanelle • Neck stiffness • Status epilepticus • Focal neurological signs • Focal seizures
		<ul style="list-style-type: none"> • A new lump > 2 cm 	<ul style="list-style-type: none"> • Bile-stained vomiting

CRT = capillary refill time; RR = respiratory rate.

Non-specific symptoms and signs of serious illness

Evidence was sought for symptoms and signs associated with fever which would predict wellness or serious illness in young children. These symptoms and signs could be non-specific for any feverish illness or be particular to a specific underlying disease. Some features were looked for individually. These included heart rate, capillary refill time (CRT), blood pressure, respiratory rate (RR), height and duration of fever and the assessment of dehydration.

General symptoms and signs of serious illness

Review question

In children with fever, what symptoms or combination of symptoms are associated with serious illness or mortality?

Are there any scoring systems that use symptoms of children with fever to predict the risk of serious illness?

In children with fever, what signs or combination of symptoms and signs are associated with serious illness or mortality?

Are there any scoring systems that use symptoms and signs in children with fever to predict the risk of serious illness? How accurate are they?

In children with fever, what symptoms and signs are associated with self-limiting illness?

In view of the number of different healthcare locations in which the initial assessment can take place, studies that looked just at symptoms alone were reviewed (to assist the remote assessor) and studies that used symptoms and signs were reviewed (to assist the face-to-face assessor).

To determine which clinical features in feverish children are associated with serious illness and which are associated with a non-serious illness, studies looking at children with a variety of symptoms and signs on presentation and followed up to end diagnosis or outcome were sought (prospective cohort studies).

Scoring systems have been developed to try to distinguish seriously ill children from those who have a minor self-limiting illness, based on a combination of objective symptoms and signs. Studies determining the accuracy of these scoring systems were also sought.

Individual symptoms

Four EL 2+^{93–96} and one EL 2–⁹⁷ prospective cohort studies were found that reported on the relationship between individual symptoms and the likely presence of serious illness. The studies

varied widely in terms of setting (for example, primary and secondary care, developed countries and resource-poor countries), methods of analysis, the ages of children included (0–18 years with different exclusion criteria), symptoms described, definitions and prevalence of serious illness. Due to the methodological and hence statistical heterogeneity, it was inappropriate to perform a meta-analysis.

The symptoms in children aged less than 6 months that were associated with serious illness in one or more papers were drowsiness (RR 7.6),⁹³ decreased activity (RR 5.8),⁹³ pale on history (RR 4.4),⁹³ poor feeding (less than half normal amount) (RR 4.4,⁹³ OR 2.9–6.0⁹⁸), decreased wet nappies (< 4 in 24 hours) (RR 4.1)⁹³ and bile-stained vomiting (RR 5.1).⁹³ The RR was calculated based on the reported positive predictive values (PPVs) and negative predictive values (NPVs).

Individual symptoms and signs

Six EL 2+^{93–96,98,99} and one EL 2–⁹⁷ prospective studies describing the signs and symptoms associated with serious bacterial infection (SBI) were found. There is methodological heterogeneity among the studies. For example, the setting varied from developed countries such as Australia⁹³ to aggregated data from resource-poor settings.⁹⁸ Moreover, the age of children included varied from < 2 months⁹⁸ to 3 months to 15 years.⁹⁴ The list of signs strongly associated with SBI were:

- being drowsy^{93,98}
- moderate/severe chest recession^{93,98,99}
- respiratory rate > 60 breaths/minute^{97–99}
- nasal flaring⁹⁸
- grunting⁹⁸
- crackles⁹⁸
- lump > 2 cm⁹³
- being pale⁹³
- not looking well⁹⁹
- bulging fontanelle.⁹⁸

Scoring systems of combinations of symptoms and signs

When searching for scoring systems using combinations of signs and symptoms, only prospective cohort studies recruiting children with fever without apparent source (FWS) were included.

Seven EL 2+^{100–104,106,107} and one EL 2–¹⁰⁵ prospective studies were found covering two scoring systems for febrile infants, which used clinical features of patients alone: Yale Observation Scale (YOS, see Table 4.2)^{100–105} and the Young Infant Observation Scale (YIOS).^{106,107} Other scoring systems (Rochester^{96,108,109} and Philadelphia⁹⁶) use laboratory values as part of the scale and were therefore not included in this section. There is heterogeneity among the studies as the setting varied from developed countries such as the USA to resource-poor settings such as India, and the age of children included ranged from 0–2 months¹⁰⁶ to 3–36 months.¹⁰⁵

Neither the YOS nor YIOS alone could reliably detect serious illness in infants without missing many cases. The YOS did improve the detection of serious illness in infants when combined with a physician-taken history and examination (sensitivity and NPV improved from 86% to 89–93% and from 85–97% to 96–98%, respectively).¹⁰² All the validation studies found that a low YOS score is associated with well infants. From the validation study of the YOS,¹⁰¹ in children aged 3 months to 3 years with a score of 6, the NPV is 97.4% for occult bacteraemia.

The symptoms and signs in the YOS associated with being well are:

- strong cry/no cry
- content
- pink
- eyes not sunken/skin normal (hydration)
- if awake stays awake, if asleep is easily roused

- smiles.

When deriving the YOS scoring system, the following symptoms and signs were correlated with serious illness:^{100,102}

- weak/high-pitched
- continuous cry
- unable to rouse
- pale/mottled/blue
- sunken eyes/doughy skin
- no smile.

Evidence summary

Individual symptoms and individual symptoms and signs

The evidence from prospective cohort studies demonstrates a number of individual symptoms (i.e. drowsiness, decreased activity, poor feeding, pale, reduced urine output, bile-stained vomiting) and signs (i.e. being drowsy, moderate/severe chest recession, respiratory rate > 60 breaths/minute, nasal flaring, grunting, crackles, lump > 2 cm, being pale, not looking well, bulging fontanelle) that are associated with serious illness in infants and young children. Most of the evidence is limited to data relating to infants less than 6 months in a secondary care setting. In isolation, none of these symptoms or signs are reliably associated with serious illness.

Scoring systems of combinations of symptoms and signs

Scoring more than 10 using the YOS scoring system after a history and examination may help identify other infants and children at high risk of serious illness.

A YOS of 6 with a well-appearing child makes the presence of a serious illness very unlikely. However, the development of features of serious illness including the symptoms listed on the YOS should prompt further evaluation.

In isolation, none of these symptoms are strongly associated with serious illness. A child identified as 'ill' when assessed by an experienced healthcare professional is likely to have an SBI. To ensure that children with serious illness are recognized early, many children without serious illness will need to be examined.

Health economics profile

The GDG did not identify any issues where cost-effectiveness issues were a priority for this clinical question.

GDG translation

Individual symptoms and individual symptoms and signs

Prospective cohort studies of children with fever have identified a number of symptoms and signs that are predictive of serious illness. Much of the most reliable data relates to infants up to the age of 6 months. The GDG decided that it was reasonable based on clinical experience to extrapolate the symptoms and signs to older children and use them as part of the assessment of older children with a feverish illness. The GDG is aware that there is currently a large prospective study being conducted in Australia on the predictive values of symptoms and signs in febrile children of all ages. In the UK, a project is in development on the recognition of acute illness in children (Dr R MacFaul, personal communication). It is hoped that the results of these studies will inform future guidance on the assessment of the risk of serious illness in children with feverish illness.

Scoring systems of combinations of symptoms and signs

The features used in the YOS associated with serious illness are validated and show good correlation with those children who go on to develop serious illness in children aged 3 months to 3 years. The GDG felt that these features can be extrapolated for use on children up to the age of 5 years, based on clinical experience and extrapolated to the UK population.

'Traffic light' system

The GDG attempted to summarise the results of risk stratification from the prospective cohort studies and scoring studies in a 'traffic light' system. From the scoring studies, those symptoms and signs that scored only 1 on the YOS were designated 'green'. Those individual symptoms and signs that scored 5 in the YOS were designated 'red', as a child with only one 'red' symptom and all other 'green' symptoms (i.e. scoring 10 in the YOS) was at significant risk of serious illness. Those symptoms and signs that scored 3 in the YOS were designated 'amber', because while a child with a combination of 'amber' symptoms or signs was at significant risk of serious illness, a child with only one 'amber' feature was not at significant risk of serious illness.

From the prospective cohort studies, the GDG assigned 'red', 'amber' or 'green' status to additional symptoms and signs based on their associated risk of serious illness and on clinical experience.

Common physiological measurements and their predictive values of serious illness

Several other signs were looked for specifically as it was felt they were possible markers of serious illness. These included heart rate, capillary refill time (CRT), blood pressure and respiratory rate.

Heart rate

Narrative summary

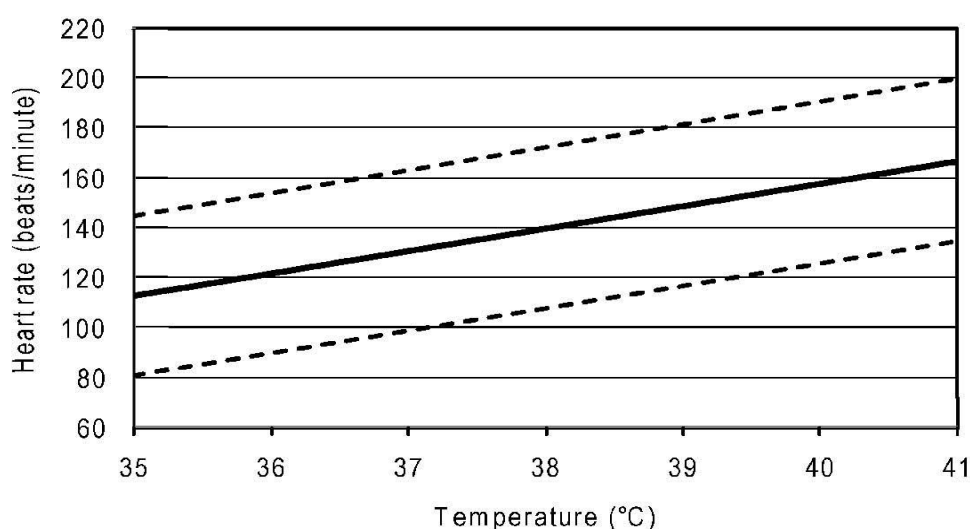
No evidence was found that provided 'normal values' for heart rate in the population of children under 5 years old. There is one EL 2+ study¹¹¹ that compared heart rate in children under 1 year with their body temperature. This study found that for every 1°C rise in body temperature, the resting heart rate rose by 9.6 beats/minute (Figure 5.1). The GDG is aware that there is an ongoing UK study to determine normal values for resting heart rate in children with fever aged 3 months to 12 years.

There are unvalidated tables of normal resting heart-rate values in young infants and children without fever which are widely taught (Figure 5.2).

Evidence summary

There is a lack of evidence regarding heart rate as a marker of serious illness. Despite this, the GDG felt that heart rate is a potentially important marker of serious illness. The Delphi panel was used to decide whether heart rate should be part of the routine assessment of a child with a fever, because a raised heart rate can be a sign of serious illness, particularly septic shock.

Figure 5.1 Heart rate rise with rising temperature in children less than 1 year old; adapted with permission from Hanna and Greenes¹¹¹



Delphi statement

'Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment.'

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	8 (15%)	39 (75%)	3 (6%)	1	52	9

Seventy-five percent of the Delphi panel agreed with this statement in round 1 (consensus achieved).

'Healthcare professionals should refer a child for specialist paediatric (children's) care if the resting heart rate is above the expected range for a feverish child.'

1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
2 (4%)	15 (30%)	33 (65%)	1 (2%)	1 (2%)	51	7

This statement did not reach consensus despite adaptations made to the original statement after round 1.

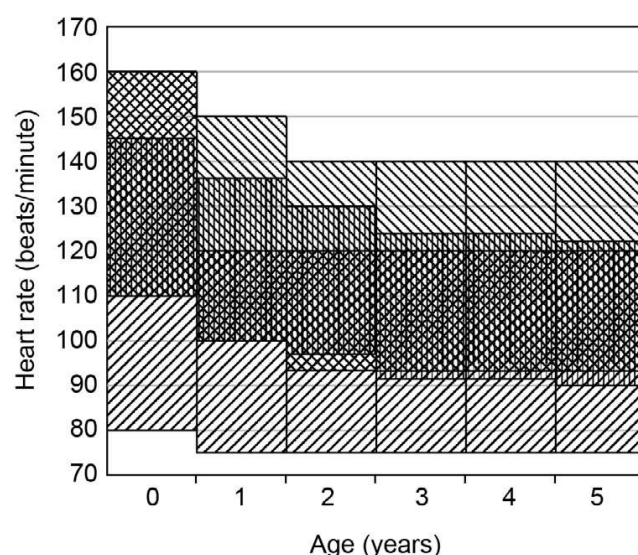
GDG translation

Heart rate was not placed in the 'traffic light' system (see below) as the Delphi panel did not agree that heart rate *per se* should be used as a basis for referral to specialist care. The statement 'healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment' was adapted and combined with the statement about the physiological parameters that should be documented as part of the assessment (see the end of Respiratory rate Section 4.5.2.4). The GDG felt it important to make healthcare professionals aware of the significance of a raised heart rate particularly in septic shock (see the recommendations at the end of Respiratory ratesection Section 4.5.2.4).

The GDG felt that basic physiological parameters in children should be backed up by a better weight of evidence. The GDG is aware that one research project on the predictive value of heart rate and

other vital signs in children with fever is currently in progress in the UK (Drs R MacFaul and M Thompson, personal communications) but it is likely that larger studies will be needed to produce definitive results. The GDG therefore recommends that studies are performed to confirm normal ranges for heart rate at various body temperatures and to determine whether children with heart rates outside these ranges are at higher risk of serious illness.

Figure 5.2 Widely quoted values for paediatric heart rates at various ages (left diagonals,²⁸⁸ right diagonals²⁸⁹) and the heart rates of children with minor blunt trauma at various ages (vertical lines¹¹²)



Capillary refill time

Narrative summary

Five studies were found investigating the prognostic value of the capillary refill time (CRT) with three EL 2+ prospective studies^{113–115} and one EL 2- retrospective study¹¹⁶ which included children in ICU post-resuscitation, which was excluded owing to the lack of relevance. In addition, there is one EL 2+ SR¹¹⁷ for signs and symptoms of dehydration which included CRT. Overall, the studies were conducted in a range of settings varying from primary care to intensive care in the UK,¹¹³ the USA¹¹⁴ and Kenya¹¹⁵ with different baselines which made meta-analysing inappropriate.

The SR¹¹⁷ showed that prolonged CRT had sensitivity of 0.60 (95% CI 0.29 to 0.91) and specificity of 0.85 (95% CI 0.72 to 0.98) of detecting 5% dehydration, which made CRT the most specific sign of dehydration. The results from prospective cohort studies showed that there was no significant association of CRT of 3 seconds with meningococcal disease, other significant bacterial illness or white blood cell count (WBC) (statistics not provided).¹¹³ In one prospective cohort study, the receiver operating characteristic (ROC) curve showed that the best performance was obtained when a CRT of 3 seconds was taken to be 'prolonged'; furthermore, a prolonged CRT (> 3 seconds) was associated with a more urgent triage category, the administration of fluid bolus and the length of hospital stay (all $P < 0.05$).¹¹³ Moreover, children with dehydration had prolonged CRT of 2 seconds, with a sensitivity of only 44% for predicting a fluid deficiency of < 5% or more of body weight (other statistics not provided).¹¹⁴ Overall agreement for CRT was moderate ($k = 0.42$), and was better for normal values (= 1 second) ($k = 0.48$) and clearly abnormal values (= 4 seconds) ($k = 0.49$).¹¹⁵

Furthermore, in a search of the specific signs and symptoms of meningococcal disease, CRT was found to be indicative (the OR of CRT > 3 seconds of having meningococcal disease is 29.4 (95% CI 9.4 to 92.6))¹¹⁸ in children with a petechial rash. In another SR¹¹⁷ that included four trials investigating the usefulness of prolonged CRT to indicated dehydration, the findings showed that the pooled sensitivity of prolonged CRT (defined differently in different studies) was 0.60 (95% CI 0.29 to 0.91), with a specificity of 0.85 (95% CI 0.72 to 0.98), for detecting 5% dehydration.

Evidence summary

The authors used different cut-offs of CRT and it appeared that CRT of 2 seconds was a weak predictor of dehydration and serious illness while a CRT = 3 seconds is associated with dehydration and significant illness (e.g. meningococcal disease) in children.

GDG translation

The GDG noted that CRT is quick to carry out and exhibits moderate reproducibility. A statement about measuring CRT was combined with the statement about the physiological parameters which should be documented as part of the assessment (see the end of Respiratory rate Section 4.5.2.4). The GDG considered that a CRT of = 3 seconds was an 'amber' sign (see the recommendations at the end of Respiratory rate section Section 4.5.2.4).

Respiratory rate

Evidence summary

Refer to Sections 4.5.1 (General symptoms and signs of serious illness), 4.5.4 (Assessment of dehydration), and 4.6.6 (Pneumonia), for evidence relating to respiratory rate.

GDG translation

An abnormal respiratory rate has been shown to be a non-specific marker of serious illness, a specific feature of pneumonia and required for the assessment of dehydration. The GDG felt that respiratory rate is therefore an important physiological parameter which needs to be assessed by healthcare professionals. A statement about measuring respiratory rate was combined with the statement about the physiological parameters which should be documented as part of the assessment (see below).

Height and duration of fever and its predictive value of serious illness

When a child with a febrile illness is being assessed, healthcare professionals often ask about the degree and duration of fever. The reason for these questions is that it is often assumed that these variables can be used to help differentiate serious bacterial illnesses from less serious self-limiting viral infections. Regarding the height of recorded fever, it is often thought that there is a higher risk of serious illness with increasing body temperature. Regarding duration of fever, it is sometimes thought that an SBI is more likely with increasing duration of fever. This is on the grounds that viral illnesses will usually resolve spontaneously over a shorter period of time. There is also a converse view that children with serious illness will present to healthcare professionals earlier in the illness because they may have other features that lead parents and carers to suspect the child is seriously unwell.

Height of fever

Review question

Can the height of body temperature in a young child with fever be used to predict the risk of serious illness or mortality?

Narrative evidence

The literature search was restricted to prospective cohort studies because this would yield the highest quality evidence (EL 2). Twelve prospective cohort studies,^{93,95,98,99,120–127} of which three were EL 2-^{124,125,127} were found that reported on the relationship between height of fever and the outcome in terms of serious illness. The studies varied widely in terms of setting (e.g. hospital emergency department or paediatric assessment units in different countries such as Australia,⁹³ the UK¹²¹ or the USA, and Puerto Rico¹²⁰), ages of children included (e.g. < 28 days¹²⁷ to 3–36 months¹²⁸), definition of fever (e.g. rectal temperature = 38°C or rectal temperature = 39°C) and outcomes measured. There was also wide variation in the methods of analysis. For these reasons it was not possible or appropriate to pool the data.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures = 39°C in particular being associated with a higher risk. Other studies did not report this association. The sensitivity of a high body temperature to detect SBI is low. With one exception, the sensitivity of a temperature = 39°C to detect SBI was between 10% and 32%. In developed countries the sensitivity of a temperature = 39°C to detect SBI was between 10% and 14%. The PPV of a temperature = 39°C varied between 4% and 40% in developed countries.

Evidence summary

Twelve prospective cohort studies (nine EL 2+ and three EL 2-) that reported on the relationship between height of fever and the outcome in terms of serious illness were found.

Several large EL 2+ studies reported a higher relative risk of SBI with increasing body temperature, with body temperatures = 39°C in particular being associated with a higher risk. Other EL 2+ studies did not report this association.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted that most large EL 2+ studies suggest that the risk of serious illness increases with height of fever in young children. Body temperatures = 39°C in particular were usually associated with a higher relative risk of SBI. The strongest associations were reported in studies involving children aged less than 6 months. However, the sensitivity and PPV of temperatures=39°C were low, which suggests that most cases of serious illness would be missed if height of body temperature was used in isolation to identify children with serious illness. Furthermore, the GDG noted that other features of a child with feverish illness, such as his or her age or an 'ill appearance' were often more predictive.

The GDG concluded that healthcare professionals should be aware that there is an association between height of body temperature and risk of SBI. However, this association is not sufficiently robust to recommend immediate action or referral based on body temperature alone. An exception was made for children aged under 6 months with body temperature = 39°C because the evidence was strongest for this age group.

In addition, the GDG noted that children aged under 3 months with fever are generally at a higher risk of serious illness (see Section 8.3). The incidence of serious illness in this group, for instance, is over ten times higher than that in older children. The clinical studies that provide the evidence for this age group used a body temperature=38°C as the definition of fever. The GDG therefore decided that children aged under 3 months with a body temperature=38°C should also be included in the recommendation about risk of serious illness.

Duration of fever and its predictive value of serious illness

Review question

Can the duration of fever in a febrile young child be used to predict the risk of serious illness or mortality?

Narrative evidence

Three EL 2+ prospective studies^{126,129,130} that looked at the duration of fever as a risk factor for SBIs in general were found. One of them¹²⁹ reported that a duration of fever > 48 hours had an odds ratio of 3.85 (95% CI 1.11 to 13.3) for predicting serious illness. This relationship just reached statistical significance as an independent predictor of SBI. Another prospective cohort study¹²⁶ reported that duration of fever was longer in infants with SBIs (26.5 ± 41.5 hours) than those without (18.6 ± 21.7 hours) ($P < 0.01$). Furthermore, in comparison with < 24 hours, duration of fever > 48 hours had an odds ratio of 1.04 (95% CI 0.35 to 3.12) of having SBIs.¹³⁰ Of the other two EL 2 studies, one reported that children with SBI had statistically significant longer duration of fever while the other did not.

Two EL 2+ prospective studies^{122,123} were also found that looked at the incidence of (predominantly occult) bacteraemia in relation to duration of fever in children with temperature = 39°C. Both studies reported a higher relative risk of bacteraemia with a shorter duration of fever (RR 1.5¹²² to 4.6¹²³). The PPVs of a short duration of fever were 4% and 10%.^{122,123}

Evidence summary

It was noted that there was a weak association between duration of fever and risk of serious illness from the three studies that looked at SBI in general. There was also an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia.

Health economics

The GDG did not identify any issues that required a cost-effectiveness analysis for this clinical question.

GDG translation

The GDG noted a weak association between duration of fever and risk of serious illness from the five studies that looked at SBI in general. They also noted an apparently converse association between duration of fever and risk of one particular SBI, namely bacteraemia. The GDG concluded that the evidence was equivocal and relatively weak in both directions. They concluded that, on the basis of existing evidence, duration of fever could not usefully be included in the list of features that may be used to help predict serious illness.

The GDG was aware that longer durations of fever than those reported in the studies above may be associated with certain serious illnesses. In particular, the GDG noted that a fever lasting 5 days or more is one of the diagnostic criteria for Kawasaki disease. For this reason, it was decided to include a fever lasting 5 days or more as one of the 'amber' features in the traffic light system. A recommendation on the diagnosis of Kawasaki Disease is included in Section 5.6.

Table 5.4 Summary table for symptoms and signs suggestive of specific diseases

Diagnosis to be considered	Symptoms and signs in conjunction with fever
Meningococcal disease	Non-blanching rash, particularly with one or more of the following: <ul style="list-style-type: none"> • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • capillary refill time of ≥ 3 seconds • neck stiffness
Meningitis	Neck stiffness Bulging fontanelle Decreased level of consciousness Convulsive status epilepticus
Herpes simplex encephalitis	Focal neurological signs Focal seizures Decreased level of consciousness
Pneumonia	Tachypnoea (RR > 60 breaths/minute, age 0–5 months; RR > 50 breaths/minute, age 6–12 months; RR > 40 breaths/minute, age > 12 months) Crackles in the chest Nasal flaring Chest indrawing Cyanosis Oxygen saturations $\leq 95\%$
Urinary tract infection	Vomiting Poor feeding Lethargy Irritability Abdominal pain or tenderness Urinary frequency or dysuria

	Offensive urine or haematuria
Septic arthritis	Swelling of a limb or joint
	Not using an extremity
	Non-weight bearing
Kawasaki disease	Fever for more than 5 days and at least four of the following: <ul style="list-style-type: none"> • bilateral conjunctival injection • change in mucous membranes • change in the extremities • polymorphous rash • cervical lymphadenopathy

RR =respiratory rate.

Number Research recommendation

Meningococcal disease

There is a need for a prospective study to assess the prognostic value of symptoms such as limb pain and cold hands and feet that have been identified as possible early markers of meningococcal disease.

Management by the -paediatric specialist

Children less than 3 months old

An EL 1+ SR comprising six studies¹⁶⁵ which examined whether procalcitonin (PCT) was a useful marker of SBI in neonates and children was also found. A significant increase in serum PCT concentration during sepsis was found in both term neonates and a heterogeneous group of preterm neonates. However, PCT lacked specificity compared with C-reactive protein (CRP) as an early marker in the diagnosis of SBI. The performance characteristics of CRP as a marker of SBI varied as different cut-off levels were used in the various studies.

C-reactive protein

A heterogeneous group of 11 EL II prospective cohort studies^{166–174,178} evaluating CRP was identified. Age ranges for these studies were birth to 16 years, but only three EL II studies contained data on children older than 36 months.^{166,172,174} Conditions studied were SBI, MCD, bacterial meningitis, bacteraemia, OBI and bacterial pneumonia. The cut-off value for CRP varied from 27.5 to 70 mg/litre. Table 8.1 shows sensitivities, specificities and relative risks for CRP values in identifying serious illness or discriminating non-serious from serious illness for each study.

Two other EL II studies^{170,171} looked at differences in CRP depending on the timing of the sample from the onset of symptoms. There was no significant difference in sensitivity or specificity between those CRP values collected more than 12 hours after the onset of feverish illness compared with those collected less than 12 hours after onset.¹⁷⁰ Slightly lower sensitivity (61.3% versus 63.5%) and specificity (80% versus 84.2%) was reported for CRP in infants when taken less than 12 hours after the onset of symptoms, but this was at a lower cut-off value of 19 mg/litre.¹⁷⁰ Furthermore, the study which evaluated the differences in CRP performance at greater than and less than 12 months old was examined. At a CRP cut-off value of 40 mg/litre, for children less than 12 months old, sensitivity and specificity were reported to be 94% and 84%, respectively (RR 31.5), whereas for those greater than 12 months old, sensitivity and specificity were reported as 80% and 59%, respectively (RR 4.0).

This study also demonstrated increased post-test probability of SBI with increasing CRP (10% at CRP < 40 mg/litre versus 86% at CRP > 100 mg/litre).

Table 8.1 Summary of sensitivity, specificity and relative risk of included studies evaluating CRP

Study	CRP cut-off (mg/litre)	Sensitivity (%)	Specificity (%)	Relative risk
Galetto-Lacour ^{178a}	40	79	79	6.1
Galetto-Lacour ^{178a}	40	89	75	12.75
Carrol ¹⁶⁶	30	81	89	3.79
Thayyil ¹⁶⁷	50	75	68.7	5.23
Kohli ¹⁶⁸	40	95	86	33.5
Pulliam ¹⁶⁹	70	79	91	13
Isaacman ¹⁷⁰	44	63	81	5.0
Fernandez ¹⁷¹	27.5	63.5	84.2	1.97
Gendrel ¹⁷²	20	73	88	5.43
Lembo ¹⁷³	10	80	55	2.3
Moulin ^{174b}	60	69.8	52	1.94
Moulin ^{174b}	20	88.4	40	2.14

^aGaletto-Lacour *et al.* produced two papers from the same data set

^bMoulin *et al.* performed analysis at two CRP cut-off values

Procalcitonin

An EL 1+ SR¹⁶⁵ looking at 46 articles which evaluated the role of PCT as an early marker of infection in neonates and young children was identified. Neonatal studies regarding the investigation of children less than 3 months of age are discussed in Section 7.3 of this chapter. The findings of the SR against each clinical condition are summarised below.

Health economics

An economic evaluation was undertaken to assess the cost-effectiveness of CRP versus PCT to investigate the presence of SBI in children without apparent source (Appendix D). Health economic evaluation was required since PCT is not routinely used. All other diagnostic tests are offered on the NHS and are part of the usual package of tests for children over 3 months where SBI is suspected. The results indicated that under certain assumptions CRP is both less costly and more effective than PCT in correctly diagnosing and ruling out SBI in children with FWS. However, the results were sensitive to the prevalence of SBI. CRP no longer dominated PCT when the prevalence of SBI was over 27%, keeping all the other baseline assumptions constant. However, given the lack of robust evidence underpinning these baseline assumptions, the analysis cannot support the replacement of CRP with PCT at present. The GDG has recommended more research on the performance characteristics of CRP and PCT in children with feverish illness of uncertain cause.

Response to antipyretic medication

It has been suggested that response to antipyretic medication may help differentiate serious from non-serious illness in febrile children. This could occur in two ways:

- a decrease in fever
- improved clinical appearance.

Decrease in fever after antipyretics

Some healthcare professionals think that a decrease in fever with antipyretic therapy indicates a lower likelihood of SBI. It is also assumed that a lack of response to antipyretic therapy makes an SBI more likely. In contrast to this, other healthcare professionals fear that giving antipyretics to reduce fever in febrile children may make the detection of serious illness more difficult as the high fever of bacterial

illness is 'masked' by antipyretics. Evidence about fever response to antipyretics in children with both serious and non-serious illness would be useful to help in the assessment of these children.

Improved clinical appearance after antipyretics

Antipyretics may also improve the child's general condition. Many healthcare professionals feel that clinical review of a febrile child 1–2 hours after they have been given antipyretics improves the ability to differentiate between serious and non-serious illness. The antipyretic and analgesic effect of antipyretics may lead to the improvement of features which may suggest serious illness (e.g. irritability, tachycardia, etc). If this improvement in features occurred only in those with non-serious illness, this would help to identify these children. However, if this improvement also occurred in children with serious illness, then these children may not have their illness identified correctly.

Evidence about improved clinical appearance after antipyretics would be useful to help in the assessment of children and would also be relevant to the use of observation in febrile children.

Review question

In a child with fever, does a failure to respond to antipyretics increase the likelihood of a serious illness?

Sub-question

Conversely, does a reduction in body temperature in response to antipyretics increase the likelihood of a self-limiting illness?

Narrative evidence

Five EL 2+ prospective cohort studies^{162,184–187} and one EL 4 conference abstract,¹⁸⁸ which was judged to be important for inclusion, investigating the relationship between a reduction of body temperature due to antipyretics and the likelihood of serious illness were identified. Four of these^{162,184,185,187,188} were conducted in the USA and one in Japan.¹⁸⁶ All these studies were hospital cohorts with different dosages and type of antipyretics (paracetamol 15 mg/kg^{184,185} or 10 mg/kg of paracetamol or aspirin^{162,185,186}), different ages of children included (3–24 months,^{162,185,186} 8 weeks to 6 years¹⁸⁷ or < 24 months¹⁸⁸), different definitions of fever and different methods of measuring body temperature. The evidence suggests that a change in temperature 1–2 hours after antipyretics does not help identify children with serious illness. However, assessment with YOS 1 hour after antipyretics seems more specific. The mean repeat YOS was 13.7 in children with serious illness compared with 10.0 in the children without serious illness ($P = 0.004$).¹⁸⁹

Evidence summary

The results from prospective cohort studies showed that a change in temperature 1–2 hours after antipyretics does not help identify children with serious illness. However, children with serious illness generally appear more ill than those without serious illness after antipyretics.

GDG translation

Some healthcare professionals think that a decrease in temperature after antipyretics makes an SBI less likely. The GDG concluded that this is not supported by evidence. Children with YOS > 10 mostly have 'amber' or 'red' features. The GDG found some evidence that if these children are reassessed after antipyretics, the features may have resolved in those without serious illness. Reassessment after antipyretics may help differentiate those with and without serious illness but the GDG recognised that more research could usefully be undertaken on this subject.

Antipyretic interventions

Physical and drug interventions

Drug interventions

Narrative evidence

Two EL 1+ reviews^{210,214} and four EL 1+ RCTs^{215–218} comparing paracetamol and ibuprofen were found. Paracetamol and ibuprofen were both shown to be effective at reducing fever in children.^{210,214,215,217,218} Both reviews^{210,214} demonstrated that ibuprofen had a more pronounced and/or longer lasting effect on fever compared with paracetamol. However, in many of those studies paracetamol was used in doses below those currently recommended in the UK.

Adverse effects of antipyretic drugs

One EL 1+ meta-analysis²¹⁰ which compared patients receiving single doses of paracetamol or ibuprofen was found. Despite the widespread use of ibuprofen and paracetamol, adverse events were rare. No evidence was found to suggest a difference in the risk of either minor or major harm between the two drugs. However, there have been reports of serious suspected adverse reactions even at therapeutic doses for both drugs.^{4,219} There is greater experience with the use of paracetamol but ibuprofen use is increasing and different adverse effect profiles may emerge.

Delphi consensus

There is a lack of evidence regarding indications for when children should be given antipyretic drugs. The GDG therefore decided to use the Delphi survey to provide information for these questions. After two rounds of Delphi the results below were obtained.

Delphi statement 8.1

Antipyretic drugs should be given to all children with fever.

1 to 3	4 to 6	7 to 9	Don't now	Missing	Total	Median
10 (19%)	11 (21%)	29 (56%)	2 (4%)		52	7

After two rounds of Delphi this question failed to reach consensus and this statement was not therefore included in the draft version of the guideline. The second question to answer was Statement 8.2 of the Delphi consensus.

Delphi statement 8.2

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better.

1 to 3	4 to 6	7 to 9	Don't now	Missing	Total	Median
3 (6%)	5 (10%)	43 (83%)	1 (2%)		52	8

This reached agreement by consensus of 83% of respondents after round 2 and is therefore included as a recommendation in the guideline.

Evidence summary

Paracetamol and ibuprofen are both effective antipyretics. Physical methods of temperature reduction offer little additional benefit and cause crying and shivering in some children. There is no evidence of a significant difference in the incidence of adverse events between the two drugs. On current evidence both drugs are equally effective but paracetamol has a longer established safety record.

There is no evidence for any specific indications for the administration of antipyretics. Care should, however, be taken with all drugs, including antipyretics if given in combination with other drugs, or if the child is suffering other complications or conditions such as dehydration. Delphi consensus provided strong agreement that antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better, but not that they should be given to all children with fever.

Health economics

Since no evidence of difference in the effectiveness of paracetamol and ibuprofen was identified, decisions on which should be used in the NHS should be based on individual prices available to trusts at the time of purchase.

GDG translation

Ibuprofen and paracetamol are widely used as antipyretic drugs. Although adverse effects and toxicities are possible with their use, paediatric formulations are safe in most children. Healthcare professionals and others involved in the supply of these drugs should ensure that parents understand how to administer them safely.

Despite their common use, there is no evidence regarding the indications for the administration of antipyretic drugs. Consequently, the GDG included questions on this in the Delphi survey. The results of this partly confirmed the lack of evidence, with no consensus on the statement that antipyretic drugs should be given to all children with fever. However, there was strong support for the statement that antipyretics should be offered to children who are miserable with fever because they may make them feel better. In response to stakeholder comments that antipyretics should not be given just because a child has a fever, the GDG decided to revisit the question as to whether all children with fever should be given antipyretics. The GDG achieved consensus among themselves that children with fever do not necessarily need to be given antipyretic agents, especially in light of the following recommendation that children who are miserable with fever may benefit from treatment. Because of the uncertainties about the benefits of antipyretic agents and their indications, the GDG recommended that more research should be conducted on the topic.

Because both drugs are safe and effective, no recommendation can be made about which should be used. The health economic analysis suggests that decisions on which should be used in the NHS should be based upon individual prices available to trusts at the time of purchase.

Research recommendation

Research recommendation on drug interventions for reducing temperature

Efficacy and cost-effectiveness studies are required which measure symptom relief associated with fever relief.

Combining pharmacological treatments

Paracetamol and ibuprofen, the drugs most commonly used to treat fever, are often used together by healthcare professionals, parents and patients, either in combination or alternately.²²⁰

Narrative evidence

Two EL 1- RCTs^{221,222} investigating the combination of antipyretic drug therapies and one EL 1+ RCT²²³ and one EL 1- RCT²²² investigating the alternation of antipyretic drug therapies were found.

Combination treatment

One EL 1- RCT²²¹ from the UK examined the administration of paracetamol, ibuprofen or both. It has to be noted that this study had no blinding and small numbers ($n=37, 35, 36$) in each arm. A statistically significant difference between the combination and paracetamol groups was found, but this was only 0.35°C and was not considered to be clinically significant. Follow-up of the majority of patients was only for 1 hour and therefore failed to detect any delayed differences. A second EL 1- RCT²²² from India with small patient numbers ($n=80$) showed that ibuprofen combined with paracetamol and nimesulide and paracetamol had almost identical antipyretic effects. No marked adverse effects were detected. Statistical data were not reported.

Neither study was of sufficient methodological quality to provide reliable evidence on the combined use of paracetamol and ibuprofen, which is therefore not recommended.

Alternating treatment

Two RCTs^{222,223} were found which examined the use of alternating regimens of antipyretic agents.

One EL 1+ RCT²²³ from Israel assigned children to receive either paracetamol or ibuprofen or to receive alternating paracetamol and ibuprofen for 3 days. The group given the alternating regimen was characterised by a lower mean temperature, more rapid reduction of fever, receiving less antipyretic medication, less stress, and less absenteeism from day care as compared with the other groups; all of the differences were statistically significant ($P < 0.05$). However, the study involved the use of a double dose loading dose, used low paracetamol maintenance doses and relied on parental temperature measurement and documentation at home. The second EL 1- RCT²²⁴ from Lebanon randomly allocated patients into one of two treatment groups: an intervention group where a single oral dose of ibuprofen was administered at baseline followed by a single oral dose of paracetamol

4 hours later; and a control group where a similar dose of ibuprofen was administered initially, followed by placebo 4 hours later. Those in the intervention group were significantly more likely than those in the control group to become afebrile at 6, 7 and 8 hours ($P < 0.05$). The two groups had similar maximum decline in temperature. No serious adverse reactions were observed. Although these results suggest the superiority of the combined alternating regimen, the findings need to be confirmed in larger trials, since the study had small numbers in each arm and failed to achieve its calculated sample size.

Evidence summary

Current limited evidence from a small number of RCTs suggests that combination treatment offers no advantage over single drug therapy and would not lead to clinically significant further reduction of body temperature. There is also inadequate evidence to demonstrate the safety of combination treatment. An individual case report has highlighted potential interactions between these drugs.²²⁵ More methodologically sound studies are therefore required to investigate the use of antipyretic combination treatment before recommendations can be made.

There is some limited evidence to suggest that alternating ibuprofen and paracetamol treatment is superior to monotherapy, although the safety of this treatment has not been studied.

GDG translation

The GDG recognises that combinations of paracetamol and ibuprofen, or regimens alternating the two drugs, are in common use by healthcare professionals and families. There is insufficient evidence to support or refute these practices. The potential for adverse drug reactions of the two used together is not known. Theoretical interactions are recognised and reliable safety data do not exist. Furthermore, each drug is known to be effective as a single agent and the potential for confusion and drug administration errors is increased by using more than one drug.

The studies examining administering paracetamol and ibuprofen at the same time have demonstrated no benefit above giving either agent alone, but these had low patient numbers. The two studies which have claimed benefit from an alternating regimen of ibuprofen and paracetamol do not provide sufficient evidence to support such a recommendation. The GDG is aware that an HTA study is currently examining the use of combined regimens of paracetamol and ibuprofen and will report in 2009.

The GDG noted that, from the evidence, antipyretic agents do not appear to be effective in the prevention of febrile convulsions. There is very limited evidence regarding the effect of paracetamol on activity and other areas contained within the clinical question, which showed inconsistent effects.

Research recommendation

Research recommendation on combining pharmacological treatment to reduce temperature

The GDG recommends that a study is conducted on the effectiveness and safety of alternating doses of paracetamol and ibuprofen in reducing fever in children who remain febrile after the first antipyretic.

Effects of body temperature reduction

In addition to the underlying illness, fever may be accompanied by a number of unpleasant symptoms including pain, reduced eating and drinking, and reduced activity. In some cases, for example pain, this is likely to be the result of the illness causing the fever. However, in other cases it is not always clear whether these are the direct result of the fever, or of the underlying illness, or a combination of the two. The GDG therefore considered the use of antipyretic interventions in the treatment of these symptoms.

Because fever is a normal response to infection, some studies have been undertaken to look at the effect of the treatment of fever on specific conditions, including malaria,²²⁶ chickenpox²²⁷ and various viral infections.²²⁸ These showed that antipyresis does appear to slow recovery, and makes little

difference to some aspects of wellbeing, although the clinical significance of these findings is marginal. As these studies were undertaken on patients who had a diagnosis, these fell outside of the scope of this guideline, and are not discussed further.

A particular concern of many parents about fever in children is that it may cause fits, or febrile convulsions.²⁰⁶ These are common in young children, and are very rarely associated with epilepsy or other problems in later life.²³⁰ Because antipyretics reduce temperature, there is a theoretical rationale for their use in the prevention of febrile convulsions.

Review question

Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following:

- time to recovery
- wellbeing
- activity
- eating and drinking
- prevention of febrile convulsions?

We did not find any evidence against other interventions.

Narrative evidence

Although there are some studies looking at the effect of pharmacological antipyresis on recovery from specific conditions such as chickenpox and malaria, and viral conditions, these fell outside of the scope of this guideline.

Research regarding the use of antipyretics in the prevention and treatment of febrile convulsions is limited. One EL 1+ review²³¹ that was judged to be adequate for inclusion owing to its clinical relevance, after obtaining methodological details from the author, and one EL 1+ SR²³² examining the use of antipyretic drugs as prophylaxis against febrile convulsions were found.

The first²³¹ investigated the hypothesis that paracetamol and ibuprofen, used prophylactically, will reduce the incidence of febrile convulsions across a wide variety of conditions. It found no evidence that the prophylactic use of antipyretics has any effect in reducing the incidence of febrile convulsions. The second review²³² assessed 12 studies of the effects of paracetamol for treating children in relation to fever clearance time, febrile convulsions and resolution of associated symptoms. It also found no evidence that the use of prophylactic paracetamol influenced the risk of febrile convulsions.

An EL 1+ double-blind RCT²²⁸ analysing ²²⁵ datasets was also identified, which found that there was no significant difference in mean duration of fever (34.7 hours versus 36.1 hours, *P* not given) or of other symptoms (72.9 hours versus 71.7 hours). Children treated with paracetamol were more likely to be rated as having at least a 1-category improvement in activity (*P* = 0.005) and alertness (*P* = 0.036).

Evidence summary

Limited evidence was found regarding the use of antipyretic medications in the promotion of wellbeing, activity, eating and drinking, and no evidence of cost-effectiveness. One study suggested that parents could identify some improvement in activity and alertness after the administration of paracetamol, but not in mood, comfort, appetite or fluid intake. There is no evidence that the use of antipyretic agents reduces the incidence of febrile convulsions. (EL 1)

GDG translation

The GDG noted that, from the evidence, antipyretic agents do not appear to be effective in the prevention of febrile convulsions. There is very limited evidence regarding the effect of paracetamol on activity or other areas contained within the clinical question, which showed inconsistent effects.

Appendix K Proposed changes to original recommendations

In the 2013 guideline the term meningitis has been replaced with bacterial meningitis, where appropriate.

Recommendation [2007]	Replaced with	Reason for change/deletion
The oral and rectal routes should not routinely be used to measure the body temperature of children aged 0–5 years.	Do not routinely use the oral and rectal routes to measure the body temperature of children aged 0–5 years. [2007]	The wording of the recommendation was changed to make it an active statement.
In infants under the age of 4 weeks, body temperature with an electronic thermometer in the axilla	In infants under the age of 4 weeks, measure body temperature with an electronic thermometer in the axilla. [2007]	The wording of the recommendation was changed to make it an active statement.
In children aged 4 weeks to 5 years, healthcare professionals should measure body temperature by one of the following methods: <ul style="list-style-type: none"> • electronic thermometer in the axilla • chemical dot thermometer in the axilla • infra-red tympanic thermometer. 	In children aged 4 weeks to 5 years, measure body temperature by one of the following methods: <ul style="list-style-type: none"> • electronic thermometer in the axilla • chemical dot thermometer in the axilla • infra-red tympanic thermometer. [2007] 	The wording of the recommendation was changed to make it an active statement.

Children with the following symptoms or signs should be recognised as being in a high-risk group for serious illness:

- unable to rouse or if roused does not stay awake
- weak, high-pitched or continuous cry
- pale/mottled/blue/ashen
- reduced skin turgor
- bile-stained vomiting
- moderate or severe chest indrawing
- respiratory rate greater than 60 breaths/minute
- grunting
- bulging fontanelle
- appearing ill to a healthcare professional.

Recognise that children with any of the following symptoms or signs are in a high-risk group for serious illness:

- pale/mottled/ashen/blue skin, lips or tongue
- no response to social cues*
- appearing ill to a healthcare professional
- does not wake or if roused does not stay awake
- weak, high-pitched or continuous cry
- grunting
- respiratory rate greater than 60 breaths per minute
- moderate or severe chest indrawing
- reduced skin turgor. [new 2013]

'Bile-stained vomiting' was removed from the traffic light system because it was incorrectly included in the 2007 system, and no evidence was found to support its inclusion in the recommendation.

The order of the bullet points in the recommendation have been changed to reflect the order in the Traffic light system.

Children with any of the following symptoms should be recognised as being in at least an intermediate-risk group for serious illness:

- wakes only with prolonged stimulation
- decreased activity
- poor feeding in infants
- not responding normally to social cues/no smile
- dry mucous membranes
- reduced urine output
- a new lump larger than 2 cm
- pallor reported by parent or carer
- nasal flaring.

Recognise that children with any of the following symptoms or signs are in at least an intermediate-risk group for serious illness:

- pallor of skin, lips or tongue reported by parent or carer
- not responding normally to social cues
- no smile
- wakes only with prolonged stimulation
- decreased activity
- nasal flaring
- dry mucous membranes
- poor feeding in infants
- reduced urine output
- rigors. [new 2013]

'New lump > 2cm' was removed from the traffic light system because it was incorrectly included in the 2007 system, and no evidence was found to support its inclusion in the recommendation.

The order of the bullet points in the

* A child's response to social interaction with a parent or healthcare professional, such as response to their name, smiling and/or giggling.

		recommendation have been changed to reflect the order in the Traffic light system.
Children who have all of the following features, and none of the high or intermediate risk features, should be recognised as being in a low-risk group for serious illness:	Recognise that children who have all of the following features, and none of the high- or intermediate-risk features, are in a low-risk group for serious illness:	The wording of the recommendation was changed to make it an active statement.
<ul style="list-style-type: none"> • strong cry or not crying • content/smiles • stays awake • normal colour of skin, lips and tongue • normal skin and eyes • moist mucous membranes • normal response to social cues. 	<ul style="list-style-type: none"> • normal colour of skin, lips and tongue • responds normally to social cues[†] • content/smiles • stays awake or awakens quickly • strong normal cry or not crying • normal skin and eyes • moist mucous membranes. <p>[new 2013]</p>	
Healthcare professionals examining children with fever, should be aware that a raised heart rate can be a sign of serious illness, particularly septic shock.	Removed	This recommendation was superseded by a new recommendation on tachycardia
Healthcare professionals should measure and record temperature, heart rate, respiratory rate and capillary refill time as part of the routine assessment of a child with fever.	Measure and record temperature, heart rate, respiratory rate and capillary refill time as part of the routine assessment of a child with fever. [2007]	The wording of the recommendation was changed to make it an active statement.
A capillary refill time of 3 seconds or longer should be recognised as an intermediate-risk group marker for serious illness (amber sign).	Recognise that a capillary refill time of 3 seconds or longer is an intermediate-risk group marker for serious illness ('amber' sign) [2013]	The wording of the recommendation was changed to

[†] A child's response to social interaction with a parent or healthcare professional, such as response to their name, smiling and/or giggling.

		make it an active statement.
Healthcare professionals should measure the blood pressure of children with fever if the heart rate or capillary refill time is abnormal and the facilities to measure blood pressure are available.	Measure the blood pressure of children with fever if the heart rate or capillary refill time is abnormal and the facilities to measure blood pressure are available. [2007]	The wording of the recommendation was changed to make it an active statement.
Children with fever should be assessed for signs of dehydration. Healthcare professionals should look for: <ul style="list-style-type: none"> • prolonged capillary refill time • abnormal skin turgor • abnormal respiratory pattern • weak pulse • cool extremities. 	Assess children with fever for signs of dehydration. Look for: prolonged capillary refill time <ul style="list-style-type: none"> • abnormal skin turgor • abnormal respiratory pattern • weak pulse • cool extremities. [2007] 	The wording of the recommendation was changed to make it an active statement.
Healthcare professionals should look for a source of fever and check for the presence of symptoms and signs that are associated with specific diseases (see table 2)	Look for a source of fever and check for the presence of symptoms and signs that are associated with specific diseases (see table 5.66). [2007]	The wording of the recommendation was changed to make it an active statement.
Meningococcal disease should be considered in any child with fever and a non-blanching rash, particularly if any of the following features are present: <ul style="list-style-type: none"> • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • a capillary refill time of 3 seconds or longer • neck stiffness. 	Consider meningococcal disease in any child with fever and a non-blanching rash, particularly if any of the following features are present [‡] : <ul style="list-style-type: none"> • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • a capillary refill time of 3 seconds or longer • neck stiffness. [2007] 	The wording of the recommendation was changed to make it an active statement.
Meningitis should be considered in a child with fever and any of the following features: <ul style="list-style-type: none"> • neck stiffness • bulging fontanelle • decreased level of consciousness • convulsive status epilepticus. 	Consider bacterial meningitis in a child with fever and any of the following features:‡ <ul style="list-style-type: none"> • neck stiffness • bulging fontanelle • decreased level of 	The wording of the recommendation was changed to make it an active statement.

[‡] See [Bacterial meningitis and meningococcal septicaemia](#). NICE clinical guideline 102 (2010).

	consciousness • convulsive status epilepticus. [2007]	statement.
Healthcare professionals should be aware that classic signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis.	Be aware that classic signs of meningitis (neck stiffness, bulging fontanelle, high-pitched cry) are often absent in infants with bacterial meningitis. § [2007]	The wording of the recommendation was changed to make it an active statement.
Herpes simplex encephalitis should be considered in children with fever and any of the following features: • focal neurological signs • focal seizures • decreased level of consciousness.	Consider herpes simplex encephalitis in children with fever and any of the following features: • focal neurological signs • focal seizures • decreased level of consciousness. [2007]	The wording of the recommendation was changed to make it an active statement.
Pneumonia should be considered in children with fever and any of the following signs : • tachypnoea (respiratory rate greater than 60 breaths per minute, age 0–5 months; greater than 50 breaths per minute, age 6–12 months; greater than 40 breaths per minute, age older than 12 months) • crackles in the chest • nasal flaring • chest indrawing • cyanosis • oxygen saturation of 95% or less when breathing air.	Consider pneumonia in children with fever and any of the following signs: • tachypnoea (respiratory rate greater than 60 breaths per minute, age 0–5 months; greater than 50 breaths per minute, age 6–12 months; greater than 40 breaths per minute, age older than 12 months) • crackles in the chest • nasal flaring • chest indrawing • cyanosis • oxygen saturation of 95% or less when breathing air. [2007]	The wording of the recommendation was changed to make it an active statement.
Urinary tract infection should be considered in any child younger than 3 months with fever.**	Consider urinary tract infection in any child younger than 3 months with fever. [2007]	The wording of the recommendation was changed to make it an active statement.
Septic arthritis/osteomyelitis should be	Consider	septic The wording

§ See [Bacterial meningitis and meningococcal septicaemia](#), NICE clinical guideline 102 (2010).

** See [Urinary tract infection in children](#), NICE clinical guideline 54 (2007).

considered in children with fever and any of the following signs:

- swelling of a limb or joint
- not using an extremity
- non-weight bearing.

arthritis/osteomyelitis in children with fever and any of the following signs:

- swelling of a limb or joint
- not using an extremity
- non-weight bearing. [2007]

of the recommendation was changed to make it an active statement.

Kawasaki disease should be considered in children with fever that has lasted longer than 5 days and who have 4 of the following 5 features:

- bilateral conjunctival injection
- change in mucous membranes in the upper respiratory tract (for example, injected pharynx, dry cracked lips or strawberry tongue)
- change in the extremities (for example, oedema, erythema or desquamation)
- polymorphous rash
- cervical lymphadenopathy

Healthcare professionals should be aware that, in rare cases, incomplete/atypical Kawasaki disease may be diagnosed with fewer features.

Consider Kawasaki disease in children with fever that has lasted longer than 5 days and who have 4 of the following 5 features:

- bilateral conjunctival injection
- change in mucous membranes in the upper respiratory tract (for example, injected pharynx, dry cracked lips or strawberry tongue)
- change in the extremities (for example, oedema, erythema or desquamation)
- polymorphous rash
- cervical lymphadenopathy.

Be aware that, in rare cases, incomplete/atypical Kawasaki disease may be diagnosed with fewer features. [2007]

The wording of the recommendation was changed to make it an active statement.

When assessing a child with feverish illness, healthcare professionals should enquire about recent travel abroad and should consider the possibility of imported infections according to the region visited.

When assessing a child with feverish illness, enquire about recent travel abroad and consider the possibility of imported infections according to the region visited. [2007]

The wording of the recommendation was changed to make it an active statement.

Table 1 Traffic light system for identifying risk of serious illness Children with fever and any of the symptoms or signs in the red column should be recognised as being at high risk. Similarly, children with fever and any of the symptoms or signs in the amber column and none in the red column should be recognised as being at intermediate risk. Children with symptoms and signs in the green column and none in the amber or red column are at low risk. The management of children with fever should be directed by the level of risk.

	Green – low risk	Amber – intermediate risk	Red – high risk
Colour	<ul style="list-style-type: none"> Normal colour of skin, lips and tongue 	<ul style="list-style-type: none"> Pallor reported by parent/carer 	<ul style="list-style-type: none"> Pale/mottled/ashen/blue
Activity	<ul style="list-style-type: none"> Responds normally to social cues Content/s miles Stays awake or awakens quickly Strong normal cry/not crying 	<ul style="list-style-type: none"> Not responding normally to social cues Wakes only with prolonged stimulation Decreased activity No smile 	<ul style="list-style-type: none"> No response to social cues Appears ill to a healthcare professional Does not wake or if roused does not stay awake Weak, high-pitched or continuous cry
Respiratory		<ul style="list-style-type: none"> Nasal flaring Tachypnoea:RR > 50 breaths/minute, age 6–12 monthsRR > 40 breaths/minutes, age > 12 months Oxygen saturation ≤ 95% in air Crackles 	<ul style="list-style-type: none"> Grunting Tachypnoea:RR > 60 breaths/minute Moderate or severe chest indrawing
Hydration	<ul style="list-style-type: none"> Normal skin and eyes Moist mucous membranes 	<ul style="list-style-type: none"> Dry mucous membranes Poor feeding in infants CRT ≥ 3 seconds Reduced urine output 	<ul style="list-style-type: none"> Reduced skin turgor
Other	<ul style="list-style-type: none"> None of the amber or red symptoms or signs 	<ul style="list-style-type: none"> Fever for ≥ 5 days Swelling of a limb or joint Non-weight bearing/not using an extremity A new lump > 2 cm 	<ul style="list-style-type: none"> Age 0–3 months, temperature ≥ 38°C Age 3–6 months, temperature ≥ 39°C Non-blanching rash Bulging fontanelle Neck stiffness Status epilepticus Focal neurological signs Focal seizures Bile-stained vomiting

The existing 2007 traffic light was amended to reflect the findings of a full update review of all symptoms and signs of fever.

Table 1 replaced by: **table 5.2** (chapter 1 – guideline summary, section 1.5 and chapter 5 – clinical assessment of the child with fever, section 5.3)

Table 2 Summary table for symptoms and signs suggestive of specific diseases (Table 2 in [2007] guideline)

Diagnosis considered	to be	Symptoms and signs in conjunction with fever
Meningococcal disease		Non-blanching rash, particularly with one or more of the following: <ul style="list-style-type: none"> • an ill-looking child • lesions larger than 2 mm in diameter (purpura) • capillary refill time of ≥ 3 seconds • neck stiffness
Meningitis		Neck stiffness Bulging fontanelle Decreased level of consciousness Convulsive status epilepticus
Herpes simplex encephalitis	simplex	Focal neurological signs Focal seizures Decreased level of consciousness
Pneumonia		Tachypnoea (RR > 60 breaths/minute, age 0–5 months; RR > 50 breaths/minute, age 6–12 months; RR > 40 breaths/minute, age > 12 months) Crackles in the chest Nasal flaring Chest indrawing Cyanosis Oxygen saturation $\leq 95\%$
Urinary tract infection		Vomiting Poor feeding Lethargy Irritability Abdominal pain or tenderness Urinary frequency or dysuria Offensive urine or haematuria
Septic arthritis		Swelling of a limb or joint Not using an extremity Non-weight bearing
Kawasaki disease		Fever for more than 5 days and at least four of the following: <ul style="list-style-type: none"> • bilateral conjunctival injection • change in mucous membranes • change in the extremities • polymorphous rash • cervical lymphadenopathy

Offensive urine and haematuria were removed from the list because they are rarely seen in clinical practice.

Table 2 replaced by: **table 5.66** (chapter 1 – guideline summary, section 1.5 and chapter 5 – clinical assessment of the child with fever, section 5.5)

Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see chapter 9).	Children with 'green' features and none of the 'amber' or 'red' features can be cared for at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see chapter 10). [2007]	The wording of the recommendation was changed to make it an active statement.
<p>If any 'amber' features are present and no diagnosis has been reached, healthcare professionals should provide parents or carers with a 'safety net' or refer to specialist paediatric care for further assessment. The safety net should be 1 or more of the following:</p> <ul style="list-style-type: none"> • providing the parent or carer with verbal and/or written information on warning symptoms and how further healthcare can be accessed (see chapter 9) • arranging further follow-up at a specified time and place • liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required. [2007] 	<p>If any 'amber' features are present and no diagnosis has been reached, provide parents or carers with a 'safety net' or refer to specialist paediatric care for further assessment. The safety net should be 1 or more of the following:</p> <ul style="list-style-type: none"> • providing the parent or carer with verbal and/or written information on warning symptoms and how further healthcare can be accessed (see chapter 10) • arranging further follow-up at a specified time and place • liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required. [2007] 	The wording of the recommendation was changed to make it an active statement.
Urine should be tested on children with fever as recommended in 'Urinary tract infection in children' (NICE clinical guideline 54). [2007]	Test urine in children with fever as recommended in 'Urinary tract infection in children' (NICE clinical guideline 54). [2007]	The wording of the recommendation was changed to make it an active statement.
Oral antibiotics should not be prescribed to children with fever without apparent source. [2007]	Do not prescribe oral antibiotics to children with fever without apparent source. [2007]	The wording of the recommendation was changed to make it an active statement.

Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). ^{††} .	Give parenteral antibiotics to children with suspected meningococcal disease at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). ^{††} [2007]	The wording of the recommendation was changed to make it an active statement.
<p>Lumbar puncture should be performed on the following children (unless contraindicated):</p> <ul style="list-style-type: none"> • infants younger than 1 month • all infants aged 1–3 months who appear unwell • infants aged 1–3 months with a white blood cell count (WBC) less than 5×10^9/litre or greater than 15×10^9/litre. [2007] 	<p>Perform lumbar puncture in the following children with fever (unless contraindicated):</p> <ul style="list-style-type: none"> • infants younger than 1 month • all infants aged 1–3 months who appear unwell • infants aged 1–3 months with a white blood cell count (WBC) less than 5×10^9/litre or greater than 15×10^9/litre. [2007, amended 2013] 	The wording of the recommendation was changed to make it an active statement.
When indicated, a lumbar puncture should be performed without delay and, whenever possible, before the administration of antibiotics. [2007]	When indicated, perform a lumbar puncture without delay and, whenever possible, before the administration of antibiotics. [2007]	The wording of the recommendation was changed to make it an active statement.
<p>Parenteral antibiotics should be given to:</p> <ul style="list-style-type: none"> • infants younger than 1 month • all infants aged 1–3 months who appear unwell • infants aged 1–3 months with WBC less than 5×10^9/litre or greater than 15×10^9/litre. [2007] 	<p>Give parenteral antibiotics to:</p> <ul style="list-style-type: none"> • infants younger than 1 month with fever • all infants aged 1–3 months with fever who appear unwell • infants aged 1–3 months with WBC less than 5×10^9/litre or greater than 15×10^9/litre. [2007, amended 2013] 	The wording of the recommendation was changed to make it an active statement.
<p>Children with fever without apparent source presenting to paediatric specialists with one or more 'red' features should have the following investigations performed:</p> <ul style="list-style-type: none"> • full blood count • blood culture • C-reactive protein 	<p>Perform the following investigations in children with fever without apparent source who present to paediatric specialists with one or more 'red' features:</p> <ul style="list-style-type: none"> • full blood count • blood culture • C-reactive protein 	The wording of the recommendation was changed to make it an active statement.

^{††} See [Bacterial meningitis and meningococcal septicaemia](#), NICE clinical guideline 102 (2010).

<ul style="list-style-type: none"> urine testing for urinary tract infection. 	<ul style="list-style-type: none"> urine testing for urinary tract infection.^{††} [2013] 	
<p>Routine blood tests and chest X-rays should not be performed on children with fever who have no features of serious illness (that is, the 'green' group).</p>	<p>Do not routinely perform blood tests and chest X-rays in children with fever who have no features of serious illness (that is, the 'green' group). [2007, amended 2013]</p>	<p>The wording of the recommendation was changed to make it an active statement.</p>
<p>When a child has been given antipyretics:</p> <ul style="list-style-type: none"> healthcare professionals should not rely on a decrease or lack of decrease in temperature after 1–2 hours to differentiate between serious and non-serious illness children in hospital with 'amber' or 'red' features should be reassessed after 1–2 hours. 	<p>When a child has been given antipyretics, do not rely on a decrease or lack of decrease in temperature at 1–2 hours to differentiate between serious and non-serious illness. Nevertheless, in order to detect possible clinical deterioration, all children in hospital with 'amber' or 'red' features should still be reassessed after 1–2 hours. [new 2013]</p>	<p>The recommendation was revised for style and clarity.</p>
<p>Children with fever presenting to specialist paediatric care or an emergency department should be given immediate parenteral antibiotics if they are:</p> <ul style="list-style-type: none"> shocked unrousable showing signs of meningococcal disease. 	<p>Give immediate parenteral antibiotics to children with fever presenting to specialist paediatric care or an emergency department if they are:</p> <ul style="list-style-type: none"> shocked unrousable showing signs of meningococcal disease. [2007] 	<p>The wording of the recommendation was changed to make it an active statement.</p>
<p>Children with fever and symptoms and signs suggestive of herpes simplex encephalitis should be given intravenous aciclovir.</p>	<p>Give intravenous aciclovir to children with fever and symptoms and signs suggestive of herpes simplex encephalitis (see recommendation 26). [2007]</p>	<p>The wording of the recommendation was changed to make it an active statement.</p>
<p>Healthcare professionals should refer to local treatment guidelines when rates of bacterial antibiotic resistance are significant.</p>	<p>Refer to local treatment guidelines when rates of bacterial antibiotic resistance are significant. [2007]</p>	<p>The wording of the recommendation was changed to make it an active</p>

^{††} See [Urinary tract infection in children](#), NICE clinical guideline 54.

statement.

In addition to the child's clinical condition, healthcare professionals should consider the following factors when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses that affect the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek healthcare advice repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness.

In addition to the child's clinical condition, consider the following factors when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses that affect the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek healthcare advice repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness. [2007]

The wording of the recommendation was changed to make it an active statement.

If it is decided that a child does not need to be admitted to hospital, but no diagnosis has been reached, a safety net should be provided for parents and carers if any 'red' or 'amber' features are present. The safety net should be 1 or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further healthcare can be accessed (see chapter 9)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure direct access for the child if further assessment is required.

If it is decided that a child does not need to be admitted to hospital, but no diagnosis has been reached, provide a safety net for parents and carers if any 'red' or 'amber' features are present. The safety net should be 1 or more of the following:

- providing the parent or carer with verbal and/or written information on warning symptoms and how further healthcare can be accessed (see section 10.2)
- arranging further follow-up at a specified time and place
- liaising with other healthcare professionals, including out-of-hours providers, to ensure

The wording of the recommendation was changed to make it an active statement.

	direct access for the child if further assessment is required. [2007]	
Children with 'green' features and none of the 'amber' or 'red' features can be managed at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see chapter 9).	Children with 'green' features and none of the 'amber' or 'red' features can be cared for at home with appropriate advice for parents and carers, including advice on when to seek further attention from the healthcare services (see chapter 10). [2007, amended 2013]	The wording of the recommendation was changed to make it an active statement.
Children with suspected meningococcal disease should be given parenteral antibiotics at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). [2007]	Give parenteral antibiotics to children with suspected meningococcal disease at the earliest opportunity (either benzylpenicillin or a third-generation cephalosporin). [2007]	The wording of the recommendation was changed to make it an active statement.
Either paracetamol or ibuprofen can be used to reduce temperature in children with fever.	Consider using either paracetamol or ibuprofen in children with fever who appear distressed. [new 2013]	The wording of the recommendation was changed to make it an active statement. The recommendation was separated to improve clarity.
The use of antipyretic agents should be considered in children with fever who appear distressed or unwell. Antipyretic agents should not routinely be used with the sole aim of reducing body temperature in children with fever who are otherwise well. The views and wishes of parents and carers should be taken into consideration.	Do not use antipyretic agents with the sole aim of reducing body temperature in children with fever. [new 2013]	The wording of the recommendation was changed to make it an active statement. The recommendation was separated to improve clarity.

Paracetamol and ibuprofen should not be administered at the same time to children with fever.

(Recommendation [1.6.1.5] in [2007] guideline)

Paracetamol and ibuprofen should not routinely be given alternately to children with fever. However, use of the alternative drug may be considered if the child does not respond to the first agent.

Two recommendations were merged in the following recommendation:

When using paracetamol or ibuprofen in children with fever:

- continue only as long as the child appears distressed
- consider changing to the other agent if the child's distress is not alleviated
- do not give both agents simultaneously
- only consider alternating these agents if the distress persists or recurs before the next dose is due. [new 2013]

Two recommendations were merged to improve clarity. The wording of the recommendation was changed to make it an active statement.

Parents or carers should be advised to manage their child's temperature as described in chapter 8. [2007]

Advise parents or carers to manage their child's temperature as described in chapter 9. [2007]

The wording of the recommendation was changed to make it an active statement.

Parents or carers looking after a feverish child at home should be advised:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration by looking for the following features:
 - sunken fontanelle
 - dry mouth
 - sunken eyes
 - absence of tears
 - poor overall appearance
- to encourage their child to drink more fluids and consider seeking further advice if they detect signs of dehydration
- how to identify a non-blanching rash
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness

Advise parents or carers looking after a feverish child at home:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration by looking for the following features:
 - sunken fontanelle
 - dry mouth
 - sunken eyes
 - absence of tears
 - poor overall appearance
- to encourage their child to drink more fluids and consider seeking further advice if they detect signs of dehydration
- how to identify a non-blanching rash
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists but to notify the school or nursery of the illness. [2007]

The wording of the recommendation was changed to make it an active statement.

Appendix L The formal consensus survey

Background

NICE clinical guidelines are typically based on a review of evidence from published literature, ideally from large, well-conducted studies. The methods used to develop these guidelines are explicit and transparent. They include literature search, assessment and synthesis of evidence and the final judgements made by the Guideline Development Group (GDG) to reach final decisions. While the use of formal consensus methods in NICE guideline is not customary, there are circumstances when they may be warranted, in the absence of robust evidence.²³⁴ This process is separate from the stakeholder consultation of the draft guideline.

A core objective of this guideline on feverish illness in children was to provide practical recommendations for the clinical assessment of children (aged 0–5 years) presenting with a feverish illness, including risk stratification. An extensive review of the literature revealed major deficiencies with the evidence to answer some of the key clinical questions. The main problems were the poor quality of the studies retrieved (small, poorly conducted studies, or incomplete reporting) and generalisability (studies were often conducted in very different settings from the NHS). Moreover, there was recognition that opinions diverged considerably in these areas among clinicians and parents.

Against this background, the GDG decided to use a formal consensus approach with a larger external group of consultees on selected questions. Formal consensus methods are used increasingly in combination with the best available evidence to develop clinical practice guidelines.^{235–237} The purpose of the consensus was to obtain the opinions of an external multidisciplinary group to assist the GDG in making reliable recommendations in areas where evidence was deficient.

Methods

Choosing the consensus method

The GDG chose a modified Delphi method.²³⁸ Delphi is one of the most widely used formal consensus techniques for obtaining opinions from groups of experts and stakeholders.²³⁹ It involves sending participants questionnaires and asking them for their views. The responses are collated and sent back to participants in a summary form allowing them to revise their original opinion in light of the group feedback.^{240,241} This process is repeated several times, with the aim of obtaining consensus. The GDG used a two-round postal/e-mail survey.

Defining the project plan

A plan protocol was designed initially that incorporated all stages and details of the work, including the consensus method to be used, recruitment of participants, data collection and analysis. Importantly, the GDG agreed the ground rules they would use for analysing the results and for formulating the recommendations based on the results from the survey. These are presented in box M.1.

A timetable was drawn up early in the process to ensure the work could be carried out during the timeline of the guideline development. The Royal College of Paediatrics and Child Health and the Patient and Public Involvement Programme (PPIP) unit at NICE confirmed that the consensus work did not require ethical approval.

Box L.1 Ground rules agreed by the GDG for making recommendations from survey results

- The results of the group ratings will be presented to the GDG, together with comments.
- Whenever appropriate the GDG will aim to formulate a recommendation for each statement. The statements will be worded in a way that can be directly translated into recommendations.
- The GDG will explicitly state the basis for its decision using the 'translation' template currently used with other recommendations for which there is evidence.
- Statements for which 75% or more of the ratings fall in the 7 to 9 range will be classified as agreement and the GDG will use the statement as a basis for making a recommendation.
- Statements for which 75% or more of the ratings fall in the 1 to 3 range will be classified as disagreement. The GDG will usually make a negative recommendation (e.g. does not recommend). In certain circumstances the GDG may decide to make a research recommendation or discard the statement. The decision not to make a negative recommendation will need to be agreed unanimously by the GDG and it will need to be justified.
- In all other cases, the GDG will discard the statement. Exceptionally, it may decide to make a recommendation, depending on the degree of variation in the ratings for that statement. Again, this decision will need to be justified and agreed unanimously by the GDG.
- In cases where there is agreement in the rating group but the GDG considers there are grounds to discard the results, the GDG reserves the right to use its own opinion in making the recommendation. This will need to be agreed unanimously by the GDG. In such cases, the GDG will explain in detail the reasons why it rejected the results.

Selecting clinical questions for formal consensus

A systematic search for the evidence was conducted on all clinical questions and relevant published studies were assessed. On examining the evidence the GDG identified a number of questions/issues for which they did not think they could competently make recommendations based on the published studies, or on their collective experience. These questions are listed in box X.2.

The following criteria were used for selecting the questions:

- there was no appropriate published evidence to answer the question
- there was some evidence but the GDG failed to reach consensus among themselves as to what the recommendation should be.
- the GDG did not think the question could be answered by standard quantitative studies
- the GDG was concerned that the evidence found was not applicable or acceptable to practice in England and Wales.

Developing the statements

The statements focused on issues that were commonly seen in practice and were clinically important both for health professionals and for parents/carers. They were generated for each selected question based on the literature review using the following steps:

- a member of the topic group with the help of the systematic reviewer drafted a background summary describing what was known about the issue, based on available evidence and known current practice as agreed by the GDG
- the summary was presented to the GDG, together with a draft statement for discussion
- the GDG finalised the statement.

The statements were worded as recommendations to ensure that the final guideline recommendations reflected the results from the consensus.

Piloting the statements

The draft statements, background and instructions were piloted for clarity and readability with ten people, including members from another GDG, parents and colleagues at the National Collaborating Centre for Women's and Children's Health. They were asked to read through all the documentation and to provide any feedback on potential improvements. Seven responses were received. On the whole, respondents felt the statements and background were clear. There were comments relating to

presentation and ratings for some statements. Based on these suggestions some of the sections were re-ordered, the wording was clarified when relevant and the rating scale for two sets of statements was modified. A member of the Patient and Public Involvement Programme (PPIP) unit at NICE checked the final wording to ensure it was understandable for parents and carers.

Box L.2 Ground rules agreed by the GDG for making recommendations from survey results

Question 2

How accurate are the different types of thermometer in the measurement of body temperature in young children and how do they compare in their ability to detect fever?

Question 3

How accurate are the readings of temperature from different sites of the body in young children and how do these sites compare in the ability to detect fever?

Question 12

In a child with fever what are the benefits, if any, of a period of observation on an assessment facility?

Question 21

Does the use of antipyretic interventions in children with fever serve a benefit or harm in terms of any of the following:

- time to recovery
- wellbeing
- activity
- eating and drinking
- prevention of febrile convulsions?

Question 22

In children with fever at home following a clinical encounter, what indications should direct the parents or carers to seek further advice?

Need to consider:

- height of temperature
- length of temperature
- colour
- drowsiness
- rash
- poor feeding
- fluid intake
- reduction in urine output
- altered consciousness
- rigors
- parental anxiety/instinct
- inconsolable crying
- irritability.

Question 23

What advice should be given to parents for further management of a febrile child?

Need to consider:

- hydration
- feeding
- frequency of temperature monitoring
- methods of cooling
- when to attend nursery or school.

Question 24

What factors other than the child's clinical condition should be considered when deciding to admit a child with fever to hospital?

Need to consider:

- • social
- • comorbidity
- • parental wishes and instinct
- • distance from home
- • time of day
- • contacts with other serious illness
- • recent travel abroad.

Selecting participants

Number of participants

There is little evidence about the effect the number of participants has on the reliability or validity of consensus. This depends on the purpose of the study and the diversity of the targeted population.²³⁵ It was aimed to obtain at least 50 ratings for each statement with a response rate of at 80%. This was based on the assumption that if 75 people were invited to take part at least 65 would agree.

Inviting and recruiting participants

The purpose of the consensus was to seek the opinions of an external multidisciplinary group including the health professionals and patients/carers /parents who are directly involved with or are affected by the issue covered. Three key groups were identified: professionals from primary care including NHS Direct, professionals from secondary care, and parents/carers. It was aimed to obtain 25 nominations in each of the three groups.

Key professional and patient organisations registered as stakeholders were asked to nominate potential participants. Sure Start was approached separately to identify parents from disadvantaged backgrounds. In addition, a message was posted on the NICE website inviting parents to participate.

A letter of invitation was sent to each nominee, together with a document explaining the background to the survey, its aim, and the task involved, including timing and deadlines. An example of a background summary and statement was provided as illustration. Nominees were asked to respond within 2 weeks. They were requested to sign a letter of confidentiality before participating. table L.1 shows the number of nominations received and the numbers who responded.

Rating

The GDG generated 35 statements for consensus. A pack containing a covering letter, the statements/background and response document, an instruction sheet and background notes was sent to each of the 61 people who had agreed to take part. Respondents were asked to indicate their agreement with each statement using a scale of 1–9 (1 being strongly disagree, 9 being strongly agree). For statements 2.1 and 5.2, participants were asked to indicate which optimum time they preferred. A 'Don't know' box and space for comments were provided. The ratings were done independently. box L.3 shows an example of a statement sent for the first round. For the full list see Annex A.1 on the accompanying CD-ROM.

For each round, participants were given 2 weeks to return their ratings. Most documents were sent by e-mail. A self-addressed labelled envelope was included for postal respondents. The participants were contacted after a week to remind them about the deadline.

Data analysis and presentation to the GDG

Results were analysed using Stata (version 8). In addition to the agreed ground rules (e.g. 75% or more of ratings 7 to 9 = agreement, 75% or more 1 to 3 = disagreement), the median score was calculated for each statement as a measure of central tendency classified as agreement (7 to 9), disagreement (1 to 3), or uncertainty (4 to 6). For statements 2.1 and 5.2 there was agreement if 75% of the ratings were in one of the response categories.

The results were presented to the GDG. For each statement, the results included the median, distribution of ratings for each of the three categories and the comments. All the information was anonymised. Statements for which there was no agreement (according to the ground rules) were

discussed. When appropriate, the GDG reworded the background and/or statement, using the participants' comments as a guide.

The statements were sent for a second round of rating. The results from the first round described above were included without the comments but participants were able to obtain them on request. The participants were asked to consult their first round ratings and to compare them with their second rating.

Table L.1 Nominations to and acceptance of participation in the Delphi survey

Group/profession	Organisation	Number of nominations received	Number who accepted
Paediatrician	Royal College of Paediatrics and Child Health	6	6
Paediatrician (A&E)			
Paediatrician (infectious diseases)			
A&E consultant	College of Emergency Medicine	2	2
Paediatric nurse, A&E nurse	Royal College of Nursing	20	20
Parent/carer	Stakeholder and NICE website (through PPIP)	2	2
	Sure Start		
General practitioner	Royal College of General Practitioners	33(25 selected)	15
Practice nurse	Primary care trusts	9	6
Out-of-hours provider	Primary care trusts	2	1
Community pharmacist	Royal Pharmaceutical Society	1	1
NHS Direct	NHS Direct	6	5
Total		79	61

Results

Round 1

Fifty-seven participants (93%) completed their ratings but only 53 returns were used in the analysis as four were received too late. There were 32 missing responses (2%) out of a total of 1855 and 79 (4%) 'Don't know'. table L.2 shows the distribution of ratings. The ratings for each statement are shown in Annex A.1 on the accompanying CD-ROM together with the comments. There was agreement with 12 out of the 35 statements and disagreement with three (on rectal thermometers). For statement 2.1, 43 (83%) of the ratings fell into the 2 hours category. This was accepted as agreement. For the remaining 20 statements there was a range of response across the three categories. Statement 8.1 had agreement (75% in the 7 to 9 category). However, the GDG decided to reword the first two statements in Section 8 in the light of comments made by the participants and also because they realised that the original statements could not be used to make unambiguous recommendations. Therefore statement 8.1 was included in the second round, taking the number of statements for re-rating up to 21. In general, the comments indicated that several statements/background needed clarifying or to be made more specific.

Box L.3 Example of a statement sent for first round consensus**Background**

Most of the care of feverish children takes place at home and is provided by parents or other carers. Some parents/carers will seek initial advice from healthcare professionals. Most of these children will recover without problems. In some cases, however, their condition may change or fail to improve. Parents need to know when to seek further help and may require further advice about the best way to care for their child.

Statement 3.1

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at home should seek further advice if:

a) the child suffers a fit

Table L.2 Distribution of ratings and median for all statements after round 1

Statement	Rating category			Responses			
	1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1.1	0	1 (2%)	48 (96%)	1 (2%)	3	50	9
1.2	0	6 (12%)	42 (84%)	2 (4%)	3	50	8.5
1.3	8 (16%)	17 (33%)	24 (47%)	2 (4%)	2	51	7
1.4	2 (4%)	11 (22%)	35 (70%)	2(4%)	3	50	8
1.5	1 (2%)	5 (10%)	43 (81%)	1 (2%)	3	50	8.5
3.1a	0	0	52 (98%)	1 (2%)		53	9
3.1b	0	2(4%)	50 (94%)	1 (2%)		53	8
3.1c	0	9 (17%)	43 (81%)	1 (2%)		53	8
3.1d	4 (8%)	14 (27%)	33 (63%)	1 (2%)	1	52	7
3.1e	1 (2%)	0	50 (96%)	1 (2%)	1	52	9
3.1f	1 (2%)	5 (9%)	46 (87%)	1 (2%)		53	9
4.1	2 (4%)	8 (15%)	39 (75%)	3 (6%)	1	52	9
4.2	7 (14%)	14 (28%)	21 (42%)	8 (16%)	3	50	7
5.1	4 (8%)	10 (19%)	36 (69%)	2 (4%)	1	52	8
6.a	7 (13%)	20 (38%)	25 (47%)	1 (2%)		53	6
6.b	2 (4%)	17 (32%)	32 (60%)	2 (4%)		53	7
6.c	1 (2%)	14 (26%)	37 (70%)	1 (2%)		52	8
6.d	6 (12%)	23 (44%)	22 (42%)	1 (2%)	1	53	6
6.e	13 (25%)	22 (42%)	17 (32%)	1 (2%)		53	6
6.f	12 (23%)	20 (38%)	20 (38%)	1 (2%)		53	6
6.g	4 (8%)	17 (32%)	28 (53%)	4 (8%)		53	7
6.h	7 (13%)	12 (23%)	32 (60%)	2 (4%)		53	7
6.i	7 (13%)	15 (28%)	30 (57%)	1 (2%)		53	7
6.j	2 (4%)	13 (25%)	37 (70%)	1 (2%)		53	8
6.k	2 (4%)	13 (25%)	36 (70%)	1 (2%)	1	52	7

Statement	Rating category		Responses				
	1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
7.1	8 (15%)	6 (12%)	29 (56%)	9 (17%)	1	52	8
7.2	2 (4%)	4 (8%)	44 (85%)	2 (4%)	1	52	9
7.3	45 (87%)	3 (6%)	3 (6%)	1 (2%)	1	52	1
7.4	46 (88%)	4 (8%)	1 (2%)	1 (2%)	1	52	1
7.5	47 (92%)	3 (6%)	0	1 (2%)	1	51	1
8.1	3 (6%)	10 (20%)	39 (75%)	0	1	52	8
8.2	12 (23%)	18 (35%)	20 (38%)	2 (4%)	1	52	5.5
8.3	2 (4%)	18 (35%)	28 (55%)	3 (6%)	2	51	7
	2 hours	6 hours	12 hours	24 hours	Don't know	Total	Median
2.1	43 (83%)	5 (10%)	1 (2%)	0	3 (6%)	52	2
	2 hours	4 hours	6 hours	12 hours	Don't know	Total	Median
5.2	2 (4%)	7 (13%)	19 (37%)	10 (19%)	14 (27%)	52	6

Statement for which there was no agreement

Statement for which there was disagreement

Round 2

Fifty-three (93%) of the 57 participants completed the task. There were three missing responses out of 1325. There were 26 'Don't know' responses, 12 of which were for statement 5.2, about the period of observation in hospital. table L.3 shows the distribution of ratings. The ratings for each statement are shown in Annex A.2 on the accompanying CD-ROM together with the comments. There remained 10 statements for which agreement could not be reached.

Formulating the recommendations

The GDG discussed all the statements again after the two consensus rounds. They removed nine of the ten statements with no agreement. In addition,, statement 5.2 was discarded because there was a high degree of uncertainty about the optimum time around the period of observation for assessment in hospital to help differentiate minor from serious illness. This was illustrated in the comments (see Annex A.1 on the accompanying CD-ROM). Box L.4 shows the 25 statements that were retained as recommendations. In most cases, the statement was reproduced exactly as a recommendation. While there was consensus agreement for statement 3.1d, the GDG unanimously decided to remove it because evidence was found after the consensus survey that duration of fever at 48 hours is not a sufficiently important sign to prompt review. However, the recommendation on seeking advice at 5 days, statement 3.1e, was retained because fever of this duration is unusual and Kawasaki disease and other serious causes of prolonged fever should be considered at this stage. An explanatory text was added to statement 4.1 (in italics) after comments suggested the statement needed qualifying ('Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness particularly septic shock.'). Statement 6.a, for which there was no agreement, was retained by unanimous consensus in the GDG. The GDG slightly modified the wording of statement 8.2 as comments indicated the message should be more specific. The three statements on rectal thermometers (7.3, 7.4 and 7.5) for which there was disagreement were retained because the GDG considered there was a sufficiently important need for guidance on their use. To reflect the strength of disagreement from the consensus they reworded the statements negatively.

Table L.3 Distribution of ratings and median for statements after round 2

Statement	Rating category					Responses	
	1 to 3	4 to 6	7 to 9	Don't know	Missing	Total	Median
1.3	9 (18%)	10 (20%)	32 (63%)		1	51	7
1.4	1 (2%)	5 (10%)	45 (88%)		1	51	8
3.1d	2(4%)	9 (17%)	40 (77%)	1 (2%)		52	7
4.2	2 (4%)	15 (30%)	33 (65%)	1 (2%)	1	51	7
5.1	0	6 (12%)	44 (85%)	2 (4%)		52	8
6.a	2 (4%)	17 (33%)	33 (64%)			52	7
6.b	1 (2%)	10 (19%)	41 (79%)			52	7.5
6.c	2 (4%)	7 (13%)	43 (83%)			52	8
6.d	7 (13%)	22 (42%)	23 (44%)			52	6
6.e	12 (23%)	24 (46%)	16 (31%)			52	6
6.f	14 (27%)	16 (31%)	22 (42%)			52	8
6.g	1 (2%)	8 (15%)	42 (81%)	1 (2%)		52	8
6.h	1 (2%)	2 (4%)	48 (92%)			51	8
6.i	2 (11%)	11 (22%)	38 (75%)			51	8
6.j	1 (2%)	9 (17%)	42 (81%)			52	8
6.k	2 (4%)	9 (17%)	41 (79%)			52	8
7.1	11 (21%)	8 (15%)	28 (54%)	5 (10%)		52	7
8.1	10 (19%)	11 (21%)	29 (56%)	2 (4%)		52	7
8.2	3 (6%)	5 (10%)	43 (83%)	1 (2%)		52	8
8.3	2 (4%)	15 (29%)	34 (65%)	1 (2%)		52	7
	2 hours	4 hours	6 hours	12 hours	Don't know	Total	Median
5.2	1 (2%)	3 (6%)	26 (50%)	10 (19%)	12 (23%)	52	6

Statement with no agreement

The final 25 statements were incorporated as recommendations in the guideline.

Box L.4 Statements retained for recommendations after two rounds of Delphi consensus

1. Care at home

Parents/carers looking after a feverish child at home should be advised:

- to offer the child regular fluids (where a baby or child is breastfed the most appropriate fluid is breast milk)
- how to detect signs of dehydration
- to check their child during the night
- to keep their child away from nursery or school while the child's fever persists and to notify the school or the nursery of the illness.

2. Assessment by telephone

An urgent face-to-face assessment means that the child should be seen within 2 hours.

3. When to seek medical help

Following contact with a healthcare professional, parents/carers who are looking after their feverish child at

home should seek further advice if:

- the child suffers a fit
- the parent/carer feels that child is less well than when they previously sought advice
- the parent/carer is more worried than when they previously sought advice
- the fever has not settled after 5 days
- the parent/carer is very distressed or unable to cope with their child's illness.

4. Face-to-face assessment

Healthcare professionals examining children with fever must measure and record heart rate as part of their routine assessment because a raised heart rate can be a sign of serious illness, particularly septic shock.

5. Observation in hospital

A period of observation in hospital (with or without investigations) as part of an assessment can help differentiate minor from serious bacterial illness (such as meningitis or pneumonia) in a young child who has a fever without obvious cause.

6. Other factors for admitting a feverish child to hospital

Healthcare professionals should consider the following factors, as well as the child's clinical condition, when deciding whether to admit a child with fever to hospital:

- social and family circumstances
- other illnesses suffered by the child or other family members
- parental anxiety and instinct (based on their knowledge of their child)
- contacts with other people who have serious infectious diseases
- recent travel abroad to tropical/subtropical areas, or areas with a high risk of endemic infectious disease
- when the parent or carer's concern for their child's current illness has caused them to seek help repeatedly
- where the family has experienced a previous serious illness or death due to feverish illness which has increased their anxiety levels
- when a feverish illness has no obvious cause, but the child remains ill longer than expected for a self-limiting illness.

7. Thermometers

Healthcare professionals should not routinely use the oral route to measure body temperature in children under the age of 5 years.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 0–3 months.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 3 months to 2 years.

Healthcare professionals should not routinely use electronic thermometers by the rectal route to measure body temperature in children aged 2–5 years.

8. Cooling methods

Antipyretic drugs should be offered to children who are miserable with fever because they may make them feel better.

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