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

Antenatal care

routine care for the healthy pregnant woman

Clinical Guideline

October 2003

Funded to produce guidelines for the NHS by NICE

Antenatal care: routine care for the healthy pregnant woman

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

Commissioned by the National Institute for Clinical Excellence

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Evidence tables

Study type codes

CCS	Case–control study
CCH	Controlled cohort study
CH	Cohort study
COM	Comparative study
CR	Case report
CS	Case series
CSS	Cross-sectional study
CSNR	Controlled trial without randomisation
DBP	Double blind parallel trial
DBRP	Double blind randomised placebo controlled trial
EE	Economic evaluation
EV	Evaluation
GL	Guidelines
HTA	Health Technology Assessment
ISNR	Interventional study not randomised
ISS	Interventional study with groups sequentially allocated
LS	Longitudinal study
ME	Model evaluation
NCC	Nested case–control
OB	Observational study
OPC	Open pilot cohort study
PHLS	Report from PHLS AIDS Diagnostic Working Group
QR	Quasi-randomised study
RDBC	Randomised double blind crossover trial
REC	Review by expert committee
RCSS	Review of cross-sectional studies
RCT	Randomised controlled trial
RV	Review
SA	Secondary analysis of RCT data
SR	Systematic review
SSW	Guideline report from PHLS Syphilis Serology Working Group
SV	Surveillance
TES	Test evaluation survey
TESC	Test evaluation survey on crossover

EL	Evidence level

[All other abbreviations will be found in the list of abbreviations on page ix]

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Audit Commission, 1997	10	2375 mothers who gave birth during June and July 1995 in England and Wales	Self-completion questionnaires sent to a national sample drawn by ONS	Perceived options in antenatal care Women's assessment of information and communication in antenatal care	Perceived option in where to have antenatal care: 33% yes 63% no 4% don't know Perceived option in which professional provides care: 35% yes 60% no 5% don't know Perceived option in having a scan: 52% yes 31% no 13% partly 4% don't know Perceived option in having a screening test: 60% yes 10% no 8% partly 22% don't know Information on the benefits and risks of various screening tests: 68% reported they had received enough spoken information 60% reported they had received enough written information		CSS	3
Gagnon, 2001	27	6 RCTs, 1443 women	To assess the effects of antenatal education on knowledge acquisition, anxiety, sense of control, pain, support, breastfeeding, infant care abilities, psychological and social adjustment	Satisfaction with maternal role preparation Maternal attachment behaviours Knowledge acquisition	No consistent results were found Maternal role preparation (1 RCT, n = 16): WMD 21.590, 95% CI 11.234 to 31.946 when women who received individual ANC were compared with women who received no organised antenatal education Maternal attachment behaviours (1 RCT, n = 10): WMD 52.600, 95% CI 21.818 to 83.382 when this component was added to antenatal classes compared with antenatal classes without this component Knowledge acquisition (1 RCT, n = 48): WMD 1.620, 95% CI 0.492 to 2.748 in expanded antenatal education classes versus standard antenatal education classes	The largest trial reviewed examined educational intervention to increase vaginal birth after caesarean section (n = 1275) No data from the other 5 trials (n = 168) were reported on labour and birth outcomes, anxiety, breastfeeding success, or general social support	SR	1a

Chapter 3 Woman-centred care and informed decision making (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Thornton et al., 1995	12	1691 pregnant women before 15 weeks gestation in England from 1991 to 1994	Extra information delivered individually (n = 561) vs. extra information delivered in classes (n = 563) vs. information normally given (n = 567) in a routine antenatal clinic on prenatal testing Extra information was delivered at a specifically scheduled class or one-on-one visit for the purpose of covering screening and risks related to: – Down's syndrome – Ultrasound at 18 weeks for fetal abnormalities (esp. neural tube defects) – Haemoglobinopathy (with patients from relevant ethnic groups) – Cystic fibrosis	Uptake rates of prenatal tests Levels of anxiety	Uptake of Down's syndrome screening: 37% vs. 32% vs. 34% Uptake of ultrasonography: 98% vs. 99% vs. 99% Uptake of cystic fibrosis screening: 65% vs. 62% vs. 79% Uptake of amniocentesis: 3% vs. 2% vs. 3% No differences in anxiety at 16 weeks. Anxiety at 20 and 34 weeks was lower among those offered individual information when compared with controls ($p < 0.05$)	Analysis by intention to treat Randomisation by sealed opaque envelopes	RCT	1b
O'Cathain et al., 2002	13	Women reaching 28 weeks before the intervention (n = 1386) and after (n = 1778) from 13 maternity units in Wales	Maternity units randomised by coin toss. Provision of MIDIRS informed choice leaflets to intervention units vs. no leaflets	Exercising informed choice Changes in women's knowledge Satisfaction with information	Informed choice: OR 1.15, 95% CI 0.65 to 2.06 Antenatal knowledge: mean difference 0.20, 95% CI –0.09, 0.49 Satisfied with amount of information: OR 1.4, 95% CI 1.05 to 1.88		RCT	1b
Hibbard et al., 1979	28	744 primigravid women in Cardiff, Wales	Survey at first attendance (n = 256) Survey at 35 weeks gestation (n = 237) Survey postpartum (n = 251)	Knowledge Anxiety			CSS	3

4.1 Who provides care?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Villar and Khan-Neelofur, 2003	32	3 RCTs, 3041 women	Midwife and GP-managed care vs. obstetrician and gynaecologist-led shared care	Preterm delivery (< 37 weeks) Pre-eclampsia PIH Caesarean section Antepartum haemorrhage UTI Anaemia (Hb < 10 g/dl) Perinatal mortality Maternal satisfaction	Preterm birth (2 RCTs, n = 2883): Peto OR 0.79, 95% CI 0.57 to 1.10 Pre-eclampsia (2 RCTs, n = 2952): Peto OR 0.37, 95% CI 0.22, 0.64 PIH (3 RCTs, n = 3041): Peto OR 0.56, 95% CI 0.45 to 0.70 Caesarean section (3 RCTs, n = 2972): Peto OR 0.99, 95% CI 0.79 to 1.25 Antepartum haemorrhage (2 RCTs, n = 2952): Peto OR 0.79, 95% CI 0.57 to 1.10 UTI (1 RCT, n = 1674): Peto OR 1.23, 95% CI 0.86 to 1.76 Anaemia (2 RCTs, n = 2952): Peto OR 1.00, 95% CI 0.82 to 1.22 Perinatal mortality (2 RCTs, n = 2890): Peto OR 0.59, 95% CI 0.28 to 1.26 Satisfaction was similar or higher for those with midwife and GP-led care	All 3 trials conducted in developed countries	SR	1a

4.2 Continuity of care

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hodnett, 2001	33	2 RCTs, 1815 women	Continuity of care by the same caregiver or small group of caregivers vs. usual care by multiple caregivers throughout pregnancy	Interventions during labour Maternal outcomes Infant outcomes	Clinic waiting times > 15 minutes (1 RCT, n = 1001): Peto OR 0.14, 95% CI 0.10 to 0.19 Antenatal admission to hospital (2 RCTs, n = 1815): Peto OR 0.79, 95% CI 0.64 to 0.97 Failure to attend antenatal classes (1 RCT, n = 814): Peto OR 0.58, 95%nCI 0.41 to 0.81 Unable to discuss worries in pregnancy (1 RCT, n = 1001): Peto OR 0.72, 95% CI 0.56 to 0.92 Not feel well-prepared for labour (1 RCT, n = 1001): Peto OR 0.64, 95% CI 0.48, 0.86 Intrapartum analgesia or anaesthesia (2 RCTs, n = 1815): Peto OR 0.53, 95% CI 0.44 to 0.64 Not feel in control during labour (1 RCT, n = 1001): Peto OR 0.48, 95% CI 0.34 to 0.68 Failure to enjoy childbirth (1 RCT, n = 1001): Peto OR 0.65, 95% CI 0.47 to 0.90 Perceive labour staff as unsupportive (1 RCT, n = 1001): Peto OR 0.72, 95% CI 0.56 to 0.92 Episiotomy (2 RCTs, n = 1815): Peto OR 0.75, 95% CI 0.60 to 0.94 Unable to discuss postnatal problems (1 RCT, n = 1001): Peto OR 0.64, 95% CI 0.49 to 0.85 Feel unprepared for child care (1 RCT, n = 1001): Peto OR 0.57, 95% CI 0.41 to 0.80 Neonatal resuscitation (2 RCTs, n = 1815): Peto OR 0.66, 95% CI 0.52 to 0.83 Miscarriage (1 RCT, n = 814): Peto OR 0.44, 95% CI 0.20 to 0.94 Vaginal or perineal tear (2 RCTs, n = 1815): Peto OR 1.28, 95% CI 1.05 to 1.56 First stage labour > 6 hours (2 RCTs, n = 1815): Peto OR 1.35, 95% CI 1.08 to 1.68 5-minute Apgar score < 8 (1 RCT, n = 1001): Peto OR 2.63, 95% CI 1.15 to 6.02 No significant difference in the rates of caesarean section, induction of labour, augmentation of labour, amniotomy, stillbirth, neonatal death, preterm birth, intact perineum, admission to NICU, birthweight < 2500 g, dissatisfaction with intrapartum pain relief or breastfeeding		SR	1a

4.2 Continuity of care (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Waldenstrom and Turnbull, 1998	34	7 RCTs, 9148 women	Continuity of care by the same caregiver or small group of caregivers vs. usual care by multiple caregivers throughout pregnancy	Interventions during labour Maternal outcomes Infant outcomes	Induction of labour: Peto OR 0.76, 95% CI 0.66 to 0.86 Augmentation of labour: Peto OR 0.78, 95% CI 0.70 to 0.87 Electronic fetal monitoring: Peto OR 0.19, 95% CI 0.17 to 0.21 Epidural: Peto OR 0.76, 95% CI 0.68 to 0.85 Narcotics in labour: Peto OR 0.69, 95% CI 0.63 to 0.77 Instrumental vaginal delivery: Peto OR 0.82, 95% CI 0.70 to 0.95 Episiotomy: Peto OR 0.69, 95% CI 0.61 to 0.77 Perineal tears: Peto OR 1.15, 95% CI 1.05 to 1.26 No significant difference in the rates of caesarean section, intact perineum, admission to NICU, postnatal haemorrhage, manual removal of placenta, antenatal admission to hospital, postnatal complications and readmissions to hospital, or duration of labour No maternal deaths reported Perinatal mortality: Peto OR 1.60, 95% CI 0.99 to 2.59 Satisfaction with care was reported in 6/7 trials but not included in the meta-analysis due to lack of consistency between measures. Women in the intervention group were more satisfied with care during all phases of pregnancy and differences were statistically significant for each study separately. Women in the continuous care group were more pleased with information giving and communication with the caregivers and felt more involved in the decision making and more in control		SR	1a

4.4 Documentation of care

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Lovell et al., 1987	44	246 women from antenatal clinic in deprived inner city area in London	Carrying their own case notes vs. cooperation card Questionnaires were administered at 8 to 16 weeks of gestation (before randomisation), 32 to 34 weeks gestation and 2 to 7 days postpartum Clinical and background information was extracted from the case notes and interviews with 20 healthcare professionals involved in maternity care were carried out	Extensive qualitative results on women's perceptions and beliefs Clinical safety of carrying own notes	Women's attitudes towards carrying their own case notes were very positive. Both groups wanted their own notes in future pregnancies. Also would have preferred to have access to notes while in hospital Did not cause anxiety but may reduce it. Experimental group felt their preferences had been taken more into account Women read notes with great interest. No one lost or forgot to bring notes to hospital. More lost notes in control group Women carrying their own notes were more likely to say that they felt in control of their pregnancy: rate ratio 1.45, 95% CI 1.08 to 1.95 and they were more likely to say they found it easier to talk to the doctors and midwives during pregnancy: rate ratio 1.73, 95% CI 1.16 to 2.59 Experimental group less likely to miss antenatal clinic appointments No difference in the availability of notes for clinic appointments but approximately 1 hour of hospital clerical time was saved per week because of not having to retrieve and re-file notes Obstetric outcomes similar in both groups Majority of health professionals and staff in favour of women having their own notes but with reservations. All believed that women liked having them	48 women (19%) dropped out at some stage but all details given in report	RCT	1b

4.4 Documentation of care (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Elbourne et al., 1987	42	290 women attending a rural consultant clinic in Berkshire, England	Carrying full case notes until 10 days after delivery (n = 147) vs. cooperation card while case notes held by hospital (n = 143) Information about women's attitudes and behaviour obtained from 4 questionnaires (booking, 34 weeks, 10 days postnatal, 6 months postnatal) Cotinine assay on polled urine samples from each group at 34 weeks. Clinical information from notes. Observations in medical records department and informal interviews with staff		Two groups of women comparable in terms of sociodemographic characteristics, smoking behaviour and in answers to socio-psychological questions in the recruitment questionnaire Women with own notes nearly 1.5 times more likely to say that they felt in control of their pregnancy (RR1.45 95% CI 1.08 to 1.95) and more than 1.5 times more likely to say that they found it easier to talk to the doctors and midwives antenatally (RR 1.73 95% CI 1.16 to 2.59). No statistically significant differences between groups in terms of women's feelings of being well informed, anxious, confident, depressed, satisfied with their care or about involvement by baby's father, clinical outcomes, women's health-related behaviours. 91% of women in own notes group wanted the same in next pregnancy compared with coop card where 58% wanted a coop card next time. No difference in availability of notes in antenatal clinic. Approx. 1 hour of clerical time saved in peripheral clinic per week	Power calculation shown. 85% response rate at 6 months postnatal. Not as many differences between groups as expected. Possible dilution of difference between groups due to Hawthorn effect and halo effect	RCT	1b
Homer et al., 1999	43	150 English speaking pregnant women from an Australian metropolitan ANC in 1997	holding antenatal record vs. keeping a co-operation card. Questionnaire administered between 34-38 weeks gestation. Audit throughout study period to monitor lost and misplaced records.	Response rate Women's feelings toward carrying their own notes	84% response rate Multiparae who carried notes were significantly more likely to report that the doctors and midwives explained everything in their records to them than multiparae with coop cards or primiparae from either group Open ended questions showed: – 89% of women carrying their own notes felt more in control, felt more informed, liked having access to their results and felt it gave them an opportunity to share information particularly with other family members and partners – 11% of women carrying their own notes thought the record was too bulky, the system inconvenient or were worried they would forget notes – No differences were noted in numbers of lost records in each group – 89% of women in the hand-held notes group wanted to carry their notes in a future pregnancy as well as 52% of the cooperation card group	Power calculation performed. Analysed on intention-to-treat basis	RCT	1b

4.5 Frequency of antenatal appointments

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Villar and Khan-Neelofur, 2003	32	7 RCTs	Provision of reduced number of visits compared with standard schedule of visits	Perinatal outcomes Satisfaction outcomes	No significant differences in preterm delivery (< 37 weeks), pre-eclampsia, caesarean section, induction of labour, antenatal haemorrhage, postnatal haemorrhage, low birth weight, SGA, postpartum anaemia, admission to neonatal intensive care unit, perinatal mortality, maternal mortality and UTI found Women from developed countries in the reduced number of visits group were less satisfied with frequency of visits (3 RCTs, n = 3393): Peto OR 0.61, 95% CI 0.52 to 0.72	4 trials in developed countries, 3 in developing countries; same 7 trials as Carroli review[46] exact n not specified and not calculable from 'included trials' tables	SR	1a
Carroli et al., 2001	46	7 RCTs, 57,418 women	Lower number of antenatal visits (n = 30,799) compared with standard antenatal care models (n = 26,620)	Maternal and neonatal clinical outcomes Perceived satisfaction	No differences found in pre-eclampsia, urinary tract infection, postpartum anaemia, maternal mortality, low birthweight or perinatal mortality Women from developed countries in the intervention group were less satisfied with frequency of visits: rate difference –8.5%, p = 0.001	4 trials in developed countries, 3 in developing countries; the same 7 trials as Villar review[32] outcome data available for n = 26,619 in intervention group and n = 25,821 in control group	SR	1a
Petrou et al., 2003	45	17,765 women with a singleton pregnancy from England and Wales from 1994 to 1995	Data from an audit from 9 maternity units were retrospectively analysed	Range of number of visits Odds ratios for adverse perinatal outcomes by unit increase in antenatal visits for nulliparae (n = 7255) and multiparae (n = 10,510)	1 to 25 antenatal care visits Delivery by caesarean section: – primiparae OR 1.04 (95% CI 1.02 to 1.06) – multiparae OR 1.02 (95% CI 1.00 to 1.04, p = 0.036) Low birthweight (< 2500 g): – primiparae OR 1.03 (95% CI 1.00 to 1.07, p = 0.032) – multiparae OR 1.02 (95% CI 0.99 to 1.05) Admission to SCBU: – primiparae OR 1.0 (95% CI 0.97, 1.03) – multiparae OR 0.99 (95% CI 0.97, 1.02) Perinatal mortality: – primiparae OR 1.03 (95% CI 0.94, 1.12) – multiparae OR 1.0 (95% CI 0.91, 1.10)		CSS	3

4.5 Frequency of antenatal appointments (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hildingsson et al., 2002	48	3061 women attending antenatal care clinics in Sweden from 1999 to 2000	Questionnaire mailed shortly after first antenatal care visit	Preference with number of visits	Multiparous women preferred both more (RR 1.3, 95% CI 1.1 to 1.4) and fewer (RR 2.0, 95% CI 1.5 to 2.7) visits compared with primiparous women Younger women (< 25 years) preferred more visits (RR 1.2, 95% CI 1.1 to 1.4) and older women (> 35 years) fewer visits (RR 1.9, 95% CI 1.3 to 2.6) compared with 25- to 35-year-olds Single women preferred more visits when compared with married or cohabitating women (RR 1.9, 95% CI 1.3 to 2.7) Women with less education preferred fewer visits (RR 1.7, 95% CI 1.1 to 2.6) Women with a prior history of miscarriage, abortion, stillbirth or assisted conception preferred more visits	In an uncomplicated pregnancy in Sweden, a woman sees the midwife 8 to 9 times and a doctor once	CSS	3

4.6 Gestational age assessment

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Neilson, 1999	57	9 RCTs	Routine use of ultrasound vs. selective use of ultrasound at < 24 weeks	Induction rates for post-term pregnancy Detection of multiple pregnancy Perinatal mortality Neurobehavioural outcome and school function	Induction rates (6 RCTs, n = 24,195): Peto OR 0.61, 95% CI 0.52 to 0.72 Undiagnosed twins by 26 weeks (6 RCTs, n = 220): Peto OR 0.08, 95% CI 0.04 to 0.16 Perinatal mortality (8 RCTs, n = 34,245): Peto OR 0.86, 95% CI 0.67 to 1.12 Poor oral reading at school (1 RCT, n = 1,993): Peto OR 1.02, 95% CI 0.72 to 1.45 Poor reading comprehension at school (1 RCT, n = 1984): Peto OR 0.82, 95% CI 0.54 to 1.23 Poor spelling at school (1 RCT, n = 1982): Peto OR 0.73, 95% CI 0.53 to 1.0 Poor arithmetic at school (1 RCT, n = 1993): Peto OR 0.90, 95% CI 0.59 to 1.37 Reduced hearing in childhood (2 RCTs, n = 5,418): Peto OR 0.90, 95%CI 0.67, 1.21 Reduced vision in childhood (2 RCTs, n = 5417): Peto OR 0.82, 95% CI 0.66 to 1.01 Use of spectacles (2 RCTs, n = 5331): Peto OR 0.87, 95% CI 0.72 to 1.05		SR	1a
Crowther et al., 1999	52	648 women at a tertiary level hospital in Australia	Women attending for their first antenatal visit at less than 17 weeks of gestation were randomised into ultrasound (n = 321) or no ultrasound (n = 327)	Proportion of women who needed EDD adjusted due to ≥ 10-day discrepancy at 18 to 20 weeks Feelings about pregnancy Pregnancy outcomes	EDD adjusted: 9% vs. 18%, RR 0.52 (95% CI 0.34 t o 0.79) Concerned about wellbeing of pregnancy: RR 0.98 (95% CI 0.90 to 1.08) Feel worried about pregnancy in any way: RR 0.80 (95% CI 0.65 to 0.99) Do not feel relaxed about pregnancy in any way: RR 0.73 (95% CI 0.56 to 0.96) Do not feel excited about pregnancy in any way: RR 0.73 (95% CI 0.50 to 1.08) Nonviable pregnancy: RR 0.97 (95% CI 0.52 to 1.81)	Menstrual dates were not available for 16 women in the intervention group	RCT	1b

4.6 Gestational age assessment (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Savitz et al., 2002	53	3655 pregnant women in the USA from 1995 to 2001	Women at 24 to 29 weeks of gestation were recruited and gestational age estimates were compared to actual delivery dates by four algorithms Group 1: LMP only Group 2: ultrasound only Group 3: LMP except when a discrepancy ≥ 7 days existed in which case ultrasound dating was used Group 4: same as Group 3 but for ≥ 14 days	Differences in estimates between 4 groups Proportion of preterm births predicted (< 37 weeks) Proportion of post-term births predicted (> 41 weeks) Deviation between predicted and actual delivery dates	Mean duration of gestation estimate: – Group 1: 277.1 days – Group 2: 274.3 days – Group 3: 274.1 days – Group 4: 274.5 days Proportion preterm: no difference between the 4 groups, kappa = 0.72, 95% CI 0.68 to 0.75 Proportion post-term: LMP 12.1%; all other groups 3.4% to 4.5%, kappa = 0.16, 95% CI 0.11 to 0.20 Predicted vs. actual delivery: – Group 1, within 1 week, 48% – Groups 2 to 4, within 1 week, 55% to 58% predicted correctly – A further 15.7% within 2 weeks later for group 1 – A further 15.6% to 16.4% 2 weeks later for groups 2-4 – At more than 2 weeks afterward, 11.5% for group 1 and 2.3% to 3.2% for groups 2 to 4		CH	2a
Tunon et al., 1996	55	14,167 pregnant women in Norway from 1987 to 1992	Ultrasound examination at 18 weeks of gestation compared to LMP for prediction of date of delivery. LMP only used if reliable and menstrual cycle was regular	Prediction of day of delivery for term birth (282 days)	Proportion of women who delivered within 1 week of prediction for term: 61% for ultrasound and 56% for LMP calculation Proportion of women who delivered within 2 weeks of prediction for term: 88% for ultrasound and 84% for LMP calculation Estimated number of post-term births: 4.1% for ultrasound and 9.8% for LMP, $p < 0.001$		CH	2a

4.6 Gestational age assessment (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Backe and Nakling, 1994	54	1341 pregnant women in Norway from 1988 to 1989	Ultrasound performed before 20 weeks of gestation compared to LMP for prediction of term birth date	Prediction compared to actual day of delivery for term birth (280 days)	Ultrasound prediction was closer to actual day of delivery, $p = 0.03$ Proportion of women who delivered within 2 weeks of prediction for term: 87.5% for ultrasound and 79.3% for LMP calculation, chi $^2 = 33$, $p < 0.001$ Delivered more than 2 weeks after predicted date: 3% with ultrasound estimation and 13.9% with LMP, chi$^2 = 103$, $p < 0.001$		CH	2a
Blondel et al., 2002	56	44,623 births in Canada from 1978 to 1996	Comparison of 6 algorithms to assess gestational age 1: LMP 2: LMP unless discrepancy greater than 14 days; then, ultrasound 3: LMP unless discrepancy greater than 10 days; then, ultrasound 4: LMP unless discrepancy greater than 7 days; then, ultrasound 5: LMP unless discrepancy greater than 3 days; then, ultrasound 6: ultrasound alone	Rates of preterm and post-term births (< 32, 34, and 37 weeks and ≥ 41 and 42 weeks) Concordance between LMP and ultrasound estimates	At < 37 weeks: 1. 7.6% 2. 7.8% 3. 8.1% 4. 8.5% 5. 9.0% 6. 9.1% At ≥ 41: 1. 20.9% 2. 16.9% 3. 15.1% 4. 13.4% 5. 13.4% 6. 11.2% Concordance within 14 days for 90.7% of births		CH	2a

5.10 Exercise in pregnancy

5.10.1 What exercises are of benefit during pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Kramer, 2002	101	10 RCTs, 688 pregnant women	Regular aerobic exercise (at least 2 to 3 times/week) vs. reduction in frequency or intensity of such exercise	Maternal physical fitness Pregnancy outcome Self-perceived body image	5 trials (n = 171) report significant improvement in physical fitness in the exercise group but difference in measures prevents meta-analysis of results; 2 trials (n = 36) reported no significant increase in fitness in the exercise group Gestational age (3 RCTs, n = 416): WMD 0.02, 95% CI –0.4, 0.4 Preterm birth (3 RCTs, n = 421): RR 2.29, 95% CI 1.02, 5.13 Birthweight (5 RCTs, n = 476): WMD 28.64, 95% CI –65.85 to 123.13 Pre-eclampsia (2 RCTs, n = 81): RR 1.17, 95% CI 0.44 to 3.08 Body image (1 RCT, n = 15): Physical stamina, WMD –1.7, 95% CI –3.49 to 0.03 Muscular strength, WMD –2.2, 95% CI –3.62 to –0.72 Energy level, WMD –2.2, 95% CI –3.29 to –1.06 Body build, WMD -1.5, 95% CI –2.51 to –0.39	Trials either did not specify method of allocation or alternated	SR	1a

5.10.2 What exercises are associated with adverse maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Camporesi, 1996	102	Three cross-sectional studies: Study 1, 100 women who dived during pregnancy and n = 69 who did not Study 2, 72 women who dived during pregnancy Study 3, 142 dived pregnancies (i.e., some women dived during more than one pregnancy)	Retrospective questionnaires	Malformations, SGA and other infant outcomes Fetal decompression disease	Overall: fetus is at greater risk of malformations and embolisation after decompression bubbles evolve in circulation, owing to lack of pulmonary filtration and inability to resolve gas bubbles in alveoli Study 1: none among non-diving mothers; 7/100 (7%) mothers had babies with congenital abnormalities 1.4% of babies were SGA in non-diving group; 6% in diving group Raised incidence of miscarriage, stillbirth and neonatal death also reported. Study 2: no evidence of increased risk to unborn fetus in mothers who stopped diving during the first trimester and mothers who dived throughout pregnancy Study 3: n = 109 (75%) live births and n = 33 (23%) stillbirths or spontaneous miscarriages, evenly divided among dived pregnancies and non-dived pregnancies	Response rate of 169/208 (81%) in one study and the 72 from the second study were self-selected and from an initial 610 women Third study fails to mention the outcome of 4 births	RCSS	3

5.11 Sexual intercourse in pregnancy

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Berghella et al., 2002	105	966 pregnant women randomised to metronidazole in a BV trial and 320 pregnant women randomised to metronidazole in a *Trichomonas vaginalis* trial in the USA	Women identified at 16 to 23 weeks of gestation with BV or *Trichomonas vaginalis* were treated with metronidazole or placebo. Questions about sexual behaviour were asked at two points in the study: before and after treatment. Treatment was 8 capsules taken at randomisation visit and again 48 hours later, repeated at follow-up visit between 24 and 29 weeks, but at least 14 days after initial visit Analysis includes women who received metronidazole treatment only	Follow-up cultures taken after initial treatment Before treatment: effect of number of lifetime partners, number of partners since start of pregnancy and episodes of intercourse in the past 4 weeks on incidence of preterm birth After treatment: intercourse (yes or no) and frequency of intercourse Effect of sexual behaviour on efficacy of treatment	For BV trial: 846/966 For *Trichomonas vaginalis* trial: 269/320 Sexual behaviour before treatment had no effect on incidence of preterm birth ($p > 0.4$ for both trials) Intercourse between the first and second dose had no effect in either trial Intercourse between the second and third dose: – BV trial RR 0.6 (95%CI 0.4, 0.9) – *Trichomonas vaginalis* trial RR 1.0, (95% CI 0.6 to 1.6) Frequency of intercourse between second and third dose: – BV trial, more frequent intercourse associated with lower incidence of preterm birth ($p = 0.03$) – *Trichomonas vaginalis* trial, $p = 0.64$ Sexual behaviour had no effect on treatment efficacy		SA	2a
Read and Klebanoff, 1993	103	13,285 women attending antenatal care from 1984 to 1989 in the USA	Frequency of intercourse at 23 to 26 weeks assessed	Association between preterm birth and Intercourse at 23 to 26 weeks (less than once a week used as reference group)	Intercourse 1 to 2 times/week: OR 0.79, 95% CI 0.70 to 0.90 Intercourse 3 or 4 times/week: OR 0.76, 95% CI 0.64 to 0.90 Intercourse ≥ 5 times/week: 0.89, 95% CI 0.70 to 1.14 Less than once per week vs. once a week or more: OR 0.80, 95% CI 0.71 to 0.89	No data on frequency of intercourse for n = 306 women	CH	2a
Klebanoff et al., 1984	104	39,217 singleton, first pregnancies from 1959 to 1966 in the USA	Coital frequency in the previous month reported until 27 weeks, then frequencies reported for the previous two weeks up to 42 to 43 weeks	Association between coital frequency and preterm birth Association between coital frequency and perinatal mortality Association between coital frequency and mean duration of gestation	Inverse relationship between frequency of coitus and preterm delivery reported at 28 to 29 weeks and also at 32 to 33 weeks ($p < 0.001$) No statistically significant association between coital frequency at 28 to 29 weeks, 32 to 33 weeks, and 36 to 37 weeks and perinatal mortality Mean duration of gestation increased with increasing coital frequency at 28 to 29 weeks, 32 to 33 weeks, and 36 to 37 weeks ($p < 0.001$)		CH	2a

5.12 Smoking in pregnancy

5.12.1 What are the maternal and perinatal outcomes associated with smoking in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Shah and Bracken, 2000	117	20 cohort studies	Meta-analysis of any maternal smoking vs. no maternal smoking during pregnancy	Preterm delivery	Pooled OR 1.27, 95% CI 1.21 to 1.33	No information regarding the size of the studies was provided in the review	SR of CH (1966 to 1997)	2a
Castles et al., 1999	116	6 studies on placenta praevia; 8 on placental abruption; 9 on ectopic pregnancy; 6 on PPROM; 5 on pre-eclampsia in the USA and Western Europe	Meta-analysis of any maternal smoking vs. no maternal smoking during pregnancy	Placenta praevia (n = 32,444 cases, n = 18,251 controls) Placental abruption (n = 42,207 cases, n = 15,095 controls) Ectopic pregnancy (n = 2831 cases, n = 7801 controls) PPROM (n = 31,639 cases, 3029 controls) Pre-eclampsia (n = 3485 cases, n = 966 controls)	Placenta praevia: pooled OR 1.58, 95% CI 1.04 to 2.12 Abruption placenta: pooled OR 1.62, 95% CI 1.46 to 1.77 Ectopic pregnancy: pooled OR 1.77, 95% CI 1.31 to 2.22 PPROM: pooled OR 1.7, 95% CI 1.18 to 2.25 Pre-eclampsia: pooled OR 0.51, 95% CI 0.38 to 0.64		SR of CH and CCS (1966 to 1995)	2 & 3
Ananth et al., 1999	115	13 studies, 1,358,083 pregnancies	Meta-analysis of any maternal smoking vs. no maternal smoking during pregnancy	Placental abruption	Pooled OR 1.9, 95% CI 1.8 to 2.0		SR of CH and CCS (1966 to 1997)	2 & 3
Wyszynski et al., 1997	118	11 studies (109,831 infants) on cleft lip, among which 9 also looked at cleft palate	Meta-analysis of any maternal smoking vs. no maternal smoking during first trimester of pregnancy	Cleft palate Cleft lip (with and without cleft palate)	CP: pooled OR 1.32, 95% CI 1.10 to 1.62 Cleft lip: pooled OR 1.29, 95% CI 1.18 to 1.42		SR of CH and CCS (1966 to 1996)	2 & 3
Conde-Agudelo et al., 1999	119	28 cohort studies and 7 case–control studies, 833,714 women	Meta-analysis of any maternal smoking vs. no maternal smoking during pregnancy	Pre-eclampsia	Cohort studies (n = 810,649): pooled RR 0.68, 95% CI 0.67 to 0.69 Case–controls (n = 23,065): pooled OR 0.68, 95% CI 0.57 to 0.81		SR of CH and CCS (1966 to 1998)	2 & 3

5.12.1 What are the maternal and perinatal outcomes associated with smoking in pregnancy? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
DiFranza and Lew, 1995	114	13 studies on miscarriage; 23 on low birthweight; 25 on perinatal mortality; and 12 on sudden infant death syndrome	Meta-analysis of any maternal smoking vs. no maternal smoking during pregnancy	Spontaneous abortion Low birthweight Perinatal mortality Sudden infant death syndrome	Spontaneous abortion: 7 cohort (n = 86,632), pooled RR 1.24, 95% CI 1.19 to 1.30 6 case–control (n = 10,535), pooled OR 1.32, 95% CI 1.18 to 1.48 Low birthweight: 22 cohort (n = 346,899), pooled RR 1.82, 95% CI 1.67 to 1.97 1 case–control (n = 654), OR 1.99, 95% CI 1.74 to 2.28 Perinatal mortality: 23 cohort (n = 657,288), pooled RR 1.26, 95% CI 1.19 to 1.34 2 case–control (n = 22,560), pooled OR 1.23, 95% CI 1.12 to 1.41 SIDS: 12 case–control (n = 2340 cases, n = 607,809 controls), pooled OR 2.98, 95% CI 2.51 to 3.54		SR of CH and CCS	2 & 3
Clausson et al., 1998	120	96,662 singleton, live births in Sweden from 1992 to 1993	Maternal risk factors for SGA; data obtained from the Swedish Medical Birth Register	SGA and smoking vs. no smoking	1 to 9 cigarettes/day: OR 1.7, 95% CI 1.6 to 1.9 10+ cigarettes/day: OR 2.4, 95% CI 2.1 to 2.7	Maternal smoking information was missing from n = 4882 births	CH	2a
Raymond et al., 1994	604	638,242 births to women > 20 years of age in Sweden from 1983 to 1989	Risks for stillbirth; data obtained from the Swedish Medical Birth Register	Stillbirth and smoking vs. no smoking	OR 1.4, 95% CI 1.2 to 1.4	Maternal smoking information was missing from n = 42,645 births	CH	2a
Kleinman et al., 1988	122	362,261 singleton deliveries in Missouri, USA from 1979 to 1983	Effects of smoking on fetal and infant mortality; data obtained from birth and death certificates and by interviewing mother on smoking habits	Overall fetal and infant mortality rates	For primiparae (n = 134,429): < 1 pack/day, OR 1.25, 95% CI 1.13 to 1.39; ≥ 1 pack/day, 1.56, 95% CI 1.37 to 1.77 For multiparae (n = 227,832): < 1 pack/day, OR 1.30, 95% CI 1.20 to 1.41; ≥ 1 pack/day, 1.30, 95% CI 1.19 to 1.42		CH	2a

5.12.2 and 5.12.3 Do smoking cessation programmes lead to reduction in smoking rates for pregnant women and what are the characteristics of smoking cessation programmes that are most effective in reducing smoking among pregnant women?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Thorogood et al., 2002	127	2 systematic reviews of RCTs and 3 additional RCTs	Smoking cessation programme vs. no programme during pregnancy RCT 1: nicotine patches vs. placebo RCT 2: 10 to 15 minute session with midwife vs. usual care RCT 3: motivational interviewing vs. usual care	Cessation rates	Review A (44 trials, n = 16,916 women): Peto OR 0.53 95% CI 0.47 to 0.60; among trials where cessation was validated by means other than self-report (8 RCTs, n = 3829), Peto OR 0.53 95% CI 0.44 to 0.63 Review B (10 RCTs, n = 4815 pregnant women): 1.9% to 16.7% in no intervention group; 7.1% to 36.1% in intervention group; absolute risk increase with intervention vs. no intervention 7.6%, 95% CI 4.3 to 10.8 RCT 1: NS RCT 2 (1120 pregnant women): NS RCT 3 (269 women in their 28th week of pregnancy): NS		SR	1a

5.12.4 Do smoking cessation programmes decrease perinatal mortality and morbidity?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Thorogood et al., 2002	127	2 systematic reviews of RCTs and 3 additional RCTs	Smoking cessation programme vs. no programme during pregnancy RCT 1: nicotine patches vs. placebo RCT 2: 10 to 15 minute session with midwife vs. usual care RCT 3: motivational interviewing vs. usual care	Low birthweight Preterm birth Very low birthweight Perinatal mortality Mean birthweight	Review A (subset of 10 trials): low birthweight, Peto OR 0.8, 95% CI 0.67 to 0.95); preterm birth, Peto OR 0.83, 95% CI 0.69 to 0.99; birthweight higher among babies from intervention group, mean difference, 28 g, 95% CI 9 to 49; very low birthweight, NS; perinatal mortality, NS RCT 1: birthweight higher in nicotine patch group, mean difference, 186 g, 95% CI 35 g to 336 g		SR	1a

5.15 Car travel during pregnancy

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Johnson and Pring, 2000	144	200 women attending their routine mid-pregnancy anomaly scan; UK	Questionnaire on current knowledge and practice among pregnant women about the use of car restraint systems during pregnancy	Seatbelt and airbag use, sources of information about restraint systems and recommendations regarding car safety	98% (159/159) always wore seatbelts in the front 68% (109/159) always wore seatbelts in the back 48% (77/159) correctly identified where to place the seatbelt 37% (50/159) could recall receiving being advised on the correct position of seatbelts;, of these 50 women, 66% (33/50) had a correct response rate to the correct position of the three-point seatbelt, this was significantly different (p = 0.003) from the women who could not remember receiving any information, who had a 40% (44/109) correct response 87% (138/159) thought that wearing a seatbelt was beneficial to them if they were involved in an accident when pregnant 62% (98/159)) thought that wearing a seatbelt was beneficial to the fetus if they were involved in an accident 74% (118/159) knew that a three-point seatbelt was safer than a lap belt for the fetus 71% (113/159) thought that airbags increased the safety of a pregnant women in an accident 17% (27/159) thought seatbelts were potentially dangerous to a pregnant woman		CSS	3
Chang et al., 1987	145	89 women and 82 coaches at childbirth classes; USA	Minimal education (pamphlet) Moderate education (lecture and brief discussion, statistics on auto safety pertaining to pregnant women and pamphlet) Control (no education)	Observation of shoulder strap of seatbelt	Increase in seatbelt use from 19.4 to 28.6% for minimal intervention group, increase of 9.2% (95% CI –3.1 to 21.5) 13.5 to 24.2% for moderate intervention women, increase of 10.8% (95% CI 0.3 to 21.1) 16.9% to 17.9% for the women in the control group, change of 1% (95% CI –10.3 to 12.3)	Group randomisation only 4 groups (no power calculation)	ISS	2a

5.15 Car travel during pregnancy (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Klinich et al., 2000	146	Retrospective study of 43 pregnant women involved in road traffic accidents, USA		Adverse fetal outcome, adverse maternal outcome	Study of 43 pregnant women involved in road traffic accidents showed that a increase in adverse fetal outcome with improper maternal restraint use: Minor crashes: 11% (2/18) adverse fetal outcome in properly restrained women, compared to 33% (2/6) improperly restrained women Moderate crashes: 30% (3/10) adverse fetal outcome in properly restrained women, compared to 100% (1/1) improperly restrained woman Severe crashes: 100% (3/3) adverse fetal outcome in properly restrained women, and 100% (5/5) improperly restrained women There is also a correlation of maternal injury level with adverse fetal outcome		CR	3
Wolf et al., 1993	149	Women of 20 weeks gestation or greater who delivered live births or stillbirths from 1980 to 1988 in Washington State, USA, who were involved as drivers in police investigated motor vehicle crashes	Restrained or not restrained with seatbelt	Birth weight Birth within 48 hours of accident Fetal death	Unrestrained pregnant women drivers were 1.9 times more likely to have a low birth weight baby (95% CI = 1.2, 2.9) and 2.3 times more likely to give birth within 48 hours after a motor vehicle crash (95% CI = 1.1, 4.9) than restrained women drivers after adjusting for age and gestational age at crash. Fetal death was 0.5% (7/1349) in unrestrained, and 0.2% (2/1243) in restrained women		CSS	3
Crosby et al., 1972	148	Pregnant baboons, USA	Horizontal sledge accelerated and decelerated similar to head on collision Lap belt vs. three point belt	Fetal death	Fetal death rate was 8.3 % (1/12) among animals impacted with a three point restraint compared to 50% (5/10) fetal death rate of animals impacted with lap belts only	Animal study that probably would not receive ethical approval if carried out now No details of how baboons were selected to be lap belt or three-point belted	ISNR	2a

6.1 Nausea and vomiting in early pregnancy

6.1.1 What is the prevalence of nausea and vomiting in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Whitehead et al., 1992	166	1000 pregnant women at an obstetric clinic in London, England	Survey of women attending for antenatal care in the first half of their pregnancy (904/1000 (90%) between 11 to 20 weeks of gestation)	Frequency of nausea and vomiting Onset of nausea and vomiting Decline of nausea and vomiting Time of day of nausea and vomiting	Nausea: daily, 584/984 (59%); weekly, 98/984 (10%); less often, 145/984 (15%); none, 157/984 (16%) Vomiting: daily, 202/971 (21%); weekly, 90/971 (9%); less often, 215/971 (22%); none, 464/971 (48%) Onset: within 4 weeks of LMP, 275/803 (34%); within 6 weeks, 314/803 (39%); within 8 weeks, 171/803 (21%); within 10 weeks 28/803 (4%); within 12 weeks 15/803 (2%) Decline: from 12 to 16 weeks, 77% reported a reduction in vomiting and 83% a reduction in nausea; at 17 to 20 weeks, 16% reported persistent vomiting, 12% reported persistent nausea; at > 20 weeks, 10% reported persistent vomiting, 13% reported persistent nausea Time of day: 148/827 (18%) reported nausea exclusively in the morning; 477/827 (57%) reported symptoms in the morning as well as other times during the day	Denominators vary owing to missing answers on survey All women who reported vomiting reported feeling nausea as well	CSS	3
Gadsby et al., 1993	167	363 consecutive women from a teaching practice in England from 1986 through 1988	Daily symptoms diary kept by women from time of positive pregnancy test until symptoms ceased	Frequency of nausea and vomiting Onset of nausea and vomiting	71/363 (20%) reported no nausea or vomiting throughout their pregnancy; 28% had nausea only; 52% had nausea and vomiting Onset: 94% by 8 weeks Duration: 91% reported no symptoms by 16 weeks	All women who reported vomiting also reported feeling nausea	CSS	3
Feldman, 1989	168			Incidence of hyperemesis gravidum	3.5/1000 deliveries			

6.1.2 What are the adverse maternal and perinatal outcomes associated with nausea and vomiting in pregnancy? (excluding twins, trophoblastic disease, and severity requiring admission to hospital)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Weigel and Weigel, 1989	165	11 studies	Meta-analysis of previously published data on outcomes in women with nausea and vomiting during pregnancy vs. no nausea and vomiting during pregnancy	Miscarriage Perinatal mortality	Miscarriage, (6 studies, n = 14,564): OR 0.36 (95% CI 0.32 to 0.42) Perinatal mortality: too much heterogeneity between studies to assess, but among 3 studies: n = 466, OR 0.18 (95%CI 0.03 to 0.94) n = 10,441, OR 0.72 (95% CI 0.59 to 0.89) n = 903, OR 0.82 (95% CI 0.22 to 3.03)	Only analyses relevant to miscarriage and perinatal mortality reported here, therefore number of studies does not add up to 11	SR (1966 to 1988)	3
Klebanoff and Mills, 1986	169				No increased risk for fetal death, low birthweight, or congenital malformations			3

6.1.3 & 6.1.4 Are there effective interventions to treat nausea and vomiting in pregnancy and what are the maternal and perinatal outcomes associated with these interventions?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Murphy, 1998	174	10 RCTs of various alternative therapies	Alternative medicine (acupressure, ginger, pyridoxine) vs. placebo, dummy acupressure, or no treatment for nausea, vomiting and hyperemesis	Reduction in severity and frequency of nausea and vomiting	7 trials (686 women) concerning P6 pressure point (4 the same as Cochrane, 3 specifically excluded from Cochrane as crossover studies with no separate data from first treatment period); 6/7 showed positive results for reducing nausea or improving symptoms; 2nd largest trial with 161 patients showed no difference even though 92.5% participants completed protocol 1 trial for ginger (same one as in Cochrane); significant reduction of symptoms of hyperemesis, reducing both degree of nausea and frequency of attacks (p = 0.035) 3 trials for pyridoxine (2 included in Cochrane, 1 extra looking at pyridoxine as part of multivitamin preparation) No trials on hypnosis or homeopathy found	11 trials seem to have been included when looking at the narrative	SR (1996 to 1997)	1a&b
Jewell and Young, 2001	173	23 RCTs	Any treatment for persistent nausea and/or vomiting in pregnancy before 20 weeks (anti-histamines, vitamin B6, debendox/Bendectin (doxylamine, dicycloverine, pyridoxine), P6 acupressure (4 RCTs), ginger root, ACTH, oral prednisolone) vs. placebo or (or dummy acupressure)	Reduction in severity and frequency of nausea and vomiting	23 trials included; variable quality Antiemetics (12 RCTs, n = 1505): Peto OR 0.17 95% CI 0.13 to 0.21 1 trial (n = 161) looked at antiemetic effect on miscarriage, neonatal loss and fetal abnormalities, all NS Association with drowsiness (4 RCTs, n = 343): Peto OR 2.19 (95% CI 1.09 to 4.37) Bendectin, as a subset of result for all medication (3 RCTs, n = 240): effect in reducing nausea Peto OR 0.28 (95% CI 0.16 to 0.51) Vitamin B6 (pyridoxine) (2 RCTs): effect on vomiting (n = 392), Peto OR 0.91 (95% CI 0.60 to 1.38); appears to be effective in reducing the severity of nausea at dosages ranging from 10 mg to 25 mg three times daily (n = 395) P6 acupressure (2 RCTS, n = 404): Peto OR 0.35 (95% CI 0.23 to 0.54) Continuous data from 1 trial was NS Last trial not able to be included in meta-analysis and showed no effect ACTH: no evidence of benefit Ginger (1 g daily) may be of benefit based on weak evidence Very little information on effects on fetal outcome		SR	1a&b

6.1.3 & 6.1.4 Are there effective interventions to treat nausea and vomiting in pregnancy and what are the maternal and perinatal outcomes associated with these interventions? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Vickers, 1996	176	6 RCTs Systematic review, search date 1995	Stimulation of P6 acupuncture point for the treatment of nausea and/or vomiting associated with pregnancy vs. no treatment, placebo or non-acupuncture intervention	Reduction in nausea and vomiting	6 RCTS for nausea and vomiting in pregnancy; same as trials as selected in Murphy's systematic review. All 6 showing positive effect for acupuncture or acupressure or electrical stimulation at P6 point ($p < 0.05$)		SR	1a
Vutyavanich et al., 2001	172	70 women with nausea during pregnancy attending antenatal clinic in Thailand before 17 weeks of gestation from 1998 to 1999	Ginger (250 mg capsules 4 times daily) (n = 32) vs. placebo (n = 38), for four days	Visual analogue scale for severity of symptoms (0 = no nausea, 10 = nausea as bad as it could be) Likert scales to measure response to treatment Episodes of vomiting Adverse effects on pregnancy outcomes	Nausea severity average over 4 days: 0.9 ± 2.2 vs. 2.1 ± 1.9, p = 0.014 Response to treatment: 28/32 (87.5%) vs. 10/35 (28.6%) reported improvement in symptoms, p < 0.001 Episodes of vomiting after 4 days: 12/32 (37.5%) vs. 23/35 (65.7%) still vomiting, p = 0.021 Spontaneous abortion: 1/32 (3.1%) vs. 3/35 (8.6%), p = 0.615 Caesarean section: 6/32 (18.8%) vs. 4/35 (11.4%), p = 0.509 No congenital abnormalities and all infants discharged in good condition	Double blinded Table of random numbers used for treatment allocation 3 from placebo group lost to follow-up	RCT	1b
Norheim et al., 2001	177	97 pregnant women at 8 to 12 weeks of gestation invited (by flyer) to participate in Norway from 1995 to 1996	Acupressure vs. dummy wristband	Intensity of nausea and vomiting Duration of nausea and vomiting	Intensity: 71% vs. 63% reported a reduction, p = NS Duration: reduced by 2.74 hours vs. 0.85 hours, p = 0.018	Double blind 'Block-randomisation' by groups of 20 (i.e., 10 at a time randomised to either group)	RCT	1b
Mazzotta and Magee, 2000	182	RCTs and cohort studies Systematic review; search date 1998	Safety of antihistamines and pyridoxine and phenothiazines Effectiveness of phenothiazine vs. placebo	Teratogenicity Malformations Reduction of nausea and vomiting by phenothiazine (3 RCTs, n = 389)	Antihistamines and teratogenicity (24 RCTs, n > 200,000): OR 0.76 (95% CI 0.60 to 0.94) Pyridoxine and major malformations (cohort study): RR 1.05, 95% CI 0.60 to 1.84 (18/458 cases, 34/911controls) Phenothiazines and teratogenicity (7 observational studies, n = 78,440): RR 1.0, 95% CI 0.84 to 1.18) Phenothiazine vs. placebo (3 RCTs, n = 389): RR 0.31 (95% CI 0.24 to 0.42)		SR	1a, 2a & 3

6.2 Heartburn

6.2.1 What is the prevalence of heartburn?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Marrero et al., 1992	184	607 women attending an antenatal clinic in London	Self-administered questionnaire about heartburn and pharyngeal regurgitation	Symptoms of heartburn and pharyngeal regurgitation. Scores for frequency of symptoms (scale 1 = less than once a week; 2 = two or more times a week) and scores for severity of symptoms (scale = 0, no symptoms to 3, constantly disrupting activities)	Prevalence of heartburn increased with gestational age: 22% in first trimester, 39% in second trimester and 72% in third trimester, $p < 0.0001$ and similarly for severity, $p < 0.0001$ There was an increased risk of suffering heartburn with increasing gestation, $p < 0.0001$, a history of prepregnancy heartburn, $p < 0.0001$, parity, $p < 0.0001$ and inversely with maternal age, $p < 0.05$. Not with BMI, race or weight gain in pregnancy	This survey assessed women at varying stages of pregnancy not at a set week	SY	3
Ho et al., 1998	605	47 consecutive, Singaporean pregnant women (in first trimester) attending an antenatal clinic were enrolled, 35 completed the study	Standardised questionnaire Women were interviewed 4 times at first, second, third trimester and in the postpartum period	Percentage with heartburn symptoms alone Regurgitation alone Heartburn and regurgitation Incidence of heartburn during pregnancy	Heartburn symptoms alone 5.7% Regurgitation alone 17.1% Heartburn and regurgitation 17.1% Heartburn symptoms noticed in first trimester (78.6%) Heartburn symptoms disappeared in second trimester (71.4%)	Prevalence of heartburn appears less in Singapore than in UK. Small population assessed (n = 35)	SY	3
Knudsen et al., 1995	185	180 women attending an antenatal clinic at 30 weeks gestation	Self-administered questionnaire to be completed daily from 31 weeks gestation to delivery	Weekly prevalence of heartburn Prevalence of heartburn related to age	Heartburn: weekly prevalence 60% (n = 112) Heartburn positively related to age $p = 0.016$		SY	3
Bainbridge et al., 1983	186	2 groups: 200 white European women (101 primiparae, 99 multiparae), interviewed at Birmingham Maternity Hospital 100 Asian women (37 primiparae, 63 multiparae) of mixed extract from the Indian subcontinent, interviewed at Birmingham Maternity Hospital and Dudley Road Hospital	Women were interviewed	Incidence of symptomatic gastro-oesophageal reflux in primiparae and multiparae	Incidence of symptomatic gastro-oesophageal reflux: White European women 81.5% Asian women 80%	Details of interview tool not provided	SY	3

6.2.2 Are there effective interventions to treat heartburn in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Shaw, 1978	187	120 women in third trimester diagnosed with symptoms of heartburn (burning sensation in the epigastrum)	60 received compound A (Syn-Ergel, containing aluminium phosphate, an antacid with a protective mucosal coating agent) 60 received compound B (active placebo)	Pain relief after 1 hour	Pain eased or gone after 1hour: Treatment group n = 40 (80%) Placebo group n = 13 (31%)	No intention to treat analysis	RCT	1b
Kovacs et al., 1990	606	50 women, > 20 weeks pregnant, suffering severe to moderate heartburn at least once in the preceding 7 days Recruited between May 1985 and June 1987	Mucaine (antacid) without oxethazaine (n = 17) Mucaine (n = 15) Placebo (n = 18)	Heartburn severity Heartburn relief Scored on a scale: 1, mild or no relief to 5, severe total relief	Heartburn severity mean scores: Mucaine w/o oxethazaine 3.0 Mucaine 2.9 Placebo 2.9 p = 0.9 Heartburn relief scores: Mucaine w/o oxethazaine 3.3 Mucaine 3.9 Placebo 2.9 p = 0.05	Mucaine containing oxethazaine meant to have anaesthetic properties. The results suggest that Mucaine with oxethazaine has some benefit over the Mucaine that does not	DBP	1b
Briggs and McKay Hart, 1972	607	Pregnant women Numbers not clear	Randomised double blind crossover trial Alcin tablets (aluminium salicylate) (test product) vs. aluminium hydroxide tablets	Episodes of heartburn Intensity of heartburn Relief of heartburn	Numbers not clear to derive accurate figures	It appears that there is no difference in the effectiveness of these treatments. Concern about the carry over effect of the drugs used in this study design Numbers unclear	RDBC	1b

6.2.2 Are there effective interventions to treat heartburn in pregnancy? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Lang and Dougall, 1989	188	207 pregnant women < 38 weeks gestation recruited 157 women randomised	Prescribed 2 weeks of:10 ml Algicon® (alginate) suspension (n = 79) vs. 10 ml magnesium trisilicate (n = 78) To be taken after meals and at bedtime	Numbers cured or improved in daytime and night time Numbers complaining of adverse events	Numbers cured or improved in daytime after 1 week: Algicon group n = 38/61 who completed week 1 Magnesium trisilicate n = 38/58 who completed week 2 Numbers cured or improved in daytime after 2 weeks: Algicon group n = 36/50 who completed week 2 Magnesium trisilicate n = 38/47 who completed week 2 Numbers cured or improved at night time after 1 week: Algicon group n = 46/61 who completed week 1 Magnesium trisilicate n = 46/58 who completed week 2 Numbers cured or improved at night time after 2 weeks: Algicon group n = 41/50 who completed week 2 Magnesium trisilicate n = 36/47 who completed week 2 Number of adverse events: Algicon group n = 18 Magnesium trisilicate n = 15	No significant difference in improvement of symptoms between the two groups	RCT	1b
Atlay et al., 1978	190	55 pregnant women complaining of heartburn (41 completed the trial and took the 3 interventions for the required time)	Crossover trial (random) Acid mixture vs. alkali mixture vs. placebo mixture 10 ml before and after meals and before bed, for 7 days with 4 day interval between each intervention	Disappearance of heartburn symptoms	Symptoms disappeared or improved: Acid treatment n = 28 (68%) Alkali treatment n = 21 (51%) Placebo n = 18 (44%) Alkali v acid p = 0.18 Alkali v placebo p = 0.66 Acid v placebo p = 0.045	Acid and alkali mixtures no difference in relief of symptoms but better relief achieved than using a placebo	RCT (cross over)	1b

6.2.2 Are there effective interventions to treat heartburn in pregnancy? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Rayburn et al., 1999	191	Pregnant women > 20 weeks of gestation	50 patients recruited to receive one week antacid therapy only; 30 patients experiencing > 4 episodes moderate–severe heartburn were randomised to antacids and liquid ranitidine vs. antacids and placebo liquid for a further 2 weeks	Heartburn intensity Global assessment of improvement	Mean heartburn intensity scores: Baseline: 7.7 Week 1: (antacid only) mean score reduced to 6.5 ($p < 0.05$) Week 2: antacid and placebo and antacid and ranitidine mean score 4.4 ($p < 0.01$) Heartburn intensity change in scores change from baseline to week 2 for antacid and ranitidine group: 7.7 to 3.7, $p < 0.001$ Global assessment of improvement: Baseline vs. placebo $p < 0.05$ Baseline vs. single pm dose ranitidine $p < 0.001$ Baseline vs. double dose ranitidine am and pm $p < 0.001$		RCT	1b
Magee et al., 1996	193	178 pregnant women who contacted a Motherrisk programme between 1985-1993 for information on gestational exposure to H_2 receptor antagonists 71% reported exposure to ranitidine (mean dose 258 ± 99 mg/day), cimetidine 16%, (487 ± 389 mg/day), famotidine 8%, (32 ± 10 mg/day) and nizatidine (5%,283± 139 mg/day) 178 controls (selected from Motherrisk database) were matched to cases	Telephone interviews	Major malformations (those having an adverse effect in either the functional or social acceptability of the individual)	Major malformations for exposure in first trimester: Cases 2.1% (3/142) Controls 3.5% (5/143) Mean difference, 1.38%, 95% CI –5.2% to 2.4%) Major malformations for exposure anytime: Cases 3% (5/165) Controls 3.1% (5/161)		CCS	3
Nikfar et al., 2002	194	5 cohort studies	Exposure to proton pump inhibitors (n = 593,593 infants) vs. no exposure (n = 15,330 infants)	Major malformations	For any exposure to proton pump inhibitors (mostly omeprazole): summary relative risk 1.18, 95% CI 0.72 to 1.94 For exposure to omeprazole: 1.05, 95% CI 0.59 to 1.85		MA of 5 CH	2a

6.3 Constipation

6.3.1 What is the prevalence of constipation in pregnant women?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Meyer et al., 1994	195	1860 consecutive series of pregnant women attending antenatal clinic in London between August 1982 and March 1984	Structured questionnaires on symptoms, health problems, at 17, 28 and 36 weeks of gestation	Prevalence of constipation at 14,28 and 36 weeks pregnancy (several other outcomes reported)	% with constipation: 14 weeks 39% (from sample n = 1513) 28 weeks 30% (from sample n = 1463) 36 weeks 20% (from sample n = 1433)		SY	3

6.3.2 Intervention for the treatment of constipation

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Jewell and Young, 2003	196	Pregnant women (in last trimester)	10 g fibre supplements (n = 27) vs. placebo (n = 13)	Increased stool frequency	OR 0.18 (95% CI 0.05 to 0.67)		SR	1a
Jewell and Young, 2003	196	Pregnant women	Stimulant laxatives (n = 70) Bulk-forming laxatives (n = 70)	Constipation not resolved Poor acceptability of treatment Effect on side effects	OR 0.3 (95% CI 0.14 to 0.61) OR 0.89 (95% CI 0.46 to 1.73) OR 2.08 (95% CI 1.27 to 3.41)		SR	1a

6.4 Haemorrhoids

6.4.1 Prevalence of haemorrhoids in pregnancy

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Abramowitz et al., 2002	197	165 pregnant women in the last 3 months of pregnancy, who gave consent for proctological examination before and after delivery between December 1996 and April 1997	Proctological examination during last 3 months pregnancy, after delivery and at any time symptoms were suggestive of anal disease (bleeding or pain)	Incidence of anal disease (thrombosed external haemorrhoids and anal fissures)	Women presenting with thrombosed external haemorrhoids (n = 13) (7.8%)		CSS	3

6.4.2 Intervention for the treatment of haemorrhoids

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Wijayanegra et al., 1992	198	100 pregnant women (12 to 34 weeks of gestation) recruited from an antenatal clinic with first- to third-degree severity of haemorrhoids	500 mg oral (hydroxyethyl)rutosides, oral tablet, twice daily for 1 month (n = 48) vs. placebo (n = 49)	Symptomatic improvement Side effects Fetal outcome (n = 97)	Symptomatic improvement after 2 weeks: 84% improvement in treatment group and 12% improvement in placebo group After 4 weeks: 94% improvement in treatment group and 14% improvement in placebo group Treatment group: abdominal discomfort (n = 1) palpitations after 2 weeks (n = 2) For all 3 patients side effects resolved by 4 weeks Treatment group (n = 48) 46 normal outcome, 1 preterm delivery, 1 congenital anomaly (mother treated at 34 weeks post-organogenesis) Placebo group (n = 49): 46 normal outcome, 1 fetal death, 1 preterm delivery, 1 SGA	Data evaluated on 97 patients	DBRP	1b

6.4.2 Intervention for the treatment of haemorrhoids (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Buckshee et al., 1997	199	50 pregnant women (amenorrhoea > 28 weeks) with history of acute internal haemorrhoids	Micronised flavonoid therapy Oral tablets (micronised diosmin 450 mg (90% and hesperidin 50 mg (10%) Three phase treatment: First phase: 6 tablets for 4 days and 4 tablets for 3 days, divided dose after lunch and dinner Second and third phase: up to 30 days after delivery, maintenance dose; 2 tablets per day, divided lunch and supper	Self-assessment of acute symptoms (0 absent to 3 severe) Relapses in the antenatal period and the postnatal period Side effects Infant outcomes	Median symptom scores assessed before and after first phase (7 day treatment) for: bleeding reduced by 1 (range 1 to 2), 95% CI, $p < 0.001$, pain reduced by 1, 95% CI, $p < 0.001$) rectal exudation reduced by 1, 95% CI $p < 0.05$ and rectal discomfort reduced by 1, 95% CI $p < 0.01$ Maintenance treatment: relapses per month before treatment 90% compared with after treatment (maintenance dose) in the antenatal period, 36.3% $p < 0.001$ Postnatal assessment: pretreatment (history 1 year prior pregnancy), % history with relapse 42% compared with assessment at 30 days post delivery % with relapses 12% Side effects: nausea and diarrhoea (n = 6) Congenital malformation (n = 1) Intrauterine death (n = 1) Birthweight: median 2.9 kg (range 2.7 to 3.1)	Recruitment to study: 50 eligible consecutive patients	CSS	3
Saleeby et al., 1991	200	25 pregnant women (age range 21 to 34 years) 22 were in 3rd trimester, 80% multiparous 88% presented with thrombosed or gangrenous haemorrhoids	Closed haemorrhoidectomy. Removal of symptomatic disease 3 quadrants removed (n = 14), 2 quadrants removed (n = 7), one quadrant removed (n = 4)	Pain relief Long term follow up (range 6 months to 6 yrs) mean 30 months Fetal outcomes	Pain relief in 24 hours (n = 24) Persistent rectal bleeding (n = 1) Additional haemorrhoidal treatment required at follow up (n = 6) No surgical related fetal outcomes		CSS	3

6.5 Varicose veins

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Bergstein, 1975 (taken from review Young and Jewell, 2003)	211	69 pregnant women at 28 weeks gestation in the Netherlands	300 mg rutoside, three times/day for 8 weeks vs. a placebo	Reduction in ankle circumference Subjective improvement in symptoms	Not estimable Improvement in symptoms: Peto OR 0.3, 95% CI 0.12 to 0.77	Paper derived from systematic review	RW of 3 RCTs	1a
Jacobs, 1996 (taken from review Young and Jewell, 2003)	211	35 healthy women with normal pregnancies and ankle oedema in the USA	EPIC for 30 minutes resting in the left-lateral position vs. 30 minutes resting in the left-lateral position (no EPIC)	Reduction in lower leg volume	Reduction in lower leg volume (WMD, fixed) –258.800 95% CI 566.914 to 49.314]	Paper derived from systematic review		1a
Katz 1990 (taken from review Young and Jewell, 2003)	211	Pregnant women, 34 to 38 weeks gestation, singleton pregnancies Numbers entered into study are not clear; only 11 completed the study	50 minutes bed rest in the lateral supine position versus the same time immersed to the waist with legs horizontal in water at 32 degrees Celsius versus the same time immersed to the shoulders in water at 32 degrees Celsius. Each crossover was done 2 to 4 days later. Only the shoulder immersion comparison is used in this review	Urine output (diuresis) one hour after treatment Participants (n = 11) Blood pressure at the end of the 50-minute treatment period Participants (n = 11)	Urine output (diuresis) one hour after treatment: WMD (fixed), –137.000 (95% CI –236.283 to –37.717) Mean arterial pressure at the end of 50 minute treatment period: WMD (fixed), –11.000 (95% CI –18.951 to –3.049)			1a

6.7 Backache

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Young and Jewell, 2003	211	3 RCTs RCT 1: 92 pregnant women at 36 weeks of gestation RCT 2: 258 women attending hospital in Sweden for an ultrasound scan RCT 3: 60 women in Sweden with pelvic or back pain arising before 32 weeks of gestation	RCT 1: Ozzlo pillow used for 1 week to support the pregnant abdomen when lying in a lateral position vs. a standard hospital pillow (control) RCT 2: 20 1-hour weekly water gymnastic classes involving exercise and relaxation in water vs. no intervention RCT 3: 10 acupuncture sessions vs. 10 physiotherapy group sessions	RCT 1: moderate or better improvement in backache; relief of insomnia RCT 2: number of days of sick leave due to back pain after 32 weeks of gestation RCT 3: numbers of women rating treatment as good or excellent	RCT 1: Effect of Ozzlo pillow on backache: (n = 184) (improvement less than moderate) OR 0.32 (95% CI 0.18 to 0.58) Effect of Ozzlo pillow on sleep: (n = 184) (benefit rated less than moderate) OR 0.35 (95% CI 0.20 to 0.62) RCT 2: Effect of water gymnastics on sick leave days due to back pain (n = 241) OR 0.38 (95% CI 0.16 to 0.88) RCT 3: Effect of acupuncture vs. physiotherapy on back pain (treatment rated as good or excellent) OR 6.58 (95% CI 1.00 to 43.16)		SR	1a
Kristiansson et al., 1996	206	200 consecutive women attending an antenatal clinic. Average age 27.9 years	Survey during pregnancy questionnaires and physical examinations	Frequency of back pain	Onset of back pain before pregnancy: 25.6% Onset of back pain during pregnancy: 61% Prevalence of back pain during weeks of pregnancy: 12 weeks: 19% 24 weeks: 47% 36 weeks: 49%		SY	3
Ostgaard et al., 1991	207	950 pregnant women attending an antenatal clinic in Sweden	Women were reviewed at 12th week and every second week until delivery	Incidence of back pain	49% complained of back pain during pregnancy but half of these had back pain before pregnancy Onset of back pain during pregnancy 27% (n = 210)		SY	3
Fast et al., 1987	208	200 women (black, white, Hispanic and oriental origin) interviewed within 24 to 36 hours after giving birth on a maternity ward (of a county hospital in the USA)	Questionnaire relating to personal data and occurrence and manifestation of low back pain	Frequency of back pain during pregnancy Month of onset of back pain	56% complained of back pain during pregnancy 48% no back pain during pregnancy 60.7% of women with back pain onset was between 5th to 7th month of pregnancy		SY	3

6.7 Backache (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Stapleton et al., 2002	209	1530 respondents to a South Australian Omnibus Population Survey, 1120 (73%) had had at least one pregnancy > 20 weeks	Population survey including specific questions on back pain during pregnancy	Incidence of back pain during pregnancy Severity of back pain during pregnancy	397/1120 (35.5%) reported back pain during one or more pregnancies 61.8%(n = 246) had at least moderately severe backache 9% (n = 35) were disabled by the pain	Survey on backache questions was dependent upon retrospective recall. Therefore reliability is unclear	SY	3
Mantle et al., 1977	210	180 women (mean age 26 years) delivering at a London Hospital between May 1973 and August 1973	Questionnaire administered to women within 24 hours of delivery, asking about back pain during pregnancy	Incidence of back pain and severity of backache during pregnancy Month of onset of backache Time of day when backache most troublesome	48% (n = 87) troublesome or severe backache 52% (n = 92) none or not worth troubling about backache Peak month of onset of pregnancy: 54% (n = 47) onset of mild or severe backache during 5th to 7th month Time of day backache most troublesome: 40% evening and 26% night		SY	3
Field et al., 1999	212	26 pregnant working women, between 14 and 30 weeks of gestation, with an interest in relaxation exercises	Randomly assigned: Massage therapy (n = 14) (x 10, 20-minute massages over 5 weeks) vs. progressive muscle relaxation class (n = 12) (a 20-minute relaxation class and encouraged to do these at home twice a week for 5 weeks)	Relief of back pain Pregnancy anxiety Sleep scale disturbance	Back pain relief scores: For massage group: first day (pre- or post-massage) 4.6/2.2 (p = 0.005) Last day (pre- or post-massage) 3.8/2.1 (p = 0.01) For relaxation group: first day (pre- or post-relaxation) 3.4/3.3 not significant Last day (pre- or post-relaxation) 3.2/3.5 (p = 0.01)	Method of randomisation not stated	RCT	1b
Ostgaard et al., 1994	213	407 pregnant women at a maternity care unit in Sweden	Random allocation (quasi) to 3 groups Group A: control group no extra intervention; any development of back or pelvic pain treated according to usual routine Group B: two 45-minute classes of back care in pregnancy Group C: five 30-minute individual lessons on back care in pregnancy	Improvement with back or posterior pelvic pain Sick leave frequency	Improvement with back or posterior pelvic pain following information on muscular training and body posture difference between group A and B ($p < 0.05$); group A and C ($p < 0.05$) Improvement with back or posterior pelvic pain following information on vocational technique training between group A and B (NS); group A and C ($p < 0.05$) Improvement with back or posterior pelvic pain and affect on sick leave: between group A and B (NS); between group A and C ($p < 0.05$)	Quasi-randomised (allocation by day of birth in month 1 to 10 Group A 11 to 20 Group B 21 to 31 Group C)	RCT	1b

6.7 Backache (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Noren et al., 1997	214	Pregnant women with any type of back pain attending an antenatal clinic in Sweden between April 1991 to February 1993	Intervention group 54 women: individually designed physiotherapy programme of 5 visits (including teaching on anatomy, posture, vocational ergonomics, gymnastics, relaxation) and an exercise programme versus control group of 81 pregnant women with back pain; no specific intervention given	Duration of sick leave	Average number of sick leave days: Intervention group: 30.4 days/woman vs. control group 53.6 days; difference in sick leave ($p < 0.001$)		CCH	2a
Tesio et al., 1994	215	16 pregnant women between 12 and 30 weeks gestation with back and/or sciatica pain onset during pregnancy and unremitting for 4 weeks	Autotraction, a mechanical treatment for back pain. Consists of a 3- to 6-second maximal pulling effort followed by 1-to 2-minute rest period for 25 minutes Three treatments every, 3 days	Pain relief recovery	Recovery: Fully recovered (n = 5) Improved (n = 8) No change (n = 3) Change in pain scores from before to after treatment: Median pain intensity as a group at start 50/100 and at end 15/100 ($p < 0.001$)	No control group	OPC	3
Guadagnino III, 1999	216	12 pregnant women (age range 14 to 34 years) with back pain attributed to pregnancy	Spinal manipulative therapy (1 to 3 techniques applied) and received treatment 2 to 3 times/week until delivery Postal questionnaire sent to mothers at end of pregnancy	Pain intensity (scale 1 to 10)	Average pain score when treatment sought: 7.58 Average pain score when maintained under care: 4.25	Method of recruitment is unclear The questionnaire included several questions that required retrospective memory of the symptoms they experienced while receiving treatment Significant bias affect in this study. Authors conclude that an RCT is required	CH	3

6.7 Backache (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
McIntyre and Broadhurst, 1996	217	20 pregnant women reporting low back pain in the second or third trimester	Rotational mobilisation exercise carried out at 3 antenatal visits	Resolution of pain	15 patients had complete resolution of pain 3 patients had 50-80% resolution 2 patients unaccounted for	Methods of study unclear	CH	3
Requejo et al., 2002	218	A 28-year-old primigravida, 20 weeks gestation with low back pain beginning at 18 weeks gestation Presented with pain limiting her to sit for 20 minutes and restricted ability to bend forward	Treatment 4 episodes during 2 weeks of manual joint mobilisation applied to symptomatic vertebral segment	Resolution of pain improved mobility	Improved mobility (able to bend forward without pain and sit longer than 1 hour without discomfort) Oswestry score reduced from 38/100 to 10/100		CR	3

8.1 Anaemia

8.1.1 Is anaemia in pregnancy associated with adverse maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Zhou et al., 1998	272	829 pregnant women in China from 1991 to 1992	Women divided into 6 groups based on their 1st-trimester Hb) concentrations (< 9.0, 9.0 to 9.9, 10.0 to 10.9, 11.0 to 11.9, 12.0 to 12.9, ≥ 13.0 g/dl) Vitamin C, iron sulphate and folic acid treatment was offered to all women with Hb levels < 110 g/dl (defined as anaemia)	Prevalence of anaemia Based on initial Hb concentrations: Risk of low birthweight Risk of preterm birth Risk of SGA	49% at enrolment; 66% in 2nd trimester; 67% in 3rd trimester Low birthweight: > 11.9 g/dl, NS; 10.0 to 10.9, RR 2.7 (95% CI 1.01 to 7.39); 9.0 to 9.9, RR 3.3 (95% CI 1.09 to 9.77); < 9.0, RR 3.0 (95% CI 0.60 to 14.76) Preterm birth: >11.9 g/dl, NS; 10.0 to 10.9, NS; 9.0 to 9.9, RR 2.6 (95% CI 1.17 to 5.90); < 9.0, RR 3.7 (95% CI 1.36 to 10.23) SGA: NS for all groups		CH	2a
Steer et al., 1995	271	153,602 pregnancies in North West Thames region, England	Retrospective analysis of information on database to determine association of lowest Hb level in pregnancy and birthweight and rates of low birthweight and preterm delivery in different ethnic groups	Birth weight, rates of low birthweight, preterm labour	Maximum mean birth weight (3483 g ± 565) achieved with lowest Hb 8.6 g/dl to 9.5 g/dl Lowest incidence of low birth weight and preterm labour occurred with lowest Hb 9.5 g/dl to 10.5 g/dl Similar for all ethnic groups		CSS	3

8.1.2 Does routine iron supplementation during pregnancy improve maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Mahomed, 2001	74	20 RCTs	Iron vs. no iron or placebo (except one trial: selective vs. routine iron) in pregnant women	Haemoglobin Measures of iron status Pregnancy outcome Side effects of treatment	Low (< 10 g or 10.5 g) predelivery Hb (12 RCTs, n = 1802): Peto OR 0.15 (95% CI 0.11 to 0.20) Low predelivery serum iron (4 RCTs, n = 726): Peto OR 0.19 (95% CI 0.12 to 0.29) Low (< 10 mg/dl) predelivery serum ferritin (4 RCTs, n = 481): Peto OR 0.12 (95% CI 0.08 to 0.17) Caesarean section (1 RCT, n = 2694): Peto OR 1.36 (95% CI 1.04 to 1.78) Blood transfusion (1 RCT, n = 2694): Peto OR 1.68 (95% CI 1.05 to 2.67) Preterm delivery (1 RCT, n = 2694): Peto OR 1.41 (95% CI 0.94 to 2.12) Low birthweight (1 RCT, n = 2694): Peto OR 1.12 (95% CI 0.72 to 1.75) SGA (1 RCT, n = 2690): Peto OR 1.10 (95% CI 0.79 to 1.52) Admission to neonatal unit (1 RCT, n = 2694): Peto OR 1.06 (95% CI 0.80 to 1.40) Congenital malformations (1 RCT, n = 2694): Peto OR 1.01 (95% CI 0.77 to 1.33) Stillbirths and deaths in first week of life (1 RCT, n = 2694): Peto OR 0.33 (95% CI 0.11, 0.99) Side effects in mothers (3 RCTs, n = 7098): Peto OR 0.41 (95% CI 0.34 to 0.50)	All pregnancy outcome results were from the trial that compared selective vs. routine iron in pregnancy	SR	1a

8.1.2 Does routine iron supplementation during pregnancy improve maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Mahomed, 2001	76	8 RCTs (5449 pregnant women with haemoglobin level > 10 g/dl	Iron and folate supplementation vs. no iron and folate or placebo	Haemoglobin Measures of iron and folic acid status	Low (< 10 g or 10.5 g) predelivery Hb (6 RCTs, n = 1099): Peto OR 0.19 (95% CI 0.13 to 0.27) Low predelivery serum iron (3 RCTs, n = 277): Peto OR 0.14 (95% CI 0.08 to 0.24) Low (< 10 mg/dl) predelivery serum ferritin (1 RCT, n = 48): Peto OR 0.04 (95% CI 0.01 to 0.14) Low (< 2.5 microgrammes/ml) predelivery serum folate (3 RCTs, n = 501): Peto OR 0.11 (95% CI 0.06 to 0.21) Low predelivery serum red cell folate (1 RCT, n = 46): Peto OR 0.12 (95% CI 0.02 to 0.89) Caesarean section (2 RCTs, n = 104): Peto OR 0.16 (95% CI 0.03 to 0.82) Preterm delivery (1 RCT, n = 48): Peto OR 8.08 (95% CI 0.80 to 81.60) Low birthweight (1 RCT, n = 48): Peto OR 7.72 (95% CI 0.47 to 127.14) Admission to neonatal unit (1 RCT, n = 48): Peto OR 7.39 (95% CI 0.15 to 372.41) Stillbirth and neonatal death (1 RCT, n = 48): Peto OR 7.72 (95% CI 0.47 to 127.14)		SR	1a

8.1.3 What are the side effects of iron supplementation in pregnancy and how can they be minimised?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Cuervo and Mahomed, 2001	274	5 RCTs, 1234 pregnant women with anaemia (Hb < 11 g/dl) in pregnancy	14 variations of interventions for anaemia, including all types of iron preparations (oral, slow release, intramuscular and intravenous iron, blood transfusions, and recombinant erythropoietin)	Women with anaemia Maternal morbidity and mortality Neonatal morbidity and mortality	Oral iron vs. placebo: anaemia (1 RCT, n = 125) Peto OR 0.12 (95% CI 0.06 to 0.24); no published data on clinically relevant outcomes	All trials were assessed to be of poor quality	SR	1a

8.2 Haemoglobinopathies

8.2.1 What is the prevalence of haemoglobinopathies in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Davies et al., 2000	275	20,333 pregnancies in Brent, England from 1986 to 1995	Universal antenatal screening for haemoglobinopathies	Prevalence	n = 1688/20,333 pregnancies tested positive for haemoglobinopathy trait or disease (8.3%): 751/20,333 with sickle trait or disease (3.7%) 265/20,333 with beta-thalassaemia trait or disease (1.3%) 272 other haemoglobinopathy 400 alpha-thalassaemia		CSS	3

8.2.2 What are the adverse maternal and perinatal outcomes associated with haemoglobinopathies?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Davies et al., 2000	275	751 pregnant women with sickle trait or disease and 265 pregnant women with beta-thalassaemia trait or disease from 1986 to 1995	Women attended counselling (n = 623/751 (83%) in sickle cases; n = 246/265 (93%) in beta-thalassaemia cases), partners tested (n = 481/623 (77%) in sickle cases; n = 234/246 (88%) in beta-thalassaemia cases), postnatal diagnosis offered	Pregnancies at risk Outcomes of pregnancies at risk Estimates of prevalence among all live births in England	Sickle cell pregnancies at risk: 113/481 (23%) Beta-thalassaemia pregnancies at risk: 22/234 (9.4%) Outcomes of at risk pregnancies: Sickle cell: 16 of 108 women who returned for follow-up accepted prenatal diagnosis (15%) 3 terminations from 4 affected pregnancies 22 affected births from 92 of 108 women who did not accept prenatal diagnosis 5 affected births among 142/623 partners not tested Beta-thalassaemia: 19 of 22 women who returned for follow-up accepted prenatal diagnosis (86%) 4 terminations from 4 affected pregnancies 0 affected births from 3 of 22 women who did not accept prenatal diagnosis 0 affected births among 12/246 partners not tested 1 beta-thalassaemia birth among 15 unaffected pregnancies Prevalence estimates: 17 infants born each year with beta-thalassaemia (0.03/1000 live births) 160 infants born each year with sickle cell disorder (0.25/1000 live births)	The prevalence estimates allow for terminations	HTA RW CSS	3

8.2.3 Does recording of racial background in the notes of pregnant women help in selective screening for haemoglobinopathies?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Aspinall et al., 2003	281	N/A	Assessing effectiveness of questions about ethnic origin	Quality of data collected	Risk group misclassification as high as 20% June quarter 2000 data from Hospital Episode Statistics indicate ethnic group data missing from 43% of records in London and 37% in England		RW	3
Modell et al., 2000	276	400 pregnancies in 138 women in the UK from 1990 to 1994	Audit to evaluate the quality of antenatal screening for haemoglobinopathy and genetic counselling	Haemoglobinopathy affected Screening offered Risk recognition	138/400 (35%) pregnancies with haemoglobinopathy 68/138 (49%) of affected pregnancies had been offered screening at first pregnancy Risk recognised in 27/63 (43%) pregnancies before 1990 and in 41/74 (55%) pregnancies after 1990	This study assumes that antenatal screening for Hb disorders is standard practice in the UK	CSS	3

8.2.4 What tests are available for detecting maternal haemoglobinopathies?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Zeuner et al., 1999	279	N/A		Screening and diagnosis algorithm	1. Estimation of red blood cell indices. MCH < 27 pg indicates thalassaemia trait 2. Subsequent quantification of HbA and HbF for thalassaemia trait (via HPLC) and identification of Hb structural variants for sickle cell traits (via isoelectric focusing) 3. If HbA and HbF > 3.5% is indicative of thalassaemia trait 4. Partner testing initiated 5. DNA analysis used when assessment of at-risk pregnancy cannot be adequately obtained by phenotyping	p. 5, 8–10	HTA	RW 4

8.2.5 Do effective interventions exist to improve outcomes for these women?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Modell et al., 1997	277	2068 cases of prenatal diagnosis in England from 1974 to 1994	Comparison of prenatal diagnosis for Hb disorders with annual number of pregnancies at risk for these disorders (ethnic group data from 1991 census)	Utilisation of prenatal diagnosis Termination of pregnancy Proportion of referrals in the first trimester	Utilisation for thalassaemias: 55% (range 10% among Bangladeshis to 89% among Cypriots) Use for sickle cell disorders: 13% by black Africans and black Caribbeans 296/305 (97%) pregnancies with fetuses diagnosed as homozygous were terminated		CSS	3
Modell et al., 2000	276	400 pregnancies in 138 women in the UK from 1990 to 1994	Audit to evaluate the quality of antenatal screening for haemoglobinopathy and genetic counselling	Uptake of prenatal diagnosis	80% uptake when offered among British Pakistanis, 35/48 (73%) agreed to prenatal diagnosis in first trimester, with 11/12 affected pregnancies terminated, compared with 11/28 (39%) accepting prenatal diagnosis in the second trimester, with 4/7 affected pregnancies terminated	This study assumes that antenatal screening for Hb disorders is standard practice in the UK	CSS	3
Ahmed et al., 2000	284	300 couples requesting prenatal diagnosis of beta-thalassaemia during 3.5 years in Pakistan	Counselling and prenatal diagnosis of beta-thalassaemia between 10 and 16 weeks (n = 15 diagnosed after 16th week)	Termination of affected pregnancies	47/53 (89%) of affected pregnancies were terminated 6/53 terminations declined for religious reasons		CSS	3

9.1 Screening for structural abnormalities

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Williamson et al., 1997	298	148 births involving neural tube defects in England and Wales from 1990 to 1991	Pregnancies of neural tube defect affected births reported to the Office of Population Census Survey were retrospectively reviewed through obstetric records	Sensitivity of ultrasound screening for anencephaly between 14 to 22 weeks (90/148 pregnancies were screened by ultrasound)	100%		CSS	3
Bricker et al., 2000	297	96,633 babies from 11 studies (1 RCT, 11 cohort) from 1986 to 1996 in Europe, USA and Korea	Literature review to assess the clinical effectiveness of routine ultrasound in pregnancy	Prevalence of fetal anomalies Sensitivity and specificity of detection with ultrasound Proportion of structural abnormalities detected with scan at less than 24 weeks	Overall: 2.09%, range 0.76 to 3.07% Detection at less than 24 weeks: 41.3% (range 15% to 71.5%) and 99.9% (range 99.4% to 100%) Detection at greater than 24 weeks: 18.6% (sensitivity only), range 18.2% to 21.7% Overall detection rate: 44.7% (sensitivity only), range 15.0% to 85.3% Structural abnormalities: Central nervous system 76.4% Pulmonary 50% Cardiac 17.4% Gastrointestinal 41.9% Urinary tract 67.3% Skeletal 23.8%	HTA report	SR	1b & 2a
Saari-Kemppainen et al., 1994	299	9310 women pregnant women from two hospitals in Finland from 1986 to 1987	Routine early ultrasound between 16 to 20 weeks gestation (n = 4691) vs. selective ultrasound (n = 4619)	Termination of pregnancy after detection of anatomical malformations in the fetus Perinatal mortality (per 1000) Screening sensitivity for major malformations	Terminations: 11 vs. 0 (no p value reported) Perinatal mortality among singleton births: 4.2 vs. 8.0, $p < 0.05$ Sensitivity: 40% vs. 27.7% Sensitivity per hospital: 75% (9/12 cases detected) and 35% (9/26 cases detected)		RCT	1b
Whitlow et al., 1999	300	6634 women carrying 6443 live fetuses in London, England	Ultrasound scan at 12 to 13 weeks of gestation	Detection rate for major structural abnormalities	Overall detection rate: 59% (37/63), 95% CI 46.5 to 72.4: CNS 84% (16/19) Face 0% (0/2) Neck 100% (13/13) Cardiac 40% (4/10) Pulmonary 33% (1/3) Gastrointestinal 100% (7/7) Urinary tract 60% (3/5) Skeletal 0% (0/7)		CSS	3

9.2 Screening for chromosomal anomalies

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
ONS, 2000	303	All children in England and Wales	Notification of Down's syndrome	Incidence of Down's syndrome per 10,000 live and still births	1986: 6.7 1988: 6.1 1990: 5.9 1992: 5.7 1994: 4.7 1996: 5.5 1998: 6.2	Report of child health statistics	SV	3
Morris et al., 2002	311	All antenatal or postnatally diagnosed and confirmed cases (via a karyotype) of Down's syndrome in England and Wales from 1989 to 1998	Collection of reports from all regional cytogenetic laboratories of cases found to have a Down's syndrome karyotype	Observed odds of maternal age specific risk of Down's syndrome	Odds at age 20 years: 1:1441 Odds at age 25 years: 1:1383 Odds at age 30 years: 1:959 Odds at age 35 years: 1:338 Odds at age 40 years: 1:84 Odds at age 45 years: 1:32	An estimated 6% of births with Down's syndrome are missed by the National Down Syndrome Cytogenetic Register; therefore, the number of births was increased by 6% to allow for those not included	SV	3

9.2 Screening for chromosomal anomalies (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Smith-Bindman et al., 2001	315	56 studies, 130,365 unaffected fetuses and 1930 cases of Down's syndrome Systematic review; from 1980 to 1999 on Medline only	Articles that assessed second trimester (15 to 24 weeks) ultrasound markers (choroid plexus cyst, nuchal fold thickening, echogenic intracardiac focus, echogenic bowel, renal pyelectasis, shortened humerus, shortened femur, and fetal structural malformations) to detect Down's syndrome fetuses	Sensitivity and specificity of each ultrasonographic marker and associated fetal loss per case diagnosed	Nuchal fold (95% CI): Sensitivity 0.04 (0.02 to 0.10) Specificity 0.99 (0.99 to 0.99) Fetal loss 0.6 Choroid plexus cyst (95% CI): Sensitivity 0.01 (0.0 to 0.03) Specificity 0.99 (0.97 to 1.0) Fetal loss 4.3 Femur length (95% CI): Sensitivity 0.16 (0.05 to 0.40) Specificity 0.96 (0.94 to 0.98) Fetal loss 1.2 Humerus length (95% CI): Sensitivity 0.09 (0.0 to 0.60) Specificity 0.97 (0.91 to 0.99) Fetal loss 1.9 Echogenic bowel (95% CI): Sensitivity 0.04 (0.01 to 0.24) Specificity 0.99 (0.97 to 1.0) Fetal loss 1.0 Echogenic intracardiac focus (95% CI): Sensitivity 0.11 (0.06 to 0.18) Specificity 0.96 (0.94 to 0.97) Fetal loss 2.0 Renal pyelectasis (95% CI): Sensitivity 0.02 (0.01 to 0.06) Specificity 0.99 (0.98, 1.0) Fetal loss 2.6		SR	2a & 3
Dick, 1994	608	4 cohort studies	Comparison of proportion of Down's syndrome pregnancies identified through triple testing with the total number of Down's syndrome pregnancies	Detection rates	Range 48% to 91% with false positive rate of 3.2 to 6%, respectively (cutoff rates from 1/190 to 1/274 used) When varying cutoff rates were accounted for, triple marker screening in the 2nd trimester with AFP, hCG, and uE_3 combined with maternal age offered 50% detection rate in women < 35 years with 5% false positive rate		SR of CH	2a

9.2 Screening for chromosomal anomalies (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Conde-Agudelo and Kafury-Geota, 1998	320	20 cohort studies, 194,326 pregnant women	Meta-analysis of effectiveness of triple marker screening for Down's syndrome	Sensitivities and false positive rates	Sensitivities for maternal age ≥ 35 years: For cutoff rates 1/190 to 1/200, 89% (range 78% to 100%), false positive rate 25% (range 20% to 29%) For cutoff rates 1/250 to 1/295, 80% (range 75% to 100%), false positive rate 21% (range 20% to 21%) Sensitivities for maternal age < 35 years: For cutoff rates 1/250 to 1/295, 57% (range 53% to 58%), false positive rate 4% (range 3% to 6%)		SR of CH	2a
Bindra et al., 2002	609	15,030 pregnant women in London from 1999 to 2001	Screening for Down's syndrome by nuchal translucency, free beta-hCG and PAPP-A and maternal age at 11 to 14 weeks	Detection rates at cutoff rate of 1/300 False positive rate for 75% and 85% detection rate Detection rate with false positive rate fixed at 5% Uptake of prenatal diagnosis	82 cases of Down's syndrome identified False positive rate at 75% detection rate: Maternal age alone, 27.7% Maternal age, free beta-hCG, and PAPP-A, 10.1% Maternal age and NT, 2.6% Maternal age, NT, free beta-hCG and PAPP-A, 0.9% False positive rate at 85% detection rate: Maternal age alone, 46.4% Maternal age, free beta-hCG, and PAPP-A, 15.2% Maternal age and NT, 9.1% Maternal age, NT, free beta-hCG and PAPP-A, 3.0% Detection rate for fixed false positive rate of 5%: By maternal age alone, 30.5% maternal age, free beta-hCG and PAPP-A, 60% Maternal age and NT, 79% Maternal age, NT, free beta-hCG and PAPP-A, 90% 89% (73/82) of women in the screen positive group chose invasive testing for prenatal diagnosis		CH	2a

9.2 Screening for chromosomal anomalies (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Wald et al., 2003	316	101 cases from 45,712 singleton pregnancies and 490 matched controls from 28,434 singleton pregnancies at 24 maternity centres in the UK and one in Austria from 1995 to 2000	Women matched on centre, maternal age and crown–rump length or biparietal diameter Comparison of efficacy of various methods and combination of methods for Down's syndrome screening Nuchal translucency obtained at 12 to 13 weeks gestation Serum and urine samples taken at 9 to 13 weeks and also included if taken at 14 to 22 weeks Serum tested for AFP, total hCG, uE_3, PAPP-A) free beta-hCG and dimeric inhibin A Urine tested for ITA, beta-core fragment, total hCG and free beta-hCG	False positive rate for 75% and 85% detection rate Detection rate with false positive rate fixed at 5% Estimates of fetal loss (stillbirth or miscarriage) due to amniocentesis or chorionic villus sampling at 85% detection rate, 80% uptake rate and 0.9% fetal loss rate attributable to procedure Outcomes of Down's syndrome pregnancies	False positive rate at 75% detection rate: Integrated test 0.3% Serum integrated test 0.8% Combined test 2.3% Quadruple test 2.5% Triple test 4.2% Double test 6.6% NT 8.6% False positive rate at 85% detection rate (95% CI): Integrated test 1.2% (1.1 to 1.3) Serum integrated test 2.7% (2.4 to 3.0) Combined test 6.1% (5.7 to 6.5) Quadruple test 6.2% (5.8 to 6.6) Triple test 9.3% (8.8 to 9.8) Double test 13.1% (12.6 to 13.6) NT 20% (18.6 to 21.4) Detection rate for fixed FPR of 5%: Serum integrated test 92% Quadruple test 92% Triple test 90% Double test 86% Fetal losses/100,000 women screened (i.e. 173 cases diagnosed) (n): Integrated test 9 Serum integrated test 19 Combined test 44 Quadruple test 45 Triple test 67 Double test 94 NT 144 71 Down's syndrome pregnancies were terminated, 4 miscarried after amniocentesis and 26 resulted in a live birth	Integrated test defined as NT and PAPP-A at 10 weeks and quadruple test markers at 14 to 22 weeks Serum integrated test is the same as above minus the NT Combined test is based on NT, free beta-hCG, PAPP-A and maternal age assessed in the first trimester Quadruple test based on AFP, uE_3, free beta-(or total) hCG, and inhibin A measurements with maternal age in the 2nd trimester Triple test based on AFP, uE_3, free beta-(or total) hCG, and maternal age in the 2nd trimester Double test based on AFP, free beta-(or total) hCG, and maternal age in the 2nd trimester	CCS	3
Alfirevic et al., 1998	323	3 RCTs, 9067 women	1st trimester CVS vs. 2nd trimester amniocentesis	Sampling failure Total pregnancy loss	Failure (1 RCT, n = 3201): Peto OR 2.86, 95% CI 1.93 to 4.24 Pregnancy loss (3 RCTs, n = 9067): Peto OR 1.33, 95% CI 1.17 to 1.52		SR	1a

9.2 Screening for chromosomal anomalies (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Alfirevic, 2000	324	3 RCTs, 1832 women	Amniocentesis vs. transabdominal CVS at 9 to 14 weeks gestation	Sampling failure Total pregnancy loss	Failure (3 RCTs, n = 1832): 0.4% vs. 2%, RR 0.23, 95% CI 0.08 to 0.65 Pregnancy loss (3 RCTs, n = 1832): 6.2% vs. 5%, RR 1.24, 95% CI 0.85 to 1.81		SR	1a
RCOG Guideline No. 8, 2000	307	N/A	Amniocentesis vs. no amniocentesis at 16 to 18 weeks (n = 4606 women) Early amniocentesis (before 14 weeks, n = 2183) vs. amniocentesis at 15 weeks or later (n = 2185)	Excess loss rate for amniocentesis vs. no amniocentesis For early amniocentesis vs. late amniocentesis: Rates of fetal loss and fetal talipes following amniocentesis Procedure analysis	Excess miscarriage rate in amniocentesis group: 1% Early vs. late amniocentesis: Total fetal loss, 7.6% vs. 5.9%, p = 0.012 Fetal talipes, 1.3% vs. 0.1%, p = 0.0001 Procedure reported difficult, 10.1% vs. 4.0%, p < 0.0001 Amniotic fluid leakage at < 22 weeks, 3.5% vs. 1.7%, p = 0.0007 Multiple needle insertion, 5.4% vs. 2.1%, p < 0.0001 First attempt success, 96.9% vs. 99.6%, p < 0.0001		SR	1b

10.1 Asymptomatic bacteriuria

10.1.1 What is the incidence of asymptomatic bacteriuria in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Foley et al., 1987	331	6883 women attending antenatal clinics; hospital in Ireland	Treatment vs. non-treatment of women with confirmed bacteriuria	Incidence of asymptomatic bacteriuria	220/6883 (3.2%)	Randomisation by coin-tossing	RCT	1b
Little, 1966	329	Women attending two antenatal clinics in two London hospitals	Antibiotic treatment vs. treatment of 'cases' only when symptomatic	Incidence of asymptomatic bacteriuria	265/5000 (5.3%)	No method of randomisation described	RCT	1b
Etherington and James, 1993	342	898 women attending antenatal clinic in a Bristol (UK) hospital	Test evaluation study	Incidence of asymptomatic bacteriuria	27/898 (3%)		TES	2a

10.1.2 What are the maternal and perinatal outcomes associated with asymptomatic bacteriuria?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Little, 1966	329	Women attending two antenatal clinics in two London hospitals 4735 women without bacteriuria 265 women with bacteriuria diagnosed by culture of midstream urine on at least two occasions Screened at first antenatal visit	Antibiotic treatment vs. treatment of 'cases' only when symptomatic Antibiotic used was sulphamethoxypyridazine for 30 days	Maternal: pyelonephritis, toxaemia Fetal: perinatal mortality, preterm birth, fetal abnormalities	Pyelonephritis: more common in women with bacteriuria when untreated (24.8% vs. 0.4% women without bacteriuria) Toxaemia: no difference between groups Perinatal mortality: no difference between groups Preterm birth: higher in the women with bacteriuria (8.7% vs. 7.6%) Fetal abnormalities: no difference between groups	Method of randomisation was not indicated	RCT	1b
Leblanc and McGanity, 1964	332	1325 women attending antenatal clinics in a US hospital; enrolled at first clinic visit Urine samples collected by catheter and initial bacteriuria defined as colony counts of greater than 10^5 of a single organism/ml	Randomisation of women found to be bacteriuric to no drug and three different drug regimens Antibiotics used were: 1. Sulfamethizole and mandelamine combination 2. Nitrofuradantoin 3. Mandelamine alone	Pyelonephritis in pregnancy Prematurity	Group [incidence of pyelonephritis]: Initially negative culture (no Rx) [21/1028 (1.9%)] Initially negative culture and long-term Rx [1/115 (0.9%)] Initial positive cultures and drug Rx [3/69 (4.3%)] Initial positive culture and no long-term Rx [8/41 (19.5%)] Group [incidence of prematurity]: Initially negative culture (no Rx) [117/1003 (11.6%)] Initially negative culture and long-term Rx [16/138 (11.6%)] Initial positive cultures and drug Rx [7/101 (6.9%)] Initial positive culture and no long-term Rx [6/27 (22.1%)]	Method of randomisation was not indicated Follow-up rate of > 90%	RCT	1b

10.1.2 What are the maternal and perinatal outcomes associated with asymptomatic bacteriuria? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Foley et al., 1987	331	220 women with asymptomatic bacteriuria Hospital in Ireland Bacteriuria defined as more than 10^5 organisms per ml in a single midstream specimen of urine	Treatment vs. non-treatment of women with confirmed bacteriuria; 100 treated, 120 not treated Antibiotics used were either sulphamethizole or nitrofurantoin	Percentage of participants with sterile urine Incidence of symptomatic urinary tract infections Incidence of pyelonephritis	Percentage with sterile urine: Treatment group: 73% Non-treatment group: 48% Incidence of symptomatic UTI: ASB group: 2.3% Sterile urine group: 0.5% Incidence of pyelonephritis: Treatment group: 3/100 (3%) Non-treatment group: 3/120 (2.5%) Peto odds ratio (95% CI): 1.21 (0.24 to 6.13)	Randomisation was by coin-tossing Allocation concealment method not indicated Follow-up rate 81% Method of analysis not indicated	RCT	1b
Kincaid-Smith et al., 1965	333	240 women with bacteriuria 500 women without bacteriuria Bacteriuria defined as 10^5 organisms/ml Confirmed on two counts Australian hospital Women attending before 26 weeks of gestation	Antibiotic treatment vs. no treatment Treatment continued till delivery Antibiotic used was sulphamethoxydiazine, changed to sulphadimidine at week 30 of pregnancy Ampicillin or nitrofurantoin was used if resistance was demonstrated to any of the above	Pyelonephritis Prematurity (excluding twin pregnancies and pregnancies complicated by pre-eclampsia) Pre-eclampsia Fetal loss	Incidence of pyelonephritis: Treated group: 4/133 (3.0%) Placebo group: 41/128 (32.0%) Incidence of prematurity: Treated group: 18/133 (13.5%) Placebo group: 25/129 (19.4%) p value: NS No bacteriuria at first antenatal visit: 13/500 (2.6%); bacteriuria at first antenatal visit: 19/140 (7.9%); p value 0.001 Incidence of pre-eclampsia: No bacteriuria at first antenatal visit: 30/500 (6%) Bacteriuria at first antenatal visit: 26/240 (10.8%) p value: < 0.05 Incidence of fetal loss: No bacteriuria at first antenatal visit: 16/500 (3.2%) Bacteriuria at first antenatal visit: 22/240 (9.2%) p value: < 0.001	Method of randomisation not clear	RCT	1b

10.1.2 What are the maternal and perinatal outcomes associated with asymptomatic bacteriuria? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Mulla, 1960	337	100 patients with bacteriuria US hospital Urine sample obtained by catheter Culture collected at 30th week of pregnancy	50 patients treated with antibiotic 50 patients not given medication until symptoms appeared Antibiotic used was sulphadimethoxine	Pyelonephritis	Incidence of pyelonephritis: Treatment group: 3/50 (6%) Placebo group: 23/50 (46%)	Method of randomisation not indicated No losses to follow up reported Method of analysis not indicated	RCT	1b
Elder et al., 1971	335	289 patients with bacteriuria diagnosed by a colony count of 10^5 organisms or more in 2 of 3 specimens of urine US hospital Samples taken at first antenatal visit Matched controls	Bacteriuric patients: Antibiotic 133 Placebo 148 Non-bacteriuric patients Antibiotic 147 Placebo 132 Antibiotic: 6 weeks of tetracycline	Pyelonephritis	Incidence of pyelonephritis: Bacteriuric (placebo): 27/148 (18%) Bacteriuric (antibiotic): 4/33 (12%) Non-bacteriuric (antibiotic): 3/146 (2.0%) Non-bacteriuric (placebo): 3/132 (2.3%)	Randomisation was by alternating with placebo and would therefore be predictable and with no allocation concealment	CSNR	2a
Gold et al., 1966	336	65 patients with bacteriuria US hospital Bacteriuria was defined as having 10^5 organisms of the same species/ml of urine on 2 consecutive laboratory reports	35 treated with sulfadimethoxine till delivery 30 treated with placebo	Prevalence of ASB Prematurity Pyelonephritis	Prevalence 65/1281 (5.1%) Incidence of prematurity: Bacteriuric (treated) group: 2/65 (3.1%) Bacteriuric (placebo) group: 0/30 Non-bacteriuric group: 168/1216 (13.9%) Incidence of pyelonephritis: Treatment group: 0/35 Placebo group: 4/30 (13.3%)	Patients were randomised according to 'odd' or 'even' number of allocation	QR	2a
Paper looking specifically at asymptomatic group B streptococcal bacteriuria								
Thomsen et al., 1987	334	69 women with GBS in the urine 1 midstream sample between weeks 27 and 31	37 patients treated with penicillin in the antenatal period	Preterm delivery (defined as delivery before the end of week 37 of gestation) Primary rupture of the membranes	Incidence of preterm delivery: Treated group: 2/37 (5.4%) Non-treated group: 12/32 (38%) p value: < 0.002	Prevalence of GBS bacteriuria was 69/4122(1.7%)	RCT	1b

10.1.3 What diagnostic tests are available for the detection of asymptomatic bacteriuria?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Comparing urine culture with reagent strips								
Shelton et al., 2001	343	200 women with attending antenatal clinic 20 identified as having ASB by urine culture US hospital	Urine dipstick-nitrite or LE vs. urine culture Commercially available reagent strips used	Sensitivity Specificity PPV NPV	LE: Sensitivity: 40 (95% CI 19 to 64) Specificity: 63 (95% CI 56 to 70) PPV: 11 (95% CI 5 to 20) NPV: 90 (95% CI 84 to 95) Nitrite: Sensitivity: 15 (95% CI 3 to 38) Specificity: 99 (95% CI 96 to 100) PPV: 60 (95% CI 15 to 95) NPV: 91 (95% CI 86 to 95) LE or Nitrite: Sensitivity: 45 (95% CI 23 to 68) Specificity: 62 (95% CI 55 to 69) PPV: 12 (95% CI 5 to 21) NPV: 91 (95% CI 85 to 95)	Using the dipstick will potentially fail to detect 55% of cases of ASB	TES	2a
McNair et al., 2000	345	528 women at first antenatal visit or admission with possible preterm labour US hospital February 1998 to March 1999	Urine culture compared with reagent strip testing Reagent strip positive if either nitrite or leucocyte esterase positive Commercially available reagent strips used	Sensitivity Specificity PPV NPV	Sensitivity: 47.2% (95% CI 30.8 to 64.3) Specificity: 80.3% (95% CI 76.4 to 83.7) PPV: 14.9% (95% CI 9.2 to 23.1) NPV: 95.9% (95% CI 92.8 to 97.1)		TES	2a
Tincello and Richmond, 1998	348	960 women attending antenatal clinics between June and September 1996	Commercial reagent strip tests for the presence of blood, protein, nitrite and leucocyte esterase vs. microscopy and culture of midstream urine Commercially available reagent strips used	Sensitivity Specificity PPV NPV of reagent strips in diagnosing asymptomatic bacteriuria (defined as 10^5 colony-forming units/ml urine)	Sensitivity: 33.3% (95% CI 26.5 to 40.1) Specificity: 91.1% (95% CI 89.1 to 93.1) PPV: 17.6% (95% CI 9.8 to 25.4) NPV: 96.0 (95% CI 94.6 to 97.4)	Blinding of investigators to the different test results is not indicated	TES	2a

10.1.3 What diagnostic tests are available for the detection of asymptomatic bacteriuria? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Etherington and James, 1993	342	898 women attending antenatal clinic UK hospital	Urine culture compared with Reagent strip testing (testing for individual reagent strips then in combination) Leuc Leucocyte Nit-Nitrite Pr-Protein Commercially available reagent strips used	Sensitivity Specificity PPV NPV Accuracy	RT S SP PPV NPV Leuc 60.0% 86.1% 16.1% 98.0% 82.3% Nit 67.5% 99.7% 90.0% 98.5% 98.2% Pr 57.4% 93.2% 29.7% 97.8% 90.6% Blood 57.4% 93.2% 29.7% 97.8% 92.0% All 4 81.8% 79.0% 10.5% 99.3% 73.6% Leuc 60.0% 86.1% 16.1% 98.0% 82.3% Nit 67.5% 99.7% 90.0% 98.5% 98.2% Either+ 73.0% 85.9% 15.9% 98.9% 83.0%		TES	2a
Bachman et al., 1993	347	1047 patients attending antenatal clinic US hospital	Urine culture compared with reagent strip testing (testing for nitrites) Commercially available reagent strips used	Sensitivity Specificity PPV	Test S SP PPV Nitrite 45.8% 99.7% 78.6% LE 16.7% 97.2% 12.1% Both + 12.5% 100% 100.0% Either+ 50.0% 96.9% 27.3%	Reagent strip testing using nitrites only will potentially fail to detect 50% of cases of ASB	TES	2a
Robertson et al., 1988	346	750 patients attending an Army Medical Centre in the USA	Urine dipstick-leucocyte esterase and nitrite compared with urine culture ASB defined as two clean-catch midstream urine cultures showing at least 10^5 cfu/ml of a single uropathogen	Sensitivity Specificity PPV NPV	Test S SP NPV PPV Nitrite 43.4% 98.9% 95.1% 79.4% LE 77.4% 96.1% 97.9% 64.0% Both + 32.2% 94.2% 99.2% 100.0% Either+ 92.0% 95.0% 99.2% 62.6%	Sensitivity of either test positive higher in this series than Shelton[343] or Bachman[347]	TES	2a
Comparing urine culture with microscopic urinalysis								
McNair et al., 2000	345	528 women at first antenatal visit or admission with possible preterm labour US hospital February 1998 to March 1999	Urine culture compared with microscopic urinalysis Urinalysis positive if there was a count of 10 leucocytes/high-power field	Sensitivity Specificity PPV NPV	Sensitivity: 80.6% (95% CI 63.4 to 91.2) Specificity: 71.5% (95% CI 67.3 to 75.4) PPV: 17.2% (95% CI 12.0 to 23.9) NPV 98.1% (95% CI 95.8 to 99.1)		TES	2a

10.1.3 What diagnostic tests are available for the detection of asymptomatic bacteriuria? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Bachman et al., 1993	347	1047 patients attending antenatal clinic US hospital	Urine culture compared with microscopic urinalysis Significant pyuria was inferred by the presence of more than 10 leucocytes/high-power field	Sensitivity Specificity	Sensitivity 25% Specificity 99%	Urinalysis will potentially fail to detect 75% of cases of ASB	TES	2a
Abyad, 1991	349	Population taken from 3000 registered patients over 7 years	Urine culture compared with microscopic urinalysis Bacteriuria > 1000 organisms/ml	Sensitivity Specificity PPV NPV	WBC/HPF: S (%) / SP (%) / PPV (%) / NPV (%) >8: 72.2 / 98.6 / 76.5 / 98.2 ≥5: 94.4 / 95.3 / 56.7 / 99.6 ≥1: 100.0 / 66.6 / 16.2 / 100.0		TES	2a
Comparing urine culture with centrifugation with Gram stain								
McNair et al., 2000	345	528 women at first antenatal visit or admission with possible preterm labour US hospital February 1998 to March 1999	Urine culture compared with centrifugation with Gram stain	Sensitivity Specificity PPV NPV	Sensitivity: 100% (95% CI 88 to 100) Specificity: 7.7% (95% CI 5.6 to 10.5) PPV: 7.3% (95% CI 5.3 to 10.1) NPV: 100% (95% CI 88.5 to 100)	Centrifugation with Gram staining will potentially detect all cases of ASB but with a poor specificity will incorrectly label over 90% of women as having ASB	TES	2a
Bachman et al., 1993	347	1047 patients attending antenatal clinic US hospital	Urine culture compared with Gram staining	Sensitivity Specificity	Sensitivity 91.7% Specificity 89.2%	Less than 10 % of cases of ASB will potentially be missed and a little over 10% of cases incorrectly labelled as having ASB	TES	2a
Other tests								
Shelton et al., 2001	343	200 women with attending antenatal clinic 20 identified as having ASB by urine culture US hospital	Urinary interleukin-8 vs. urine culture	Sensitivity Specificity PPV NPV	Sensitivity: 70% (95% CI 46 to 88) Specificity: 67 %(95%CI 59 to 74) PPV: 19% (95% CI 11 to 30) NPV: 95% (95% CI 90 to 98)	Urinary interleukin-8 will potentially fail to detect 30% of women with asymptomatic bacteriuria	TES	2a

10.1.3 What diagnostic tests are available for the detection of asymptomatic bacteriuria? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Millar et al., 2000	344	383 women with attending antenatal clinic US hospital Bacteriuria defined as 10^4 colony-forming units of a single pathogen	Rapid enzymatic screening test (detection of catalase activity) vs. urine culture	Sensitivity Specificity PPV NPV	Sensitivity: 70% (95% CI 56.5 to 83.5) Specificity: 45% (95% CI 39.5 to 50.5) PPV: 14% (95% CI 9.0 to 19) NPV: 92% (95% CI 88 to 96)	The rapid enzymatic screening test will potentially fail to detect 30% of women with asymptomatic bacteriuria	TES	2a
Graninger et al., 1992	350	1000 women attending antenatal clinic in a German hospital	Bioluminescence assay	Sensitivity Specificity Predictive accuracy	Sensitivity: 93% Specificity: 78% Predictive accuracy: 99%		TES	2a

10.1.4 Does universal screening for asymptomatic bacteriuria during pregnancy (and treatment of those found to be positive) result in improved outcomes compared with no screening?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Smaill, 2002	351	Cochrane review, updated 2000 14 RCTs Women with asymptomatic bacteriuria found on antenatal screening Various countries	Antibiotic treatment vs. placebo or no treatment	Effect of antibiotic treatment on persistent bacteriuria during pregnancy Risk of preterm delivery or low birth weight babies Development of pyelonephritis	Effect of antibiotic treatment on persistent bacteriuria during pregnancy: Treatment group: 38/293 (13%) Control group: 225/300 (75%) Peto odds ratio: 0.07 (95% CI 0.05 to 0.10) Risk of preterm delivery or low birth weight babies: Treatment group: 101/1044 (9.7%) Control group: 127/879 (14.5%) Peto odds ratio: 0.60 (95% CI 0.45 to 0.80) Development of pyelonephritis: Treatment group: 59/1125 (5.2%) Control group: 203/1064 (19.1%) Peto odds ratio: 0.24 (95% CI 0.19 to 0.32) NNT: 7	Study quality was assessed and found to be generally poor Inadequate allocation concealment except in one study No blinding of observer to treatment allocation Results were however consistent from study to study None of the studies collected adverse outcomes of antibiotic treatment	SR	1a

10.1.5 What antibiotic regimens are cost effective in treating asymptomatic bacteriuria in pregnant women?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Villar et al., 2001	352	Cochrane systematic review, updated 2000 8 RCTs comparing different antibiotic regimens	Single dose compared with 4 to 7 day course 2 RCTs	Preterm delivery Pyelonephritis	Preterm delivery: Treatment group: 5/55 (9.1%) Control group: 5/46 (10.9%) Peto odds ratio: 0.81(95% CI 0.26 to 2.57) Pyelonephritis: Treatment group: 5/54 (9.3%) Control group: 5/46 (2.1%) Peto odds ratio: 3.09 (95% CI 0.54 to 17.55)	Only two RCTs reported preterm birth rates and pyelonephritis	SR	1a

10.1.6 What are the outcomes associated with these antibiotic regimens?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Villar et al., 2001	352	Cochrane systematic review, updated 2000 8 RCTs comparing different antibiotic regimens 2 RCTs	Single dose compared with 4 to 7 day course	Gastrointestinal side effects	Treatment group: 16/231 (6.9%) Control group: 29/209 (14%) Peto odds ratio: 0.53 (95% CI 0.31 to 0.91)	Results largely influenced by a trial that was stopped mainly due to side effects of sulphadimidine	SR	1a

10.2 Asymptomatic bacterial vaginosis (BV)

10.2.1 What is the prevalence of asymptomatic BV infection in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Goldenberg et al., 1996	355	13,747 pregnant women from 7 medical centres in the USA from 1984 to 1989	Women at 23 to 26 weeks gestation were grouped according to ethnic origin (white, black, Hispanic, Asian-Pacific islander). BV was diagnosed by Gram stain score ≥ 7 in conjunction with vaginal pH > 4.5	Frequency of BV	White women (n = 4049): 8.8% Black women (n = 5285): 22.7% ($p < 0.05$ compared with white women) Hispanic women (n = 4240): 15.9% ($p < 0.05$ compared with white women) Asian-Pacific islander (n = 173): 6.1%		CSS	3
Hay et al., 1994	356	718 women attending an antenatal clinic in North West London	Swabs taken at first visit (< 28 weeks) Gram stained	BV diagnosis	At first visit: 87/718 (12%) diagnosed with BV		CSS	3

10.2.2 What are the diagnostic tests for detecting BV infection and how do they compare in terms of sensitivity and specificity?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Amsel et al., 1983	359			Criteria for BV diagnosis	Presence of 3 of the following required: – Thin white-grey homogeneous discharge – Vaginal fluid pH > 4.5 – Fishy odour on adding of alkali – Clue cells present on direct microscopy			
Nugent et al., 1991	360			Criteria for BV diagnosis	Gram-stained vaginal smear to estimate proportions of bacterial morphotypes to give 0 to 10 score: < 4 normal, 4 to 6 intermediate, > 6 BV			
Mastrobattista et al., 2000	610	69 asymptomatic pregnant women from 1996 to 1997 in the USA	Amsel criteria compared (2 of 3 criteria required) with Gram stain by Nugent criteria as the standard for BV diagnosis in women at 16 weeks gestation (mean)	Sensitivity Specificity	Sensitivity: 56% (95% CI 32 to 78) Specificity: 96% (95% CI 90 to 100)	Character of vaginal discharge not used as criteria because it is less easily characterised in pregnant women than in nonpregnant women	TES	3
Krohn et al., 1990	611	593 pregnant women from 1984 to 1986 in the USA	Clinical diagnosis of BV by Amsel's criteria (standard) compared with Gram stain (Nugent's criteria) and gas-liquid chromatography (Spiegel's criteria)	Sensitivity Specificity	Gram-stained: sensitivity 62%; specificity 95% Gas-liquid chromatography: sensitivity 78%; specificity 81%		TES	3

10.2.3 Is BV infection associated with adverse maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Flynn et al., 1999	357	8 case–control studies and 11 cohort studies	Meta-analysis to determine magnitude of risk associated with BV (vs. no BV) and preterm birth	Preterm birth (defined as < 35 weeks in two studies, < 36 weeks in one study, < 37 weeks in all others)	OR (fixed) 1.85, 95% CI 1.62 to 2.11 OR (random) 2.05, 95% CI 1.67 to 2.50 RR (fixed, 10 cohort studies): 1.56, 95% CI 1.37 to 1.78 RR (random, 10 cohort studies): 1.75, 95% CI 1.34 to 2.29		SR	2 & 3
Gratacos et al., 1998	358	635 women screened for BV in Spain at < 35 weeks	Diagnosis based on Gram-stained smears based on Nugent's criteria Positive women retested within 4 to 8 weeks	BV diagnosis at initial visit Preterm birth	125/635 (19.6%) with BV Repeat sample taken in 92/125 (73.6%) of women 47/92 (51.1%) found still positive for BV Preterm birth: BV+ at initial visit 20/125 (16%) vs. BV– at initial visit 26/510 (5%); RR 3.1, 95%CI 1.8 to 5.4 Preterm birth in BV+ persistent women 8/47 (16%) vs. BV disappearance at second visit 7/45 (15.5%)		CSS	3

10.2.4 & 10.2.5 What are the antibiotic regimens of BV infection in pregnancy and how do they compare in terms of effectiveness and does screening for and treating pregnant women found to have BV infection lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
McDonald et al., 2003	362	10 RCTs, 4249 pregnant women screened (or treated) for BV at 10 to 26 weeks of gestation	Antibiotic regimen vs. placebo or no treatment	'Test-of-cure' Preterm delivery PPROM	Failure of test-of-cure (8 RCTs, n = 2835): Peto OR 0.21, 95% CI 0.18 to 0.24 Preterm delivery, < 37 weeks (8 RCTs, n = 4062): Peto OR 0.95, 95% CI 0.82 to 1.10 Preterm delivery, < 34 weeks (5 RCTs, n = 851): Peto OR 1.20, 95% CI 0.69 to 2.07 Preterm delivery, < 32 weeks (3 RCTs, n = 3080): Peto OR 1.08, 95% CI 0.70 to 1.68 PPROM (3 RCTs, n = 3080): Peto OR 0.32, 95% CI 0.59 to 1.17		SR	1a

10.3 *Chlamydia trachomatis*

10.3.1 What is the prevalence of chlamydial infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Preece et al., 1989	365	3309 women screened for chlamydial antigen over a one year period District general hospital in Birmingham, England	Cervical swab, ELISA technique	Prevalence of chlamydia in pregnant women	Overall prevalence = 6% (198 women) Prevalence: women under 20 years, 14.5%; single women, 14.2%; black women, 16.8%		CSS	3
Goh et al., 1982	366	53 pregnant women attending GUM clinic at a hospital in London from June to December 1981	cervical swabs	Prevalence of chlamydia	Chlamydia prevalence was isolated in 20/53 (37.7%)		CSS	3

10.3.2 What re the maternal and perinatal outcomes associated with chlamydial infection in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Preece et al., 1989	370	3309 women screened for chlamydia in a district hospital in England, from September 1985 through August 1986	Screening for chlamydia in pregnant mothers on presentation in labour with ELISA Infants of mothers with chlamydia seen at 3, 6, 12, and 26 weeks	Neonatal *C. trachomatis* infection Neonatal conjunctivitis Respiratory infection	198 mothers positive for chlamydial antigen identified 174 of the 198 infants followed-up Culture positive 25% (n = 43/174) 11% (n = 20/174) infants had neonatal conjunctivitis 3% (n = 6/174) infants developed lower respiratory tract infections	Only babies born to women with chlamydia followed up	CSS	3
Schachter et al., 1986	371	131 neonates of 262 pregnant women who tested positive for chlamydia in obstetric clinic in San Francisco hospital, from 1977 to 1983	Screening of all pregnant women who presented for their first antenatal care visit and prospective follow-up of their infants plus 46 control infants whose mothers had negative chlamydia cultures before delivery	Neonatal deaths Culture positive for chlamydia in newborn Conjunctivitis in the newborn Pneumonia in the neonate	Neonatal death 4% (n = 5/131) 36% (n = 47/131) cultured positive for chlamydia 17.6% (n = 23/131) neonatal conjunctivitis 16% (n = 21/131) had pneumonia None of the controls developed any clinical disease due to *C. trachomatis* nor were any cultures positive by 9 months of age	Only 50% of infants born to infected mothers were followed up All women who were delivered by caesarean section or who refused or had moved were excluded	COM	3

10.3.3 Does screening women for chlamydial infection in pregnancy lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Brocklehurst and Rooney, 2002	369	11 RCTs included	Antibiotic therapy or alternative antibiotic therapy vs. placebo or no treatment for chlamydia in pregnant women	Eradication of maternal infection Preterm delivery Side effects, endometritis and neonatal death: no significant difference	Number of women with positive cultures reduced by 90% when treated with antibiotics compared with placebo; OR 0.06 (95% CI 0.03 to 0.12) Preterm delivery OR 0.89 (0.51 to 1.56) Side effects, endometritis and neonatal death: no significant difference	Being updated	SR	1a
Ryan et al., 1990	368	11,544 women cultured at their first prenatal care visit Tennessee, USA, from September 1982 through August 1985	Cervical culture at first antenatal care visit and prospective follow up Women who presented from September 1982 through December 1983 were not treated (n = 1110) Women who presented from Jan 1984 through Aug 1985 were treated with erythromycin (n = 1323)	Prevalence Low birthweight Infant death	21.1% (n = 2433/11544) were positive for chlamydia Increase in low birthweight in untreated group vs. treated group (19.6% vs. 11.0%, $p < 0.0001$, RR 1.78, 95% CI 1.48 to 2.18) No difference between treated and culture negative group (RR 0.94, 95% CI 0.79 to 1.10) Decrease in survival in untreated group vs. treated group (97.6% vs. 99.4%, $p < 0.001$, RR 0.98, 95% CI 0.97 to 0.99) Treated also more likely to survive than culture-negative group (99.4% vs. 98.5%, $p < 0.01$, RR 1.01, 95% CI 1.0 to 1.01)	Historical cohort different calendar periods could explain observed differences Infant death defined as those who did not leave the hospital alive	CH	2b

10.3.4 What methods should be used for screening for *Chlamydia trachomatis* in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Fitzgerald et al., 1998	372	Adults	Culture Enzyme immunoassay Serology	Sensitivities and specificities of various tests	Chlamydia culture Sensitivity 75% to 85% at best, and may be low as 55%, only appropriate for invasive samples, and labour intensive Enzyme immunoassay Sensitivity 75% to 80% compared with culture Suitable for large number of samples, requires invasive samples and high specificity only if positive results are confirmed Serology of no value in diagnosis of acute chlamydial infection	Work carried out in collaboration with Royal College of Physicians Research Unit and Members of Central Audit Group in Genitourinary Medicine	GL	4
Stary, 2001	364	Adults	Culture Direct fluorescent antibody assays Enzyme immunoassays RNA-DNA hybridisation Nucleic acid amplification	Sensitivities and specificities of various tests	Cell culture sensitivity range 40% to 85%, only appropriate for invasive samples Direct fluorescent antibody assays sensitivity range 50% to 90%, suitable for invasive and noninvasive samples, but time-consuming and therefore unsuitable for large numbers Enzyme immunoassays sensitivity range 20% to 85%, suitable for large number of samples, requires invasive samples and high specificity only if positive results are confirmed RNA-DNA hybridisation sensitivity range 70% to 85%, rapid and reliable, suitable for large numbers and requires invasive samples Nucleic acid amplification sensitivity range 70% to 95%, also has high specificity (97% to 99%), suitable for large numbers of samples, invasive and noninvasive samples may be used, but expensive and inhibitors may be a problem in urine samples	Single author, no guideline methodology given	GL	4

10.4 Cytomegalovirus

10.4.1 What is the prevalence of cytomegalovirus (CMV) infection in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Ryan et al., 1995	374	Pregnant women in England and Wales in 1992 and 1993 (1,363,123 live births)	Reports of CMV to laboratories in England and Wales	Number of cases in pregnant women Outcomes of pregnancy	47 reports of CMV infection in pregnancy Intrauterine death or stillbirth in 22 cases	Reports in pregnancy could not be linked to outcomes in live born infants Most infections with CMV in pregnancy are not recognised	SV	3

10.4.2 What is the prevalence of congenital cytomegalovirus (CMV) infection?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Preece et al., 1986	375	23,247 pregnant women 3 London hospitals Dates not given	Infants diagnosed if CMV isolated from throat swab in first week of life	Estimated prevalence of congenital CMV	69/23,247 Prevalence 2.6/1000	Estimated denominator as not all women screened	CSS	3
Peckham et al., 1983	376	14,200 babies born at three London hospitals from Sep 1979 through Aug 1982	Infants diagnosed if CMV isolated in first week of life from throat swab	Congenital infection with CMV	42 live births, rate of 3/1000 None of the 42 mothers had any signs or symptoms of acute CMV infection 26 had been positive at their first antenatal visit	Discrepancy between 14,789 mothers and 14,200 infants, i.e. approx 589 infants unaccounted for	CS	3

10.4.3 Does screening pregnant women for cytomegalovirus (CMV) infection lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Bolyard et al., 1998	377				Repeated testing is necessary to identify CMV because it can be shed Seroposivity does not offer complete protection against maternal reinfection and subsequent fetal infection No currently available vaccines or prophylactic therapy		GL	4
Stagno and Whitley, 1985	378				Maternal immunity does not prevent virus reactivation nor transmission to fetus No effective drug therapy for CMV or its transmission exists No ways to determine whether intrauterine transmission has occurred No way to determine whether infected infant will have serious sequelae		RV	4

10.5 Hepatitis B virus

10.5.1 What is the prevalence of hepatitis B viral infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Boxall et al., 1994	379	3522 anonymous serum samples collected from women attending an antenatal clinic in the West Midlands from February 1990 to January 1991	Sera tested for HBsAg using RIA or ELISA and positives confirmed using reverse passive haemagglutination	HBsAg prevalence among women of various ethnic origins	Overall prevalence 0.56% (20/3522) Breakdown: 13/20 Asian 4/20 African-Caribbean 3/20 SE Asian Prevalence in women from immigrant groups 1.04%		CSS	3
Brook et al., 1989	380	6226 women attending antenatal clinic at the Royal Free Hospital, London, from 1983/84 to 1988/89	Screening using HBsAg	Number of mothers HBsAg positive at first antenatal care visit	33/6226 (0.5%) HBsAg positive at first visit		CS	3
Chrystie et al., 1992	381	Stored serum from antenatal clinics 1990 (n = 3760) and 1988 (n = 3975) Sera of women originally collected for rubella in West Lambeth Health authority in London	Serology	Prevalence among women screened	In 1988: 38/3760 (1%) women HBsAg positive In 1990: 35/3975 (0.9%) women HBsAg positive		CSS	3
Derso et al., 1978	382	Approximately 240,000 pregnant women from antenatal clinics in West Midlands, England, from May 1974 to May 1977	Serum screening using HBsAg	Prevalence of HBsAg carriage in pregnant mothers	297 pregnant women were HBsAg positive Overall prevalence of approx 1/850 (0.1%)		CSS	3

10.5.2 What is the prevalence of congenital hepatitis B virus in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Ramsay et al., 1998	385	England and Wales from 1985 to 1996	Surveillance of laboratory reported cases to PHLS communicable disease surveillance centres	Infection in children (under 15 years) Number of cases due to mother-to-child transmission Estimated annual number of perinatal transmissions which lead to chronic carriage	Total of 173 cases reported 37/173 (21%) due to mother-to-child transmission 93/116 cases of perinatal transmission leading to carriage per year	Assumption that 80% of perinatal infections lead to chronic carriage	CSS	3
Derso et al., 1978	382	Approximately 240,000 pregnant women from antenatal clinics in West Midlands, England, from May 1974 to May 1977	Serum screening using HBsAg	Infants HBsAg positive beyond 3 months of age	Antigen detected in cord blood of 101/219 (46%) of 269 babies delivered 17/122 (14%) babies followed up beyond 3 months of age had persistently high titres of HBsAg; 64% were Chinese, 30% African-Caribbean and 8% Asian (0 European)	The paper states that 297 carrier mothers were discovered but in the table of ethnic distribution of mothers, only 100 mothers are accounted for	COM	3

10.5.3 What are the consequences for the baby of congenital hepatitis B virus?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Beasley and Hwang, 1984	384	22,707 men presenting for routine examination from 1976 to 1978 in Taiwan	Prospective follow-up through 1983	HBsAg carrier state Hepatocellular carcinoma Mortality	3,454 HBsAg positive 113/3,454 HCC cases among HBsAg carriers 3/19,253 cases among non-carriers 103/202 deaths due to cirrhosis or hepatocellular carcinoma in HBsAg carrier group 9/394 deaths due to cirrhosis or hepatocellular carcinoma in non-carrier group RR 22.3 (95% CI 11.5 to 43.2)		CH	2b

10.5.4 What are the diagnostic tests available for detection of hepatitis B viral infection and how do they compare in terms of specificity, sensitivity, and cost effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Summers et al., 1987	394	All women attending the antenatal clinic at a US hospital in New Orleans from November 1983 through October 1985	Serum collected at initial prenatal visit Patients interviewed for hepatitis B virus risk factors	Number of women identified with risk factors	136/15399 women found to be HBsAg positive (prevalence 0.88%) No patient symptomatic 54/108 (50%) pregnant women demonstrated risk factors		CSS	3
Chaita et al., 1995	395	88 Thai women attending an antenatal clinic with known HBsAg status (44 HBsAg positive)	Saliva and serum samples were collected and then analysed in Liverpool, England, using ELISA to detect HBsAg	Sensitivity and specificity of screening for HBsAg in saliva compared with serum	Sensitivity 92% (95% CI 84.5 to 99.5) Specificity 86.8% (95% CI 76.0 to 97.6)		CSS	3

10.5.5 What are the interventions to reduce mother-to-child transmission of hepatitis B virus?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Sehgal et al., 1992	386	109 HBsAg positive mothers in India from 1987 through 1989	Group 1: HBV vaccine within 24 hours of birth and 2nd and 3rd dose at 4 and 8 weeks, respectively (n = 24) Group 2: HBV vaccine and HBIG within 24 hours of birth. Further HBV vaccine doses at 4 and 8 weeks respectively (n = 27)	HBsAg carrier state in infants at 6 months	HBV carrier rate: Group 1: 1/21* (4.8%) Group 2: 3/24* (12.5%) *3 cases excluded from each group RR 2.6 (95%CI 0.29, 23.4)	58 mothers refused vaccination for their babies	RCT	1b
Xu et al., 1985	392	208 pregnant mothers with HBsAg from antenatal clinics in Shanghai from 1982 to 1984	Group 1: BIVS vaccine for hepatitis B virus within 24 hours of birth and at 1 and 6 months of age (n = 60) Group 2: NIAID vaccine for hepatitis B viruswithin 24 hours of birth and at 1 and 6 months of age (n = 60) Group 3: BIVS vaccine for hepatitis B virus plus HBIG within 24 hours of birth and further vaccine only at 1 and 6 months of age (n = 60) Group 4: placebo within 24 hours of birth and at 1 and 6 months of age (n = 28)	HBsAg carrier state in infants at 6 months (n = 5, 5, 4, and 1 lost to follow-up, for each group respectively)	HBV carrier rate: Group 1: 12/56 (21.4%) Group 2: 3/55 (5.4%) Group 3: 2/27 (7.4%) Group 4: 24/55 (43.6%) Group 4 vs. group 1: RR 0.49 (95% CI 0.27 to 0.88) Group 4 vs. group 2: RR 0.13 (95% CI 0.40 to 0.39) Group 4 vs. group 3: RR 0.17 (95% CI 0.04 to 0.67)	BIVS = Beijing Institute of Vaccine and Serum vaccine NIAID = National nstitute of Allergy and Infectious disease vaccine	RCT	1b
Nair et al., 1984	391	20 pregnant women attending antenatal clinic found positive for HBsAg and anti-HBe in USA from 1978 through 1982	HBIG (n = 12) or placebo (n = 8) within 24 hours after birth and at five week intervals for a total of 6 injections for infants	HBsAg carrier state in infants	1/20 infants became HBsAg and HBeAg positive from the HBIG group		RCT	1b

10.5.5 What are the interventions to reduce mother-to-child-transmission of hepatitis B virus? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Wong et al., 1984	387	315 pregnant women found positive for HBeAg attending antenatal clinic in Hong Kong from June 1981 to September 1983 from which 262 gave consent	Group 1: HBV vaccine at birth and at 1, 2 and 6 months after birth, plus 7 monthly HBIg injections (n = 36) Group 2: same as above, but only one HBIG injection at birth (n = 35) Group 3: vaccine only at 0, 1, 2, and 6 months (n = 35) Group 4: placebos for both vaccine and HBIg (n = 34)	HBsAg carrier state in infants	HBV carrier rate: Group 1: 2.9% Group 2: 6.8% Group 3: 21.0% Group 4: 73.2% (Rates as calculated by life-table attack-rate analysis)	By September 1983, 216 babies had been born to 262 mothers Infants excluded because of low birthweight, low Apgar score, congenital abnormality, withdrawn from study, stillbirth, or other criteria These results are for 140 babies who were at least 6 months of age by September 1983	RCT	1b
Zhu et al., 1997	388	204 HBsAg positive pregnant women from two hospital obstetric departments in Shanghai, China from February 1991 to February 1994 207 babies were born to the 204 mothers	HBIG given 3, 2 and 1 month before delivery (n = 105) vs. no treatment (n = 102)	Seroconversion to HBeAg in mothers at 3 months before delivery Prevention of intrauterine transmission of HBV	Treatment group: 37/103 (36%) Control group: 32/101 (32%) 6/105 HBsAg positive babies in treatment group (5.7%) vs. 15/102 HBsAg positive babies born in control group (14.7%) $p < 0.05$ (RR 0.39, 95% CI 0.16 to 0.95)	Method of randomisation not indicated No losses to follow up	RCT	1b
Lo et al., 1985	389	361 HBeAg positive mothers in 3rd trimester at obstetric clinic in Taipei, Taiwan from September 1982 to October 1983	Group 1: HBV vaccine alone (38 infants) Group 2: HBV vaccine and HBIG at birth (36 infants) Group 3: HBV vaccine and HBIG at birth and 1 month of age (38 infants)	Hepatitis B virus in infants at 6 months	HBV carrier rate: Group 1: 9/38 (23.7%) Group 2: 4/36 (11.1%) Group 3: 2/38 (5.3%) Group 1 vs. group 2 RR: 0.47 (95% CI 0.16 to 1.39) Group 1 vs. group 3 RR: 0.22 (95% CI 0.05 to 0.96)	Method of randomisation not specified 112 infants received vaccine and were followed-up for 6 months or longer	RCT	1b

10.5.5 What are the interventions to reduce mother-to-child-transmission of hepatitis B virus? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Beasley et al., 1983	390	1026 HbeAg positive women from 2 large hospitals in Taipei, Taiwan, attending antenatal clinics from November 1981 through December 1982	Group 1: HBIG at birth and at 3 months at which time vaccination also initiated (n = 51) Group 2: HBIG at birth and vaccine initiated at 4 to 7 days old (n = 50) Group 3: HBIG at births and vaccination initiated at 1 month (n = 58) All initial vaccination followed by booster 1 month and 6 months later 159 infants and 84 controls for analysis at least 9 months of age	Hepatitis B virus in infants at 9 months	HBV carrier rate: Group 1: 1/51 (2.0%) Group 2: 3/50 (6.0%) Group 3: 5/58 (8.6%) Group 3 vs. group 2 RR: 0.70 (95% CI 0.18 to 2.77) Group 3 vs. group 1 RR: 0.23 (95% CI 0.03 to 1.88)	Method of randomisation not indicated 159 infants whose parents gave consent, were not withdrawn from the study, who received the full treatment of the group to which they were assigned and were at least 9 months of age at time of analysis	RCT	1b
Beasley et al., 1977	383	62 asymptomatic HBsAg positive women at an antenatal clinic in Taiwan No date given	Mothers' sera tested either during pregnancy or 1 to 20 months postpartum 20 women eAg positive	Transmission rate	17/20 (85%) of babies from eAg positive mothers became HBsAg positive 13/42 (31%) of infants from eAg negative mothers became HBsAg positive RR 2.8 (95% CI 1.69 to 4.47)		CSS	3

10.7 HIV

10.7.1 What is the prevalence of HIV infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Unlinked Anonymous Surveys Steering Group, 2002	407	426,474 pregnant women in England, plus 52,707 in Scotland, tested in 2001	Survey used leftover blood from samples taken for routine clinical tests	Number HIV-1 infected HIV prevalence	London: 363/103,840 Elsewhere in UK: 143/322,634 London prevalence: 0.35% (0.05 to 0.84) Elsewhere in UK prevalence: 0.04 (0.0 to 0.43)	Results represent 72% of all live births in UK for 2001	CSS	3
Unlinked Anonymous Surveys Steering Group, 1999	613	506,462 pregnant women in Scotland and England, tested in 1998	Survey used leftover blood from samples taken for routine clinical tests	Number HIV-1 infected Prevalence Mother-to-child transmission	HIV-1 infected: London: 224/101,602 Scotland: 13/57,298 Elsewhere in UK: 53/347,562 Prevalence: London: 0.22% (0.0 to 0.62) Scotland: 0.023% (0.0 to 0.079) Elsewhere in the UK: 0.015% (0.0 to 0.12) Infected babies and births in HIV infected women: London: 37/232, 15.9% (95% CI 12.1% to 21.6%) Scotland: 2/13, 15.4% (95% CI 7.7% to 23.1%) Rest of UK: 19/86, 22.1% (95% CI 17.4% to 26.7%)		CSS	3
Unlinked Anonymous Surveys Steering Group, 2001	408	Pregnant women in Scotland and England, 484,563 women tested in 2000	Survey used leftover blood from samples taken for routine clinical tests	Number HIV-1 infected Prevalence (range)	HIV-1 infected: London: 298/103,852 Scotland: 25/53,347 Elsewhere in UK: 89/327,364 London prevalence 0.29% (0.0 to 0.73) Elsewhere in the UK prevalence 0.027% (0.0 to 0.3)		CSS	3

10.7.2 What is the prevalence of congenitally acquired infection in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Unlinked Anonymous Surveys Steering Group, 2002	407	426,474 pregnant women in England, plus 52,707 in Scotland, tested in 2001	Survey used leftover blood from samples taken for routine clinical tests	Mother-to-child transmission of HIV-1	Infected babies and births in HIV infected women in the UK: 49/561	Estimates are based on the observed proportion of maternal infections diagnosed before delivery and assume that 2% of infants will acquire HIV even if maternal infection is diagnosed before delivery	CSS	3
Unlinked Anonymous Surveys Steering Group, 2001	408	484,563 pregnant women in Scotland and England, tested in 2000	Survey used leftover blood from samples taken for routine clinical tests	Mother-to-child transmission of HIV-1	Infected babies and births in HIV infected women: 45/452	Estimates are based on observed proportions of maternal infections diagnosed before delivery and assumed that about 2% of infants will acquire HIV even if maternal infection is diagnosed prior to delivery	CSS	3
CDR Weekly, 26 April 2001	412	Paediatric surveillance data	None	Confirmed cases of HIV infection in children by the end of January 2001 in the UK (excluding Scotland)	1036 infected children, 68% probably acquired through mother-to-child transmission 1885 children born to HIV infected mothers reported by end of January 2001, 712 known to be infected, 716 known to be uninfected, 457 unresolved or unreported By the end of 1999, 697 known to be infected, 259 indeterminate, and 659 not infected out of a total of 1615 children born to HIV infected mothers In 2000, 270 babies were born to HIV infected mothers resulting in 15 HIV-positive babies, 57 not infected and 198 as yet undetermined		LS	3
Conner et al., 1994	409	RCT with 477 HIV infected pregnant women enrolled from April 1991 to December 1993 (409 births leading to 415 live-born infants)	Zidovudine vs. placebo	Efficacy of zidovudine in reducing risk of vertical transmission measured by HIV infection status of child	67.5% (95%CI 40.7 to 82.1) relative reduction in risk of HIV transmission ($z = 4.03$, $p = 0.00006$) Proportion infected at 18 months in zidovudine group 8.3% (95% CI 3.9 to 12.8) Proportion infected at 18 months in placebo group 25.5% (95% CI 18.4 to 32.5)		RCT	1b

10.7.3 What are the diagnostic tests available for detection of HIV infection and how do they compare in terms of specificity, sensitivity and cost-effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Balano, 1998	614		Rapid HIV screening during labour	Performance of rapid HIV 1 antibody testing	Sensitivity 99.9% Specificity 99.6% Positive predictive value exceeds 50% only when prevalence of HIV 1 exceeds 0.5%	Letter This paper only reported the performance of this test, i.e. did not investigate the test's performance itself		
PHLS AIDS Diagnosis Working Group, 1992	415		HIV testing algorithm	Initial assay (EIA or rapid tests). If reaction is positive, further testing with different assays (two). If both confirmatory tests are nonreactive, issue negative report. If confirmatory tests are reactive, one more test with a new specimen should be obtained to ensure no procedural errors have occurred	Available EIAs or rapid tests have similar and adequate sensitivity to be used singly to generate a negative report (unless HIV-2 assay is also needed) HIV culture and tests for p24 antigen are not of much value in diagnostic testing, as they may be insensitive, non-specific and expensive tests	In a low prevalence population such as the UK, high specificity and reasonable sensitivity are important	Report from PHLS AIDS Diagnosis Working Group	IV
Postma et al., 1999	615		Performance of ELISA as initial test for HIV as specified for use in cost effectiveness model		Sensitivity 100% Specificity 99.9%	Unclear, but these values seem to be as reported from the manufacturer		
Van Doornum, 1998	414	Serum specimens from 31,232 pregnant women in Amsterdam between 1988 and 1995	Two ELISA approach (with membrane spot assay to discriminate between infection with HIV-1 or HIV-2) vs. Western blot analysis	Evaluation of confirmatory strategy of two-ELISA approach and resolution of indeterminate results with NASBA and SIA	42 sera that were available for analysis which gave positive or borderline results by ELISA and indeterminate or negative results by Western blot All initially reactive samples (tested by EIA) were retested by a second ELISA (based on a different principle) and the initial screening assay Confirmation of reactivity with a second EIA, enhanced with a membrane spot assay to discriminate between HIV-1 and HIV-2, was necessary and useful for endorsing a negative result and confirming possible cases of HIV 2 infection The importance of requesting a new specimen upon reactive confirmation results to ensure against procedural errors was also demonstrated.		EV	3

10.7.3 What are the diagnostic tests available for detection of HIV infection and how do they compare in terms of specificity, sensitivity and cost-effectiveness? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Samson and King, 1998	413		Literature review to compile evidence-based guidelines on HIV screening in pregnancy	Recommendations on HIV testing in pregnant women	Third generation EIA kits have sensitivity 99.4%-100% and specificity 99–100% Combined EIA and Western blot protocol has sensitivity 99% and specificity 99.99%	These are guidelines for Canada		

10.7.4 What are the interventions to decrease congenitally acquired HIV?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Brocklehurst and Volmink, 2002	416	8 RCTs, various countries, HIV infected, pregnant women Cochrane review Most recent update 2002	Zidovudine monotherapy vs. placebo Zidovudine vs. zidovudine Short–short vs. long–long Long–short vs. long–long Short–long vs. long–long Nevirapine vs. zidovudine Nevirapine in mothers already taking antiretroviral therapy vs. standard ART Combination therapy (zidovudine and lamivudine) vs. placebo Antenatal and intrapartum Intrapartum and postpartum	HIV infection status of child	Zidovudine vs. placebo, 4RCTs (n = 1379): OR 0.44 (95% CI 0.33 to 0.59) Short–short vs. long–long, 1 RCT (n = 453): OR 2.46 (95% CI 1.15 to 5.27) Long-short vs. long-long, 1RCT (n = 746): OR 0.66 (95% CI 0.35, 1.24) Short–long vs. long–long, 1 RCT (n = 743): OR 1.40 (95% CI 0.82 to 2.38) Nevirapine vs. zidovudine, 1 RCT (n = 496): OR 0.50 (95% CI 0.32 to 0.79) Nevirapine + ART vs. placebo + ART, 1 RCT (n = 1174): OR 1.10 (95% CI 0.42 to 2.87) Zidovudine + lamivudine vs. placebo, 1 RCT (n = 1792): Antenatal and intrapartum: RR 0.52 (95% CI 0.35 to 0.76) Intrapartum and postpartum: RR 0.66 (95% CI 0.46 to 0.94)	In two studies, there was uncertainty about whether randomisation was adequately concealed. Another study was not blind once the randomly allocated packs were opened. The remaining 5 studies were double blind and randomised	SR	1a
Shey Wiysonge et al., 2002	616	1 RCT; 898 HIV-infected pregnant women, conducted in Kenya Cochrane review Most recent update 2002	Vaginal disinfection with disinfectant (chlorhexidine) during labour vs. no disinfection	HIV infection status of child	OR 0.93 (95% CI 0.63 to 1.38)	Generation of allocation sequence and concealment of allocation inadequate	SR	1a

10.7.4 What are the interventions to decrease congenitally acquired HIV? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
European Mode of Delivery Collaboration, 1999	417	436 women between 34 and 38 weeks pregnancy with confirmed HIV-1 diagnosis without indication (or contraindication) for caesarean section delivery in various European countries, including UK	Caesarean section delivery vs. vaginal delivery	HIV infection status of child by 18 months (n = 370)	By intention to treat: adjusted OR 0.2 (95% CI 0.1 to 0.6) By actual mode of delivery: adjusted OR 0.4 (95% CI 0.2 to 0.9)	No woman breastfed. Randomisation through computer-generated lists and analysis by intention to treat and by actual mode of delivery	RCT	1b
Mandelbrot et al., 1998	410	2,834 singleton children born to mothers with HIV infection in 85 perinatal centres in France from 1985 to 1996	Vaginal delivery vs. caesarean section plus zidovudine compared with vaginal delivery vs. caesarean section without zidovudine	HIV infection status of child	Univariate analysis: No zidovudine: RR 1.0 (95% CI 0.6 to 1.6) With zidovudine: RR 0.1 (95% CI 0.0 to 0.8) Multivariate analysis: No zidovudine: OR 1.2 (95% CI 0.6 to 2.3) With zidovudine: OR 0.2 (95% CI 0.0 to 0.9)		Cohort	2b
Kind et al., 1998	617	414 children of mothers in Switzerland known to be HIV infected from 1986 to 1 July 1996	Elective caesarean section plus zidovudine vs. caesarean section and no zidovudine AND Other modes of delivery plus zidovudine vs. other modes of delivery and no zidovudine	HIV infection status of children	Caesarean section + zidovudine: 0/31 infected (0%, 95% CI 0 to 11.0) Caesarean section + no zidovudine: 7/86 infected (8%, 95% CI 3 to 16) Other delivery mode + zidovudine: 4/24 infected (17%, 95% CI 5 to 37) Other delivery mode + no zidovudine: 55/271 infected (20%, 95% CI 16 to 24) Risk difference for zidovudine: –8 (95% CI –14 to -2) for caesarean section –3 (95% CI –19 to 12) for other delivery modes Risk difference for caesarean section: –17 (95% CI –32 to -2) for zidovudine –12 (95% CI –20 to –5) for no zidovudine		NCC	3

10.7.4 What are the interventions to decrease congenitally acquired HIV? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Shey Wiysonge, et al., 2002	618	2 RCTs, 1813 known HIV infected women who are pregnant Cochrane review Most recent update 2002	Vitamin A supplementation during pregnancy vs. placebo or micronutrient supplementation	HIV infection status of child	OR 1.09 (95% CI 0.81 to 1.45)	Both studies are described as randomised and double blind, although one study did not report the method of allocation concealment. In one study, 7.8% of women were excluded from the analysis and 5% were lost to follow-up in the other	SR	1a
Duong et al., 1999	411	Pregnant women with HIV infection reported through obstetric surveillance in the British Isles	Surveillance of mother-to-child transmission of HIV infection	Mother-to-child transmission rate by infection status of child among women who did not breastfeed Reduction of risk of mother-to-child transmission with no antiretroviral treatment and vaginal or emergency caesarean section vs. elective caesarean section and antiretroviral therapy	Mother-to-child transmission rate by infection status of child among women who did not breastfeed: 19.6% (8.0% to 32%) in 1993; 2.2% (0% to 7.8%) in 1998 Reduction of risk of mother-to-child transmission with no antiretroviral treatment and vaginal or emergency caesarean section vs. elective caesarean section and antiretroviral therapy: 31.6% (13.6% to 52.2%) to 4.2% (0.8% to 8.5%)			

Short–short (treatment with zidovudine) = 35 weeks in pregnancy for mother and until 3 days old for baby

Long–long (treatment with zidovudine) = from 28 weeks in pregnancy for mother and for the baby until 6 weeks old

Long–short (treatment with zidovudine) = from 28 weeks pregnancy for the mother and for the baby until it is 3 days old

Short–long (treatment with zidovudine) = from 35 weeks in pregnancy for the mother and for the baby until 6 weeks old

10.7.5 Does screening for HIV in pregnancy and instituting appropriate interventions lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Brocklehurst and Volmink, 2002	416	8 RCTs total, various countries, HIV infected, pregnant women Cochrane review Most recent update 2002	Zidovudine vs. placebo Zidovudine vs. zidovudine Short–short vs. long–long Long–short vs. long–long Short–long vs. long–long Nevirapine vs. zidovudine	Infant death within 1 year of birth (n = 1487, 4 RCTs)*	OR 0.57 (95% CI 0.38 to 0.85)	* Significant heterogeneity between RCTs ** Number of maternal deaths small and wide CIs *** This study was double-blind with central randomisation and a non-breastfeeding population. 2% lost to follow-up	SR	1a
				Infant death within 28 days of birth (n = 1210, 3 RCTs)	OR 1.87 (95% CI 0.68 to 5.10)			
				Infant death after 1 year of birth (n = 395, 1 RCT)	OR 1.02 (95% CI 0.14 to 7.28)			
				Incidence of stillbirth (n = 1504, 4 RCTs)	OR 0.83 (95% CI 0.36 to 1.92)			
				Incidence of preterm delivery (n = 757, 2 RCTs)	OR 0.86 (95% CI 0.57 to 1.29)			
				Incidence of low birthweight (n = 1192, 3 RCTs)	OR 0.74 (95% CI 0.53 to 1.04)			
				Any side effects in child (n = 1480, 4 RCTs)	OR 1.27 (95% CI 0.87 to 1.87)			
				Sufficient side effects in child to stop or change treatment (n = 415, 1 RCT)	OR 1.02 (95% CI 0.43 to 2.40)			
				Maternal death (n = 1391, 4 RCTs)**	OR 0.30 (95% CI 0.13 to 0.68			
				Any side effect in mother (n = 1085, 3 RCTs)	OR 1.01 (95% CI 0.66 to 1.53)			
				Sufficient side effects in mother to change or stop treatment (n = 1506, 4 RCTs)	OR 1.42 (95% CI 0.64 to 3.18)			
				Infant death within 1 year of birth (n = 434, 1 RCT)***	OR 1.93 (95% CI 0.35 to 10.63)			
				Infant death within 28 days of birth (n = 454, 1 RCT)	OR 1.94 (95% CI 0.17 to 21.54)			
				Incidence of stillbirth (n = 454, 1RCT)	OR 1.92 (95% CI 0.17 to 21.35)			
				Incidence of preterm delivery (n = 454, 1 RCT)	OR 0.47 (95% CI 0.16 to 1.39)			
				Incidence of low birthweight (n = 455, 1 RCT)	OR 0.84 (95% CI 0.47 to 1.49)			
				Any side effects in child (n = 451, 1 RCT)	OR 0.69 (95% CI 0.21 to 2.19)			
				Maternal death (n = 427, 1RCT)	OR 9.13 (95% CI 0.49 to 170.61)			

10.7.5 Does screening for HIV in pregnancy and instituting appropriate interventions lead to improved maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
				Any side effect in mother (n = 466, 1 RCT)	OR 0.42 (95% CI 0.04 to 5.39)			
				Infant death within 1 year of birth (n = 718, 1 RCT)	OR 1.19 (95% CI 0.41 to 3.44)			
				Infant death within 28 days of birth (n = 748, 1 RCT)	OR 2.38 (95% CI 0.43 to 13.06)			
				Incidence of stillbirth (n = 754, 1 RCT)	OR 0.70 (95% CI 0.17 to 2.97)			
				Incidence of preterm delivery (n = 754, 1 RCT)	OR 0.42 (95% CI 0.13 to 1.34)			
				Incidence of low birthweight (n = 751, 1 RCT)	OR 0.87 (95% CI 0.56 to 1.35)			
				Any side effects in child (n = 740, 1 RCT)	OR 0.29 (95% CI 0.08 to 1.03)			
				Maternal death (n = 725, 1 RCT)	OR 2.38 (95% CI 0.21 to 26.32)			
				Any side effect in mother (n = 769, 1 RCT)	OR 1.20 (95% CI 0.34 to 4.18)			
				Infant death within 1 year of birth (n = 711, 1 RCT)	OR 0.87 (95% CI 0.27 to 2.75)			
				Infant death within 28 days of birth (n = 744, 1 RCT)	OR 0.60 (95% CI 0.05 to 6.60)			
				Incidence of stillbirth (n = 748, 1 RCT)	OR 0.48 (95% CI 0.09 to 2.47)			
				Incidence of preterm delivery (n = 748, 1 RCT)	OR 0.21 (95% CI 0.05 to 0.97)			
				Incidence of low birthweight (n = 745, 1 RCT)	OR 0.54 (95% CI 0.33 to 0.89)			
				Any side effects in child (n = 739, 1 RCT)	OR 0.69 (95% CI 0.27 to 1.76)			
				Maternal death (n = 717, 1 RCT)	OR 0.40 (95% CI 0.02 to 9.93)			
				Any side effect in mother (n = 764, 1 RCT)	OR 0.73 (95% CI 0.17 to 3.06)			
				Infant death within 1 year of birth (n = 616, 1 RCT)	OR 0.71 (95% CI 0.36 to 1.37)			
				Incidence of stillbirth (n = 631, 1 RCT)	OR 0.49 (95% CI 0.04 to 5.40)			
				Incidence of low birthweight (n = 601, 1 RCT)	OR 1.50 (95% CI 0.75 to 3.01)			
				Maternal death (n = 618, 1 RCT)	OR 0.33 (95% CI 0.01 to 8.14)			

10.7.5 Does screening for HIV in pregnancy and instituting appropriate interventions lead to improved maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Shey Wiysonge et al., 2002	618	2 RCTs, known HIV infected women who are pregnant Cochrane review Most recent update 2002	Vitamin A supplementation during pregnancy vs. placebo or micronutrient supplementation	Stillbirths (n = 1692, 2 RCTs) Very preterm births (n = 1578, 2 RCTs) All preterm births (n = 1577, 2 RCTs) Low birthweight (n = 1486, 2 RCTs) Very low birthweight (n = 1483, 2 RCTs) Postpartum CD4 levels (n = 727, 1 RCT) Maternal death (n = 728, 1 RCT)**	OR 1.07 (95% CI 0.63 to 1.80) OR 0.86 (95% CI 0.57 to 1.31) OR 0.88 (95% CI 0.68 to 1.13) OR 0.86 (95% CI 0.64 to 1.17) OR 0.71 (95% CI 0.40 to 1.28) Weighted mean difference –4.0, 95% CI –51.06 to 43.06 OR 0.49 (95% CI 0.04 to 5.40)	No evidence of heterogeneity between the trials (p = 0.37) ** There were only 3 maternal deaths	SR	1a
Ricci and Parazzini, 2000	418	436 women between 34 to 38 weeks pregnancy with confirmed HIV-1 diagnosis without indication (or contraindication) for caesarean section delivery in various European countries, including the UK	Caesarean section delivery vs. vaginal delivery	Adverse effects of delivery in HIV-1 infected women (i.e., fever, wound infection, anaesthetic, anaemia, other)	Higher rates of fever in women who gave births by Caesarean section, but no significant differences in complication rates between women treated with zidovudine in pregnancy and those not treated	Analysis by actual mode of delivery	RCT	1b
Cunningham et al., 2002	419	242 from original PACTG (only US and French sites included) study with 25 excluded from final analysis (RCT substudy)	Emergence of nevirapine resistance mutations at 6 weeks postpartum in women receiving standard antiretroviral treatment	Detection of resistance mutations prior to receipt of study drug Detection of resistance mutations at 6 weeks postpartum among women who received the study drug (single dose oral 200 mg to mother and 2 mg/kg to infant)	Detection of resistance mutations prior to receipt of study drug: 5/217 women (2.3%) Detection of resistance mutations at 6 weeks postpartum among women who received the study drug: 14/95 (15%, 95% CI 8 to 23%)	International, multicentre substudy of PACTG 316 Risk for development of resistant mutations not correlated with CD4 cell counts or HIV-1 RNA viral load at delivery or with type of antiretroviral therapy	OB	3
Palumbo et al., 2001	420	220 HIV infected women and n24 of their HIV infected infants from 4 US cities from 1991 to 1997 who received zidovudine during pregnancy	Impact of antiretroviral resistance on vertical transmission rates	Detection of resistance mutations in mother Perinatal transmission and maternal presence of resistance mutations Detection of resistance mutation in neonate	38 women (17.3%) For zidovudine mutation: 15.8% yes, 15.1% no (NS) For nucleotide reverse-transcriptase inhibitor: 12.5% yes, 16% no (NS) 2 babies (8.3%) but mutation pattern not identical to mothers	All women received zidovudine treatment during pregnancy Phylogenetic and genotypic resistance testing	OB	3

Very preterm = < 34 weeks of gestation Preterm birth = < 37 weeks of gestation Low birthweight = < 2500 g Very low birthweight = < 2000 g

10.8 Rubella

10.8.1 What is the prevalence of rubella susceptibility in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Miller et al., 1997	423	Antenatal population in England and Wales	Impact of 1994 mumps and rubella vaccination campaign on future incidence of rubella in pregnant women	Antenatal susceptibility Incidence and risk of rubella infection in susceptible pregnant women	Susceptibility in antenatal population: 2% in nulliparous women (735/36509) and 1.2% (839/67615) in parous women for 1994/5 ($p < 0.0001$) Susceptibility in Asian (n = 5000) vs. non-Asian (n = 62,346) population was 4.4% compared with 1.3% In 1995, incidence in nulliparous 2/431 (risk/1000 = 4.6), in parous 0/547; overall risk 2/1005	Data on rubella monitored through serologically confirmed cases, terminated pregnancies because of rubella and notifications to NCRSP.	SV	3
Tookey et al., 2002	424	145,284 pregnant women from former North West Thames region from 1996-1999 from which antenatal rubella screening data were available for 137,398	Retrospective analysis of routinely collected data	Rubella susceptibility	2.5% overall Breakdown by ethnicity: 1.7% white were susceptible vs. 3.7% of women from Mediterranean region, 5.1% of Asian, 4.8% black and 8% Oriental	Database used for this analysis includes about 90% of the deliveries in the area	SV	3

10.8.2 What is the incidence of congenital rubella syndrome in babies in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Tookey, 2002	422				Annual average of 3 congenital rubella births and 4 rubella associated terminations for 1996 to 2000 Just over 60 terminations for rubella disease or contact in pregnancy for England and Wales for 1991 to 2000 (ONS 2001)	Data contained in a report provided by the UK National Screening Committee working group		4
Miller et al., 1997	423	Registered congenital rubella births with NCRSP or terminations registered with ONS	To monitor impact of rubella immunisation on congenital rubella since 1971	Numbers of congenital rubella infection births, number of congenital rubella syndrome births and number of terminations for rubella disease or contact	From 1996 to 2000: congenital rubella infection: 1 case; congenital rubella syndrome: 16 cases; 17 terminations		SV	3

10.8.3 What are the diagnostic tests available for detection of rubella infection in pregnant women and how do they compare in terms of specificity, sensitivity, and cost-effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Grageot-Keros and Enders, 1997	426	852 sera (575 negative for anti-rubella virus IgM antibodies, 98 previously reactive sera, 28 paired sera taken during the acute phase of the disease, 9 sera from follow-up of primary infections, 44 sera from follow-up of vaccinations, and 98 samples containing potentially interfering analytes)	Roche Rubella IgM eEIA recomb compared with Abbott IMx Rubella IgM test and Sorin ETI-RUBIK-M reverse test	Sensitivity and specificity	Sensitivity: Roche: 99.3% Abbott: 98.3% Sorin: 100% Specificity: Roche: 100% Abbott: 93.9% Sorin: 82.7%		EV	2a

10.8.4 Does screening pregnant women for rubella immunity lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Miller et al., 1982	425	1016 pregnant women with confirmed rubella infection at different stages of pregnancy from January 1976 to September 1978 in England and Wales	Prospective follow-up up of infants to assess consequences of congenital infection	Pregnancy outcome; infection status of infant; rubella defects in seropositive (n = 102) vs. seronegative (n = 133) infants (congenital heart disease and deafness); frequency of congenital infection	Of 966 women, 523 (54%) had elective abortions, 36 (4%) had spontaneous miscarriages 9 women had stillbirths (4 of which had severe abnormalities); 5 infants died in neonatal period Of 269 infants tested (68% of surviving infants), 117 (43%) were infected Defects found in 20 children, all from seropositive group Incidence of other defects (delayed motor development, visual defects, speech delay, etc) were not found to be different among the two groups of infants Congenital infection in first 12 weeks of pregnancy among mothers with symptoms was over 80%, reduced to 25% at end of second trimester 100% of infants infected during first 11 weeks of pregnancy had rubella defects	Diagnosis of rubella (in mothers) based on 4-fold rise in antibody titre or the detection of specific IgM Infants defined as infected if IgM antibody present at birth or persistence of IgG after 1 year.	CH	2b

10.8.4 Does screening pregnant women for rubella immunity lead to improved maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Grillner et al., 1983	428	491 cases of rubella in pregnant women from 1978 to 1980 and 118 children followed up at age 20 months, 4 years or 7 years, in Sweden	Consequences of rubella during pregnancy with special reference to infection during 17th to 24th weeks of gestation Cases identified by surveillance and outcome determined by survey	Outcome of rubella infected pregnancies Intrauterine transmission of rubella Rubella defects	101 pregnancies infected from 17 to 24 weeks of gestation; all except one resulted in liveborn infant A decline in rate of infection from weeks 9 to 16 (57% to 70%) to weeks 17 to 20 (22%) and weeks 21 to 24 (17%) From 1 to 16 weeks of gestation, 10% to 40% of surviving children had rubella defects compared with 0% to 2% of children whose mothers were infected during 17 to 24 weeks of gestation		CH	2b
Morgan-Capner et al., 1985	429	7 pregnant women with asymptomatic rubella reinfection in early pregnancy	Reports of 7 cases	Identification of rubella specific antibody (IgM) in infants or products of conception	None detected		CST	3
CDC 2001	430	680 Live births from susceptible mothers in the UK, USA, Germany and Sweden	Inadvertent rubella vaccination with HPV-77, Cendehill or RA 27/3 at 3 months before or during pregnancy	Congenital rubella syndrome	No infant born with congenital rubella syndrome		SV	3

10.8.5 Is it cost effective to screen pregnant women for rubella immunity?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Stray-Pederson, 1982	619	Model based on annual pregnant population of 50,000 in Norway and prognosis of congenital rubella in unvaccinated population (n = 38 during epidemic period; n = 6 during nonepidemic period)	Modelling to assess cost benefit of rubella vaccination programmes (with goal of preventing rubella in pregnant women and subsequent congenital rubella syndrome)	Comparison of various vaccination programmes	All strategies were cost effective Based on cost/benefit ratios, net benefit came from vaccination offered to all women in puberty, supplemented with offering vaccination to nonimmunised women after delivery and women at high risk of exposure If participation in vaccination programme < 100%, vaccination offered at two ages (e.g. childhood and puberty) gives best results in prevention of congenital cases		EE	3 (?)

10.8.6 What are the interventions for a susceptible woman who is exposed to rubella infection during pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Tookey, 2002	422				There is no treatment to prevent or reduce mother-to-child transmission of rubella once infection has been detected in pregnancy	Report provided by the UK National Screening Committee working group	REC	4

10.9 Streptococcus group B

10.9.1 What is the prevalence of streptococcus group B in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Merenstein et al., 1980	432	1218 cultures taken during routine antenatal care visits and 1441 maternal infant pairs evaluated at delivery in Colorado, USA	Swabs placed in selective broth and plated (modified Todd-Hewitt broth)	Colonisation rate within this population	Colonisation rate varied from 6.6% to 11.6% in pregnant mothers 3.8% of infants were colonised at birth	Site of swabs unspecified Todd-Hewitt broth selected for GBS isolation, because 'most effective' according to this study, but no false positive or false negative rates reported	CSS	3
Regan et al., 1991	433	7742 pregnant women from the USA (various states) from university clinical centres from Nov 1984 through Jun 1987	Vaginal and endocervical culture obtained between 23 and 26 weeks of gestation	Prevalence of GBS	18.6%		CSS	3
Hastings et al., 1986	434	1457 pregnant women in England	Low vaginal and rectal swabs from women at booking, 28 and 36 weeks	Overall GBS colonisation rate	28% with no association between maternal age, blood group or parity		CSS	3

10.9.2 What is the prevalence of GBS infection in the neonate and what are the consequences of infection?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Fey et al., 1999	437	Neonates in England and Wales between 1995 and 1997	Analysis of reports to CDSC and isolates submitted to laboratories	Rates of early onset (within first week of birth) disease Rates of late onset (between 1 week and 3 months of age) disease	0.4/1000 live births 0.2/1000 live births	Marked under-reporting suspected, as one region where all laboratories contributed reports had rates of 0.7/1000 and 0.3/1000 for early and late onset, respectively No actual numbers. Data from an abstract	SV	3
Oddie and Embleton, 2002	435	36 infants infected with GBS in the first week after birth out of 62,786 live births in the Northern health region of the UK from April 1998 to March 2000	Survey (cross-checked with surveillance by PHLS)	Isolation of GBS in infant during first week of life Effect of GBS isolated during pregnancy as risk factor for early onset disease	Prevalence of 0.57 per 1000 live births (36 of 62,786 live births) Adjusted OR 1.9 (95%CI 0.03, 142.7)		CCS	3
Health Protection Agency 2002	431	N = 537 confirmed cases of GBS in infants aged < 90 days, reported by paediatricians and microbiologists from Feb 2000 to 28 Feb 2001 in the UK	Surveillance via the British Paediatric Surveillance Unit and cases reported by microbiologists to PHLS for typing	Isolation of GBS from a normally sterile site	From 537 cases, 67% aged under 7 days (early-onset disease); 33% aged between 7 and 90 days (late-onset disease) Overall mortality rate of 9.4% Incidence for England: 0.8/1000 live births (95% CI 0.7 to 0.9); early-onset disease 0.5 (0.5 to 0.6) Incidence for Wales: 0.6/1000 live births (0.4 to 0.9); early-onset disease 0.4 (0.2 to 0.7) Most common presentations of early-onset disease: sepsis in 62%; pneumonia in 26%		SV	3
Bignardi, 1999	438	15 confirmed cases of neonatal GBS infection from January 1995 through December 1997 from among 10,525 live births	Positive blood and CSF cultures that yielded GBS at Sunderland Royal Hospital from children under three months of age	Incidence of GBS	Neonatal infection 1.42/1000 live births (95% CI 0.8 to 2.04)		CSS	3

10.9.3 What are the diagnostic tests available for antenatal detection of GBS carriage and how do they compare in terms of specificity, sensitivity, and cost-effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Schrag et al., 2002	443	A stratified random sample of 5144 live births were selected from 629,912 live births from 1998 and 1999 from 8 geographical areas in the USA. All births of infants with early-onset infection were included in the sample (n = 312)	Universal culture screening vs. screening by assessment of clinical risk factors to identify candidates for intrapartum antibiotics for GBS	Prevention of early onset GBS disease in infants less than 7 days old	Risk of early-onset disease lower in universally screened group: adjusted relative risk 0.46 (95% CI 0.36 to 0.60) After excluding all women with risk factors and adequate time for prophylaxis, adjusted relative risk was still similar: 0.48 (95% CI 0.37 to 0.63)		CH	2b
Spieker et al., 1999	442	240 pregnant women at 28 weeks of gestation in Florida, USA	Patients received written instructions on how to obtain rectovaginal swab and obtained own swab. Physician also obtained swab Reference standard was any culture obtained by physician or women found to be positive	Cultures positive for GBS	24% (24/240) cultures positive for GBS patient sensitivity 79%, physician sensitivity 83%, p = 0.365		CSS	3
Molnar et al., 1997	441	163 women presenting for their 26 to 28 week antenatal care visit at five family physician offices and eight obstetricians at a hospital in Toronto, Canada from November 1995 through March 1996	Patient survey about who women would prefer to do their swabs; vaginal/anorectal swab collected by patient on self and vaginal/anorectal swab collected by physician on same woman Any culture positive for GBS obtained by women or physician used as reference standard	Comparison of GBS detection rate	Overall prevalence of maternal GBS carriage: 24% (39/163) (95% CI 17% to 30%) Concordance between physician- and patient-collected swabs was 95% (95% CI 92% to 98%) Patients identified 38 cases for sensitivity of 97% (lower 95% CI 92%); physicians identified 32 cases for sensitivity of 82% (95% CI 70% to 94%) From 161 surveys, 54 (34%) of women preferred to do their own swab, 66 (41%) were indifferent and 41 (26%) preferred physician to do their swab		CSS	3

10.9.3 What are the diagnostic tests available for antenatal detection of GBS carriage and how do they compare in terms of specificity, sensitivity, and cost-effectiveness? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Boyer et al., 1983	440	5586 cultures from pregnant women at obstetric practices in Chicago, USA from April 1979 to Sept 1981	Cultures from vagina and rectum Colonies with suggestive haemolysis or morphology identified as GBS with CAMP test Women with positive prenatal cultures, cultures obtained again intrapartum and within three days of delivery 200 women with negative prenatal cultures also recultured	Value of prenatal culture for identifying GBS colonisation status at delivery	Overall, 22.8% (1272/5586) women were carriers of GBS In colonised women, rectal cultures were more frequently positive than vaginal cultures (82% vs. 65%) 575/1272 GBS carriers were restudied at delivery. Of 182 antenatal positive vaginal and rectal cultures, 132/182 (73%) were positive at delivery Of 67 antenatal positive vaginal cultures, 46/67 (69%) were positive at delivery Of 144 antenatal positive vaginal cultures, 86/144 (60%) were positive at delivery Of 200 antenatal negative vaginal and rectal cultures, 17/200 (9%) were positive at delivery Estimated sensitivity and specificity of prenatal culture: 70% and 90%, respectively	182/575 recultured women with incomplete or unquantified cultures were excluded	EV	3
Yancey et al., 1996	439	826 women attending antenatal clinics in the USA	Vaginal and rectal swabs at approx 35 to 36 weeks gestation and again at delivery	Overall colonisation rate Test performance by culture-delivery interval	GBS identified in 219/826 (26.5%) of women In cultures obtained 1 to 5 weeks before delivery, sensitivity 87% (95% CI 83% to 92%), specificity 96% (95% CI 95% to 98%) Among patients cultured 6 weeks or more before delivery, sensitivity 43% and specificity 85%		CSS	3

10.9.4 & 10.9.5 What are the available interventions for managing women who are GBS carriers and do these interventions improve maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Smaill, 1999	444	5 RCTs	Intrapartum antibiotics vs. no treatment	Infant colonisation with GBS Early-onset neonatal GBS sepsis Neonatal death from infection	4 trials (n = 624): Peto OR 0.10 (95% CI 0.07 to 0.14) 4 trials (n = 751): Peto OR 0.17 (95% CI 0.07 to 0.39) 2 trials (n = 427): Peto OR 0.12 (95% CI 0.01 to 2.0)	No studies used a placebo or blinded the observer to the treatment allocation	SR	1a
Gibbs and McNabb, 1996	446	15 patients admitted in labour who had GBS at 26 to 28 weeks of gestation from December 1993 to August 1994 in the USA	5ml of 2% clindamycin cream intravaginally vs. no treatment	GBS from swabs of distal vaginal and rectum in mother GBS in infant from 4 sites (throat, ear, umbilicus, and rectum)	5 of 15 were culture negative at admission Treatment group: 5/5 vaginal cultures were positive; 3/5 rectal cultures were positive 2/6 neonates positive at one or more sites No treatment group: 3/4 positive vaginally and rectally 1/4 neonates positive at all four sites RR (mothers) 1.33 (95% CI 0.76 to 2.35) RR (infants) 1.33 (95% CI 0.13 to 10.25)	Computer-generated randomisation	RCT	1b
Benitz et al., 1999	445	4 trials on antibiotics administered in antepartum period 5 trials on intrapartum prophylaxis RCTs and controlled trials	Treatment with broad-spectrum antibiotics to prevent early-onset infection and monotherapy to prevent transmission in antepartum period or intrapartum vs. no treatment	Reduced GBS colonisation in mother and infant at delivery Early onset GBS	2/4 studies on antepartum treatment reported reduction in maternal colonisation at delivery None of the antepartum treatment studies reported an effect on neonatal infections Reduction of 80% in early-onset GBS with intrapartum antibiotic treatment (pooled OR 0.188, 95% CI 0.07 to 0.53)	Literature review was conducted only on Medline and from references of other recent reviews	SR	2a
Schrag et al., 2000	447	7867 cases of invasive GBS disease in counties from 8 states in the USA from 1993 to 1998	Active surveillance of microbiology laboratories and analysis with census data	Incidence of early-onset disease from 1993 to 1998 and corresponding dates of guideline releases	Decline from 1.7/1000 live births in 1993 to 0.6/1000 live births in 1998 (65% decrease, $p < 0.001$)	Cases defined by isolation of GBS from normally sterile site (e.g. blood or cerebral spinal fluid), i.e., cases identified from amniotic fluid, placenta or urine alone were not included	SV	3

10.9.4 & 10.9.5 What are the available interventions for managing women who are GBS carriers and do these interventions improve maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Jeffrey and Moses, 1998	448	All neonates admitted to neonatal unit in Sydney, Australia. Background incidence determined from November 1986 to February 1988. Intervention from June 1988 to June 1996	Screening all women at 28 weeks (or 24 weeks with known risk factors for preterm birth) with low vaginal swab, cultured on to blood agar. Treatment of all carriers with intravenous ampicillin in labour (1 g/6 hour until delivery)	Incidence of early-onset GBS before and after intervention	Before: 5732 live births. Incidence 4.9/1000 live births After: 36,342 live births. Incidence 0.8/1000 live births ($p < 0.0001$)		CS	3

10.10 Syphilis

10.10.1 What is the prevalence of syphilis infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hurtig et al., 1998	620	139 women treated for syphilis during pregnancy and 17 children meeting the case definition of congenital syphilis from 1994 to 1997, excluding Scotland (n = 136)	National survey of genitourinary medicine specialists and paediatricians; surveillance	Incidence of syphilis detected in pregnancy and congenital syphilis	121 women were detected through antenatal screening: 31 had confirmed or probably congenitally transmissible syphilis (30 excluding Scotland); NNT = 18,600 and 55,700 (maximum numbers) to detect one woman needing treatment and to prevent one case of congenital syphilis, respectively	Over the period 1994 to 1997, over 2 million women would have been screened as part of antenatal care	CSS	3
PHLS CDSC and PHLS Syphilis Working Group, 1998	453	139 women treated for syphilis during pregnancy and 17 children meeting the case definition of congenital syphilis from 1994 to 1997, excluding Scotland (n = 136)	National survey of genitourinary medicine specialists and paediatricians; surveillance	Minimum overall prevalence of women considered to need treatment for syphilis in pregnancy	For England and Wales: 0.068 (95% CI 0.057 to 0.080) per 1,000 live births	Denominators derived from routine ONS birth statistics.	CSS	3
Flowers and Camilleri-Ferrante, 1996	452	Pregnant women in East Anglia identified by screening	Surveillance	Positive screening test for syphilis	4-8 per million pregnancies	Estimated from 1991-1995 out of an estimated 130,000 pregnancies screened.	SV	3

10.10.2 What are the maternal and perinatal outcomes associated with syphilis infection in pregnancy?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Ingraham, 1951	455	1063 women with syphilis treated with penicillin and three control groups: 302 women with untreated syphilis, 594 women with bismuth and arsenical treatment of syphilis and 10,323 women without syphilis in the USA in the 1940s	Comparison of pregnancy outcomes between the penicillin treated syphilis and control groups	Effect of untreated syphilis on pregnancy outcomes (n = 302) compared with nonsyphilitic pregnancy (n = 10,232)	Early syphilis (n = 220): 25% stillborn (vs. 2.6%) 14% died in neonatal period (vs. 2.2%) 41% live birth to infected infant (vs. 0%) 20% live birth without syphilis (vs. 95%) Late syphilis (n = 82): 12% stillborn (vs. 2.6%) 8.5% died in neonatal period (vs. 2.2%) 2% live birth to infected infant (vs. 0%) 77% chance of birth to healthy, uninfected infant (vs. 95%)	Because penicillin became widely available in 1950s, no prospective observational studies in developed countries All differences between the early untreated group and the treated group were reported to be significant but the level of significance was not reported	CS	3
Fiumara et al., 1952	458	1005 pregnant women admitted in labour in Boston, USA in 1951	Syphilis diagnosis occurred either before pregnancy, antenatally or after delivery	Pregnancy outcomes Preterm birth defined as gestational age less than 37 weeks	24 had syphilis, 13 of which were old and treated cases, 11 diagnosed antenatally or after delivery None resulted in congenital syphilis 6/24 preterm births (25%) compared with 113/981 (11.5%) among women without syphilis (NS)		CS	3
Rotchford et al., 2000	459	1783 pregnant women from 12 clinics in South Africa screened for syphilis at first antenatal care visit between June and Oct 1998	Adequate (n = 108) vs. inadequate (n = 50; includes n = 30 no treatment) with penicillin Inadequate = less than 2 doses Adequate = at least 2 doses	Perinatal outcome in mother (because data on how many live births were twin pregnancies not available)	Of 1783 women, 158 tested positive for syphilis, data on pregnancy outcome available for 142 women 17 perinatal deaths among 15 women; stillbirths among 6 women; 9 women had early neonatal deaths Of 43 inadequately treated women for whom pregnancy outcome was known, 11 experienced perinatal death compared to 4 among treated women (99 for whom pregnancy outcome was known); $p < 0.0001$ Risk reduction (adjusted for age and gravidity) for each additional dose of penicillin: 1 dose: 41% (95% CI 2% to 64%) 2 doses: 65% (95% CI 42% to 79%) 3 doses: 79% (95% CI 66% to 88%)	Baseline findings from RCT Treatment: 3 weekly intramuscular injections of 2.4 mega-units of benzathine penicillin (as per DoH South Africa) Perinatal death defined as stillbirth or early neonatal death	CS	3

10.10.3 What is the prevalence of congenitally acquired syphilis infection and what are the consequences of infection?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
PHLS CDSC and PHLS Syphilis Working Group, 1998	453	Children under 2 years old in England and Wales between 1988 and 1995 Children identified through the British Paediatric Surveillance Unit	Surveillance of genitourinary medicine clinic data Surveillance programme from June 1993 to July 1997	Cases of syphilis in children Cases of syphilis in children as defined by US CDC Annual incidence	34 cases of early congenital syphilis reported from genitourinary medicine clinics; 2 more cases reported in 1996 9 reported with presumptive syphilis and 8 possible cases of congenital syphilis. No definite cases reported by paediatricians in the UK Rate of 0.06/1000 live births	Possible that some children with congenital syphilis were being treated outside genitourinary medicine clinic system; i.e., these estimates are conservative	SV	3

10.10.4 What are the diagnostic tests available for detection of syphilis infection and how do they compare in terms of specificity, sensitivity, and cost-effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Egglestone and Turner, 2000	449	N/A	Algorithm for treponemal antibody screening and confirmatory testing		FTA-abs still generally considered to be the gold standard, but TPHA is more sensitive, except in the third and fourth weeks of infection. TPHA is also more specific. Therefore most appropriate for confirming reactive EIA results at present. If TPHA is used for screening, then EIA can be used as the confirmatory test Further evaluation of immunoblotting as confirmatory test is needed		SSW	4
PHLS CDSC and PHLS Syphilis Working Group, 1998	453	N/A	Treponemal tests: TPIIA, FTA-Abs, EIAs Non-treponemal tests: RPR, VDRL		EIAs: over 98% sensitive, over 99% specific All treponemal tests sensitive at all stages of syphilis (except early primary syphilis) 98% and 98% to 99% specific May result in false negatives, particularly in very early or late syphilis, in patients with reinfection or who are HIV positive Predictive value of these tests is poor when used alone in low-prevalence populations	This information is from a report to the UK National Screening Committee (unpublished)	SR	4

10.10.5 What are the available interventions for managing women who are infected with syphilis?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Walker, 2001	462	Pregnant women with a confirmed diagnosis of syphilis, with and without concomitant HIV infection Cochrane review, most recent update 2001	To determine the most effective antibiotic treatment regimen of syphilis	Maternal resolution of clinical symptoms, miscarriage, stillbirth, neonatal deaths, and congenital syphilis	No RCTs identified	Available evidence is insufficient to determine the optimal penicillin regimen	SR	1a
Hashisaki et al., 1983	465	Pregnant woman with history of allergy to penicillin diagnosed with primary syphilis	Two successive course of erythromycin therapy	Efficacy of erythromycin treatment	Failure to cure infection. Subsequent successful treatment with penicillin after desensitisation		CR	3

10.10.6 Do these interventions improve maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Alexander et al., 1999	463	448 were diagnosed with syphilis from 28,552 women who delivered at a hospital in Texas, USA, from September 1997 to August 1989	Treatment with 2.4 million units of intramuscular benzylpenicillin (penicillin G) for primary, secondary or early latent syphilis and 7.2 million units of intramuscular benzylpenicillin for women with late latent syphilis (over 3 weeks)	Syphilis status of child	340 diagnosed antenatally Treatment prevented congenital syphilis in all 27 maternal primary and 136 maternal late infections Congenital syphilis prevented in 100/102 in maternal early latent infection group 4/75 treatment failures in maternal secondary syphilis group 2 congenital syphilis cases stillborn Overall, a 98.2% success rate for preventing congenital syphilis	108 were diagnosed postpartum and therefore not included in the study group Women screened (RPR and VDRL) for syphilis at first prenatal visit, 28 to 32 weeks prenatal visit and at delivery (confirmed with microhaemagluttinin assay) Clinical stage assigned by clinical examination of dark field microscopy	CH	2b
Watson-Jones et al., 2002	464	1688 pregnant women at an antenatal clinic in Tanzania from September 1997 to November 1999 (556 RPR positive and 1132 RPR negative)	Treatment with single dose benzylpenicillin in women with a positive RPR. Screen for syphilis. Serum samples also tested at reference laboratory by TPHA. FTA assay performed on sera that gave conflicting results from RPR and TPHA	Pregnancy outcomes (stillbirth, IUGR or preterm birth and birthweight) in seronegative vs. women treated for syphilis	No significant differences in adverse pregnancy outcomes between the two groups: 17.3 vs. 15.2 for all outcomes ($p = 0.86$) No significant difference in mean birthweight between the two groups ($p = 0.24$)		CH	2a

10.10.7 Is it cost effective to undertake universal screening for syphilis infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Conner et al., 2000	602	Data provided by 8 laboratories that performed a total of 169,140 antenatal screening tests for syphilis in one year, approximately one-fifth of the number of antenatal tests conducted in the UK	Estimation of costs based on the assumption that 40 women a year are detected and treated through antenatal screening and that the number of screening tests performed equalled the number of live births in the UK (annual births 750,000)	Cost of screening in the UK based on the cost of screening tests, treatment, and follow-up of infected women and their infants	Costs of screening estimated to be £672,366 (£161,849 to £2,306,382), or £0.90 per pregnancy screened NNT = 18,602 women screened to detect one woman who needs treatment for syphilis and a maximum of 55,713 women need to be screened to prevent one case of congenital syphilis. This is the equivalent of £16,670 for each woman treated for syphilis, or £49,928 for each case of congenital syphilis prevented	Targeted screening of high-risk groups would detect 70% of cases but would be practically difficult. Costs for targeted screening strategies are also presented for women in the Thames region, pregnant women in nonwhite ethnic groups and women born outside the UK. Targeting or stopping screening would save relatively little money		

10.11 Toxoplasmosis

10.11.1 What is the prevalence of toxoplasmosis immunity in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Ades et al., 1993	467				Toxoplasmosis immunity in pregnant women in the UK has fallen from approx 22% to 8%			

10.11.2 What is the incidence of new toxoplasmosis infection in pregnant women in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Eskild, 1996	466	Pregnant women in Europe	Medline search from 1983 to 1996	Incidence of toxoplasmosis in pregnancy	Range of 2.4 (Finland) to 16 (France) per 1000 susceptible women USA: 2/1000 to 6/1000 susceptible women	No data for the UK were found	SR	3
Ryan et al., 1995[621]	621	All pregnant women in England and Wales from 1981 to 1992	Surveillance	Number of reports of toxoplasmosis related to pregnancy	423 cases reported		SV	3

10.11.3 What is the prevalence of neonatal toxoplasmosis infection and what are its consequences?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Pratlong et al., 1996	471	286 pregnant women infected with toxoplasmosis between 7 and 34 weeks of gestation in France from 1985 to 1993	Detection of fetal abnormalities by ultrasound and of toxoplasma in amniotic fluid and in fetal blood	Risk of congenital infection by time of maternal infection	18% (52/286) overall; 11% (17/155) at 7 to 15 weeks; 26% (28/109) at 16 to 28 weeks; 32% (7/22) at 29 to 34 weeks		CS	3
Dunn et al., 1999	472	603 confirmed maternal toxoplasmosis infections in France from 1987 to 1995	Data collected from routinely collected information in medical records Diagnosis of fetal infection based on cordocentesis or amniocentesis with clinical examination after birth at 2, 5, 8 and 12 months and annually thereafter for a median of 4.5 years	Pregnancy outcome Risk of congenital infection by time of maternal infection Clinical outcome of liveborn infants with toxoplasmosis (n = 153) Risk of development of clinical signs in infant by time of maternal infection	Planned termination: 5 women; miscarriage: 3 women; stillbirth: 3 women; live birth: 591; unknown: 1 woman Congenital infection confirmed in 153 infants; excluded in 396 infants; 42 infants lost to follow-up Overall transmission rate among liveborn infants: 26% (153/591); 6% (95% CI 3 to 9) at 13 weeks of gestation; 40% (95% CI 33 to 47) at 26 weeks of gestation; 72% (95% CI 60 to 81) at 36 weeks of gestation 27% (41/153) of infected infants had chorioretinal lesions (n = 33), intracranial calcification (n = 14) and/or hydrocephaly (n = 2) Risk of clinical sign at 13 weeks: 61% (95% CI 34% to 85%); at 26 weeks: 25% (95% CI 18% to 33%); at 36 weeks 9% (95% CI 4% to 17%)	Three women gave birth to twins; data reported on firstborn twin only	CS	3
Foulon et al., 1999	473	144 women with confirmed toxoplasmosis infection from 5 European centres	Fetal infection detected by cordocentesis, amniocentesis or both Antibiotic treatment of 119/144 affected women Congenital toxoplasmosis determined by cord and neonatal blood samples. Infants followed-up to 1 year of age	Overall transmission Risk of congenital infection by time of maternal infection Clinical signs in infant	44% (64/144) gave birth to an infected infant (antibiotics made no difference in transmission rate, p = 0.7) At 6 to 10 weeks of gestation: 21%; 11 to 15 weeks: 19%; 16 to 20 weeks: 23%; 21 to 25 weeks: 60%; 26 to 30 weeks: 65%; 31 to 35 weeks: 93% 4 fetuses aborted; therefore, from 140 infants, 14% (19/140) either died in utero, had neurological abnormalities, hydroencephalus, cerebral calcifications, and/or choroidal scars with or without visual impairment	Analysis on infected (n = 64) vs. uninfected infant not presented	CS	3

10.11.3 What is the prevalence of neonatal toxoplasmosis infection and what are its consequences? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Lappalainen et al., 1995	622	16,733 pregnant women in Finland from 1988 to 1989	Screening for primary toxoplasmosis in mother Follow-up of 37 liveborn infected children	Mothers with toxoplasmosis Annual incidence of congenital toxoplasmosis	42 mothers with toxoplasmosis infection 4 infants with confirmed congenital toxoplasma infection; 0.3/1000 live born children per year		CS	3
Lebech et al., 1999	469	99,246 consecutive deliveries in Denmark from 1992 to 1996	Mothers screened at delivery for toxoplasma infection and infants of positive mothers followed for 12 months after delivery	Prevalence of toxoplasma infection in infants	0.3 per 1000	This study represented about one-third of all deliveries in Denmark	CS	3

10.11.4 What are the common sources of toxoplasmosis infection and how can pregnant women avoid infection?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Cook et al., 2000	470	252 pregnant women with acute toxoplasma infection and 858 controls from 5 centres in Europe from 1994 to 1995	Infection identified by antenatal screening Data collected by interview after diagnosis of infection	Associated risk with food and environmental factors for toxoplasmosis	Any cat in home: OR 1.0 (95% CI 0.7 to 1.5) Contact with soil: OR 1.8 (95% CI 1.2 to 2.7) Tasting meat while cooking: OR 1.5 (95% CI 1.0 to 2.4) Raw or undercooked beef: OR 1.7 (95% CI 1.1 to 7.2) Raw or undercooked lamb: OR 3.1 (95% CI 1.4 to 7.2) Raw or undercooked pork: OR 1.4 (95% CI 0.7 to 2.8)		CS	3

10.11.5 What are the diagnostic tests available for detection of toxoplasmosis infection and how do they compare in terms of specificity, sensitivity and cost effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Cubitt et al., 1992	474	Sera from 1000 pregnant women booking for antenatal care at a London hospital	Serological screening for antibodies to toxoplasmosis with gold standard based on repeat testing results	Comparison of DA, LA and EIAs	49/1000 discordant results among all assays and required repeat testing; 9 remained undetermined EIAs: 0/773 false positives, 2/218 false negatives LA: 0/218 false negatives, 1/773 false positives DA: 0/218 false negative, 23/773 false positives		TES	3

10.11.6 What are the available interventions for managing women who are infected with toxoplasmosis?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Peyron et al., 2002	476	0 RCTs	Treatment vs. no treatment of toxoplasmosis in pregnancy to reduce the risk of congenital toxoplasma infection	Congenital infection and clinical congenital infection	No RCTs identified		SR	1a
Wallon et al., 1999	477	9 studies identified	Treatment (spiramycin alone, pyrimethamine-sulphonamides, or a combination of the two) vs. no treatment of toxoplasmosis in pregnancy to reduce the risk of congenital toxoplasma infection	Congenital toxoplasmosis infection vs. no infection	5 studies showed effectiveness of treatment ($p < 0.001$): 22% vs. 52% 13% vs. 100% 21% vs. 47% 0% vs. 100% 4% vs. 83% 4 showed treatment was not effective: 5% vs. 17% 0% vs. 10% 10% vs. 10% 24% vs. 21%		SR	2a

10.11.7 Does screening pregnant women for toxoplasmosis infection lead to improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Bader et al., 1997	479	N/A	Decision analysis to compare no testing for congenital toxoplasmosis, targeted screening in cases of abnormalities noted on ultrasound and universal serological screening of pregnant women followed by amniocentesis to diagnose fetal infection in cases of maternal seroconversion	Pregnancy loss avoided	By medical treatment: universal screening reduced the number of cases of congenital toxoplasmosis at the 'cost' of 18.5 additional pregnancy losses for each case avoided By pregnancy termination: additional 12.1 pregnancy losses for each case avoided		ME	3

11.1 Gestational diabetes

11.11.1 What are the maternal and perinatal outcomes associated with gestational diabetes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Mestman et al., 1972	485	360 pregnant women in the USA	All had GTT and prednisolone GTT. All women followed up for 5 years	Abnormal GTT at pregnancy Abnormal GTT five year after pregnancy	During pregnancy: 51/360 with elevated fasting blood sugar; 181/360 abnormal GTT; 90/360 positive PGTT; 38/360 normal 5 years later: with elevated fasting blood sugar, 17/51 had abnormal GTT; with abnormal GTT, 59/181 still had abnormal GTT; with positive PGTT, 12/90 had abnormal GTT; 0/38 normal had abnormal GTT		CH	2a
Jensen et al., 2000	486	143 women diagnosed with gestational diabetes and 143 controls (with at least one risk factor, but normal OGTT) in Denmark from 1989 to 1996	Retrospective study of case notes. Women screened by risk factors, urinanalysis, and FPG. Diagnosis established if FPG or 75 OGTT met WHO criteria for diabetes mellitus in nonpregnant state Women with GDM were treated with diet and/or insulin	Maternal outcomes in cases vs. controls Fetal outcomes in cases vs. controls	Hypertensive disorders: 28 (20%) vs. 15 (11%), p = 0.046 Caesarean section: 47 (33% vs. 30 (21%), p = 0.033 Induced labour: 88 (62%) vs. 34 (24%), p < 0.0001 Preterm delivery: 15 (11%) vs. 7 (5%), p = 0.12 Gestational age: 39.0 ± 2 weeks vs. 39.9 ± 1.8, p < 0.0001 Ponderal index (kg/m^3): 25.5 ± 2.8 vs. 24.9 ± 2.2, p = 0.05 Macrosomia (birthweight ≥ 4500 g): 20 (14%) vs. 9 (6.3%), p = 0.049 Admission to neonatal unit: 66 (46.2%) vs. 17 (11.9%), p < 0.0001 Birthweight (corrected for gestational age), length at birth, Apgar score at 5 minutes, jaundice, congenital malformations and perinatal deaths were not significantly different		CCS	3
O'Sullivan et al., 1973	487	187 GDM patients and 259 negative control patients in Boston, USA from 1962 to 1970	GDM diagnosed with GTT	Perinatal mortality (28th week of gestation to 14 days postpartum)	GDM: 12/187 (6.4%) babies died; normal GTT: 4/259 (1.5%) babies died, p < 0.05		CCS	3

11.1.2 How do the following tests for the detection of GDM (risk factor screening, urinalysis, timed random blood glucose, Mini GTT, Full GTT) compare in terms of specificity, sensitivity, likelihood ratios and cost-effectiveness?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Marquette et al., 1985	490	434 pregnant women from an obstetric clinic in the USA	Glucose screen at 28 weeks of gestation with 50 g GCT after fasting. All positive women tested again within 2 weeks with 3hour OGTT. Maternal risk factors included obesity, excessive weight gain, glycosuria, family history of diabetes, and poor obstetric history	Comparison of 182 women with maternal risk factors vs. 252 women without risk factors Analysis by number of risk factors present	Number of positive screens: 56 (30.8%) vs. 56 (22.2%), p = 0.06 Number with GDM: 6 (3.2%) vs. 6 (2.4%), p = 0.57 6/252 (2.4%) had no risk factors present; 5/144 (3.5%) had one risk factor present; 1/31 (3.2%) had two risk factors present; 0/7 had more than two risk factors. NS difference in rates of diabetes among these groups. Sensitivity 50% Specificity 58%		CH	2b
O'Sullivan et al., 1973	491	18,812 antenatal patients from 1954 to 1959 from Boston , USA and 752 pregnant women from 1956 to 1957 (i.e., the entire antenatal care population from Boston City hospital during this period)	For 18,812: a venous blood sugar was obtained at 1 hour after 50-g GCT from all women and risk factors were obtained from clinical histories Those with high blood sugar levels or risk factors were scheduled for GTT For 986: 1-hour, 50-g GCT compared with 3 hour, 100-g GTT	For 18,812: proportion of general antenatal population (i.e., excluding those with diagnosed GDM) found to have one or more risk factors Risk factors included birth of baby > 9 lb, history of adverse pregnancy outcome, and family history of diabetes For 986: sensitivity and specificity of 1-hour, 50-g GCT	56.2% were negative to all factors; 43.8% had at least one risk factor Sensitivity of GCT 79% Specificity of GCT 87%		CH	2a
Gribble et al., 1995	494	2745 pregnant women in Wisconsin, USA from 1991 to 1993	Retrospective analysis of urinanalysis compared with 24- and 28-week blood glucose screening after 50-g GCT followed by 100-g OGTT for glucose levels > 140 mg/dl from 50-g test	Sensitivity and specificity	Sensitivity 7% Specificity 98%		CS	3

11.1.2 How do the following tests for the detection of GDM (risk factor screening, urinalysis, timed random blood glucose, Mini GTT, Full GTT) compare in terms of specificity, sensitivity, likelihood ratios and cost-effectiveness? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hooper, 1996	495	610 pregnant women in Baltimore, USA	Retrospective analysis of urinanalysis compared with 50-g GCT between 24 and 28 weeks of gestation followed by 100-g, 3-hour, GTT for glucose levels > 135 mg/dl from 50-g test	Glycosuria Sensitivity and specificity	Glycosuria: 6 women with GDM and 9 without GDM No glycosuria: 7 with GDM and 588 without GDM Sensitivity 46.2% Specificity 98.5%		CS	3
Watson, 1990	493	500 consecutive patients at an antenatal clinic in Germany	Urinanalysis compared with 50g, 1 hour, GCT at 28 weeks gestation followed by 100 g, 3 hour, OGTT for glucose levels >140 mg/dl from 50g test	GDM Glycosuria Sensitivity and specificity	22/500 (4.4%) diagnosed with GDM 85/500 (17%) showed some degree of glycosuria (defined as present at at least two antenatal visits) 6/22 (27%) of women with GDM showed glycosuria Sensitivity 27.3% Specificity 83.5%		CH	2b
McElduff et al., 1994	496	714 women attending antenatal clinic in New South Wales, Australia	RPG measured within two hours of a meal (≥ 6.1 mmol/l considered positive) compared with 1-hour, 50-g GCT at 28 weeks GDM diagnoses confirmed by 100-g GTT	GDM Sensitivity and specificity of RPG	28/714 (3.9%) with GDM Sensitivity 46% Specificity 86%		CH	2b
Jowett et al., 1987	497	110 pregnant women with suspected GDM in England	RPG levels tested over 24-hour period (0800, 1200, 1500, 1700, 2200 hours) and 75-g GTT administered	Sensitivities and specificities at various thresholds and at various times of day of RPG test	At threshold 5.6 mmol/l: sensitivity range 29% to 80%; specificity range 74% to 80% At threshold 6.1 mmol/l: sensitivity range 41% to 58%, specificity range 74% to 96% Highest sensitivities reported at 1500 hours		TES	3
Reichelt et al., 1998	498	5010 pregnant women in Brazil from 1991 to 1995 with no prior diagnosis of diabetes	FPG at 24 to 28 weeks of gestation was compared with 2-hour, 75-g GTT (used for diagnosis)	GDM Optimal threshold for maximising sensitivity and specificity of FPG	379/5010 (7.6%, 95% CI 6.8 to 8.3) women with GDM At 89 mg/dl (4.9 mmol/l), sensitivity and specificity maximised at 88% and 78%, respectively	Period of fasting not specified	2	IIa

11.1.2 How do the following tests for the detection of GDM (risk factor screening, urinalysis, timed random blood glucose, Mini GTT, Full GTT) compare in terms of specificity, sensitivity, likelihood ratios and cost-effectiveness? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Perucchini et al., 1999	499	520 women in Switzerland from 1995 to 1997	FPG compared with 1-hour, 50-g GCT between 24 and 28 weeks of gestation One week later, all patients also took 3-hour, 100-g GTT	GDM Optimal threshold for maximising sensitivity and specificity of FPG and 1-hour, 50-g GCT	53/520 (10.2%) women with GDM At 4.8 mmol/l, sensitivity and specificity for FPG maximised at 81% and 76%, respectively, (155/520 (30%) of women would have had to proceed to GTT for diagnosis) At 7.0 mmol/l, sensitivity and specificity maximised at 68% and 82%, respectively	Results were irrespective of last time women had eaten	CH	2a
Lewis et al., 1993	500	10 women with GDM and 12 controls from Chicago, USA	Between 26 and 32 weeks of gestation, each person underwent 3 GCT tests within a 2-week period (order of tests was randomised for each person) Test 1: 50-g GCT in fasting state Test 2: 50-g GCT 1 hour after a meal Test 3: 50-g GCT 2 hours after a meal	Plasma glucose levels after each test for women with GDM vs. controls	Cases: fasting = 10.5 mM plasma glucose, 1-hour = 11.0 mM plasma glucose, 2-hour = 9.3 mM plasma glucose ($p < 0.03$) Controls: fasting = 7.8 mM plasma glucose, 1-hour = 6.7 mM plasma glucose ($p < 0.01$), 2-hour = 6.4 mM plasma glucose 7/12 (58%) controls with glucose ≥7.8 mM in fasting state		TESC	3

11.1.3 Does screening for and instituting interventions for GDM result in improved maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Walkinshaw, 2000	504	4 RCTs (612 women with impaired glucose tolerance or gestational diabetes)	Diet therapy vs. no specific treatment	Maternal and fetal complications associated with diabetes	Caesarean section (4 RCTs, n = 612): Peto OR 0.97 (95% CI 0.65 to 1.44) Preterm birth (1 RCT, n = 158): Peto OR 0.57 (95% CI 0.10 to 3.36) Birthweight > 4000 g (2 RCTs, n = 457): Peto OR 0.78 (95% CI 0.45 to 1.35) Birthweight > 4500 g (2 RCTs, n = 457): Peto OR 0.85 (95% CI 0.28 to 2.56) Birth trauma (2 RCTs, n = 457): Peto OR 0.13 (95% CI 0.02 to 0.96) Perinatal death: not estimable Admission to NICU (1 RCT, n = 126): Peto OR 0.55 (95% CI 0.16 to 1.90) Maternal hypertensive disorder (1 RCT, n = 126): Peto OR 0.66 (95% CI 0.11 to 3.93)		SR	1a
Persson, 1985	505	202 pregnant women with impaired glucose tolerance from 1981 to 1984 in Sweden	Treatment by diet (n = 105) vs. diet and insulin (n = 97) (insulin doses adjusted according to blood glucose values)	Obstetric complications Fetal complications	Proteinuria, hypertension, pre-eclampsia, and polyhydramnios not significantly different No perinatal deaths. Birthweight, gestational age, and skinfold thickness not significantly different 30 in diet group and 40 in insulin group showed one or more episodes of neonatal morbidity	Insulin was instituted in 15/105 (14%) of women whose control exceeded 7 mmol/l (fasting) or 9 mmol/l (postprandial) who were originally randomised to the diet only group	RCT	1b
Avery et al., 1997	507	33 women at less than 34 weeks of gestation selected from a health maintenance organisation in the USA	30 minutes of exercise 3 to 4 times weekly (n = 15) vs. control group (n = 14)	Mean haemoglobin A1c Caesarean section Neonatal outcomes	Mean haemoglobin A1c (5.2% vs. 5.2%, NS) Caesarean section: 3 (20%) vs. 3 (21.4%), p = 1.0 Birthweight: 3419 ± 528g vs. 3609 ± 428 g, p = 0.30 Neonatal hypoglycaemia (NS) Gestational age: 39.4 ± 1.2 weeks vs. 39.7 ± 0.9 weeks, p = 0.7 No preterm births	144 women were approached for the study, 43 did not meet inclusion criteria and 68 declined From the original 33, 1 from the experimental and 3 from the control group dropped out	RCT	1b

11.1.3 Does screening for and instituting interventions for GDM result in improved maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Naylor et al., 1996	506	3778 women presenting for antenatal care in Toronto, Canada, from 1989 to 1992	50-g, 1-hour GCT screening at 26 weeks of gestation and diagnostic 100-g, 3-hour OGTT at 28 weeks of gestation (for all women) Group 1: known and treated GDM (n = 143) Group 2: untreated borderline GDM (n = 115) Group 3: false positive group (positive result on GCT, normal result on OGTT) (n = 580) Group 4: negative screenees (less than 7.8 mmol/l on GCT and normal result on OGTT) (n = 2940)	Macrosomia Pre-eclampsia Caesarean delivery	Macrosomia (> 4000 g): Group 1 15 (10.5%) Group 2 33 (28.7%) Group 3 14 (80%) Group 4 395 (13.7%) Macrosomia (> 4500 g): Group 1 5 (3.5%) Group 2 7 (6.1%) Group 3 12 (2.1%) Group 4 56 (1.9%) Pre-eclampsia: Group 1 12 (8.4%) Group 2 10 (8.7%) Group 3 31 (5.4%) Group 4 144 (4.9%) Caesarean: Group 1 48 (33.6%) Group 2 34 (29.6 %) Group 3 136 (23.9%) Group 4 585 (20.2%)(In multivariate model, caesarean vs. spontaneous vaginal delivery in Group 4 vs. Group 1: OR 2.2 (95% CI 1.3 to 3.7)		CH	2a
Wu Wen et al., 2000	492	1,729,225 pregnant women and 1,738,863 infants from 1984 to 1997 in Canada	Universal screening after guidelines introduced in 1985 vs. one area where no universal screening was implemented and retrospective analysis of medical records by ICD-9 codes	Number of women diagnosed with GDM Pregnancy complications in areas of universal screening vs. no universal screening	Overall: 38,274 women with GDM; an increase of 0.3% in 1984 to 2.7% in 1996; universal screening: 1.6% in 1990 to 2.2% in 1996 vs. 1.4% to 1.0 in no screening area Caesarean section: 18.8% vs. 18.9% Pre-eclampsia: 2.9% vs. 3.5% Polyhydramnios: 0.3 vs. 0.5 Amniotic infection: 0.9 vs. 0.5 Fetal macrosomia: 12.5% vs. 12.7% of newborn in each region		CS	3

11.1.3 Does screening for and instituting interventions for GDM result in improved maternal and perinatal outcomes? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Goldberg et al., 1986	508	58 pregnant women and 58 controls from an antenatal diabetes clinic in the USA from 1979 to 1984	Home glucose monitoring vs. controls Insulin therapy begun in subjects of either group if glucose values were > 95 mg/dl or if postprandial values were > 120 mg/dl	Use of insulin Neonatal outcomes Caesarean section	Use of insulin: 29 (50%) vs. 12 (21%), $p < 0.01$ Birthweight: 3231 ± 561 vs. 3597 ± 721, $p < 0.002$ Macrosomia (≥ 4000 g): 5 (9%) vs. 14 (24%), $p < 0.05$ Large for gestational age: 7 (12%) vs. 24 (41%), $p < 0.005$ Caesarean section: 32% vs. 25%, NS		CCS	3

11.2 Pre-eclampsia

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Barton et al., 2001	515	748 women with a singleton pregnancy with hypertension in the USA from 1995 to 1998	Women from 24 to 35 weeks of gestation with no proteinuria by dipstick (0 or trace) at admission to study monitored for progression to proteinuria	Progression to proteinuria Progression to severe pre-eclampsia Rate of progression to proteinuria by gestational age at enrolment Incidence of SGA babies	Proteinuria developed in 343/748 (46%) women Severe pre-eclampsia developed in 72/748 (9.6%) women Rate of progression greater in women enrolled at less than 30 weeks compared with 34 to 35 weeks, $p = 0.008$ SGA in women with proteinuria versus hypertension alone: 24.8% vs. 13.8%, $p < 0.001$	Gestational hypertension defined as maternal blood pressure greater than or equal to 140 mmHg systolic or 90 mmHg diastolic. Proteinuria defined as greater than or equal to 1+ (by dipstick) on at least two occasions. Severe pre-eclampsia defined as either 1) severe hypertension (160/110 mmHg on 2 occasions), 2) mild hypertension with severe proteinuria (greater than or equal to 3+) or 3) development of thrombocytopenia	CSS	3
Page and Christianson, 1976	516a	14,833 singleton pregnancies in California, USA from 1959 to 1967	Levels of mean arterial pressure in the middle trimester (121 to 180 days) assessed in relation to pregnancy outcomes	Stillbirth rate Neonatal mortality rate Incidence of SGA babies (weighing less than 2500 g at gestations greater than or equal to 37 weeks)	Middle trimester: progressive rise in stillbirth and neonatal death rate above 85 mmHg, with sharp rise after 90 mmHg An increase in frequency of SGA babies above 85 mmHg		CH	2a

11.2 Pre-eclampsia (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Page and Christianson, 1976	516b	12,954 singleton pregnancies in California, USA from 1959 to 1967	Levels of mean arterial pressure in the middle (121 to 180 days) and third (after 180 days) trimester assessed in relation to pregnancy outcomes in women with or without proteinuria	Fetal mortality and morbidity Stillbirth rate/1000 Perinatal death/1000	In third trimester: increase in fetal deaths and morbidity above 95 mmHg Middle trimester, stillbirth rate: In white women (n = 10,074): – without proteinuria and < 90 mmHg = 8.4 – without proteinuria and ≥ 90 mmHg = 14.8 – with proteinuria and < 90 mmHg = 15.4 – with proteinuria and ≥ 90 mmHg = 47.6 In black women (n = 2880): – without proteinuria and < 90 mmHg = 10.8 – without proteinuria and ≥ 90 mmHg = 28.5 – with proteinuria and < 90 mmHg = 37.7 – with proteinuria and ≥ 90 mmHg = 142.9 Middle trimester, perinatal death rate: In white women (n = 10,074): – without proteinuria and < 90 mmHg = 15.2 – without proteinuria and ≥ 90 mmHg = 25.8 – with proteinuria and < 90 mmHg = 38.5 – with proteinuria and ≥ 90 mmHg = 17.0 In black women (n = 2880): – without proteinuria and < 90 mmHg = 20.3 – without proteinuria and ≥ 90 mmHg = 34.6 – with proteinuria and 90 mmHg = 56.6 – with proteinuria and ≥ 90 mmHg = 142.9		CH	2a

11.2 Pre-eclampsia (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Cuckson et al., 2002	525	11 devices for blood pressure monitoring from 15 studies	Meta-analysis of accuracy of devices in pregnancy and pre-eclampsia. Mean pressure differences of mercury devices compared with mean pressure differences of automated devices	Mean pressure differences (MPD) and standard deviation (SD)	MPD of mercury devices in pregnancy (SD): systolic 1.0 (6), diastolic 1.7 (7) MPD of mercury devices in pre-eclampsia (SD): systolic 5.5 (9), diastolic 7.9 (8) MPD of automated devices in pregnancy (SD): systolic -3.0 (12), diastolic -4.0 (8) MPD of automated devices in pre-eclampsia (SD): systolic 18.7 (11), diastolic 8.2 (7)		TES	3
Brown et al., 1998	527	220 woman with diastolic hypertension after 20th week of pregnancy in Australia	Management with K4 (n = 103) vs. management with K5 (n = 117)	Severe hypertension Prolonged pregnancy Requirements for antihypertensive treatment Laboratory data (including serum creatinine, uric acid, aspartate aminotransferase, platelet count and haemoglobin) Birthweight Fetal growth restriction Perinatal mortality Eclampsia Maternal death	No significant difference in number of episodes of severe hypertension, however more women were found to have severe diastolic hypertension with K4: 34 (33%) vs. 20 (17%), p = 0.006) No significant difference in proportion of women who needed antihypertensive treatment or in laboratory data No significant difference in birthweight, fetal growth restriction, prolonged pregnancy, or perinatal mortality No cases of eclampsia or maternal death	Analysis was by intention to treat Blinded endpoint analysis, but patients, doctors and midwives were aware of random allocation Severe hypertension defined as systolic greater than or equal to 170mm Hg, diastolic greater than or equal to 110mm Hg	RCT	1b

11.2 Pre-eclampsia (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Duckitt, 2003	512	Pregnant women	Systematic review of studies on risk factors for pre-eclampsia to July 2002	Parity Age History of previous pre-eclampsia Family history of pre-eclampsia Underlying medical conditions Multiple pregnancy BMI	Nulliparity OR 2.71, 95% CI 1.16 to 6.34 (14 studies) Maternal age over 40 years and primiparous OR 2.17, 95% CI 1.36 to 3.47; maternal age over 40 years and multiparous OR 2.05, 95% CI 1.47 to 2.87 (15 studies) Pre-eclampsia in first pregnancy OR 8.23, 95% CI 6.49 to 10.45; pre-eclampsia in second pregnancy OR 11.51, 95% CI 5.76 to 22.98 (10 studies) Positive family history of pre-eclampsia OR 5.27, 95% CI 1.57 to 17.64 (1 cohort study) Pre-existing diabetes (type 1) OR 4.53, 95% CI 3.30 to 6.23 (5 studies) Multiple pregnancy (regardless of parity) OR 2.76, 95% CI 1.99 to 3.82 (9 studies) BMI over 35 at booking OR 2.29, 95% CI 1.61 to3.24 (2 studies)		CH & CCS	2b and 3
Villar and Khan-Neelofur, 2001	32	3 RCTs, 3041 women	Midwife and GP-managed care vs. obstetrician and gynaecologist-led shared care	Pre-eclampsia	Pre-eclampsia (2 RCTs, n = 2952): Peto OR 0.37, 95% CI 0.22 to 0.64	Please refer to section 4.1 for other outcomes and results of this study.	SR	1a

11.3 Preterm birth

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Buekens et al., 1994	542	5440 women from antenatal clinics in Belgium, Denmark, Hungary, Ireland, Italy, Portugal and Spain from 1988 to 1990	Routine cervical examination at every antenatal appointment (n = 2719) vs. avoidance of cervical examination if possible (n = 2721)	Median number of appointments Preterm birth (< 37 weeks) Low birthweight (< 2500g) Premature rupture of the membranes (PROM) Stillbirth	Median number of appointments for women in both groups: 8 Preterm birth: 5.7% vs. 6.4%, RR 0.88, 95% CI 0.72 to 1.09 Low birthweight: 6.6% vs. 7.7%, RR 0.86, 95% CI 0.71 to 1.04 PROM: 27.1% vs. 26.5%, RR 1.02, 95% CI 0.94 to 1.12 Stillbirth: 8.7% vs. 8.0%, RR 1.09, 95% CI 0.61 to 1.94	Computer generated randomisation in sealed envelopes	RCT	1b
Iams et al., 1996	543	2915 women from 10 university affiliated antenatal clinics in the USA from 1992 to 1994	Vaginal ultrasonography at approximately 24 and again at 28 weeks of gestation (2531/2915)	Preterm birth (< 35 weeks) Sensitivity and specificity	At 24 weeks, compared with women with cervical lengths (CL) above the 75th percentile: – women at or below 75% (CL 40 mm) had RR 1.98, 95% CI 1.2 to 3.27 – women at or below 50% (CL 35 mm) had RR 2.35, 95% CI 1.42 to 3.89 – women at or below 25% (CL 30 mm) had RR 3.79, 95% CI 2.32 to 6.19 – women at or below 10% (CL 26 mm) had RR 6.19, 95% CI 3.84 to 9.97 – women at or below 5% (CL 22 mm) had RR 9.49, 95% CI 5.95 to 15.15 – women at or below 1% (CL 13 mm) had RR 13.99, 95% CI 7.89 to 24.78 At 28 weeks, compared with women with cervical lengths above the 75th percentile: – women at or below 75% (CL 40 mm) had RR 2.8, 95% CI 1.41 to 5.56 women at or below 5o% (CL 35 mm) had RR 3.52, 95% CI 1.79 to 6.92 – women at or below 25% (CL 30 mm) had RR 5.39, 95% CI 2.82 to 10.28 – women at or below 10% (CL 26 mm) had RR 9.57, 95% CI 5.24 to 17.48 – women at or below 5% (CL 22 mm) had RR 13.88, 95% CI 7.68 to 25.10 – women at or below 1% (CL 13 mm) had RR 24.94, 95% CI 13.81 to 45.04 Sensitivity for at 24 and 28 weeks for less than or equal to 30 mm CL: 54% and 70% Specificity for at 24 and 28 weeks for less than or equal to 30 mm CL: 76% and 69%		CH	2a

11.3 Preterm birth (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Goldenberg et al., 2000	544	10456 women with singleton pregnancies in the USA from 1995 to 1998	Measurement of fetal fibronectin values at 8 to 22 weeks	Preterm birth (greater than or equal to 13 weeks and less than 35 weeks)	Comparing fetal fibronection level in greater than or equal to 90th percentile with less than 90th percentile: – at 13 to 14 weeks, 12.1% vs. 5.5%, RR 2.19, 95% CI 1.27 to 3.80 – at 15 to 16 weeks, 13.5% vs. 4.4%, RR 3.06, 95% CI 1.73 to 5.41 – at 17 to 18 weeks, 5.9% vs. 3.8%, RR 1.54, 95% CI 0.74 to 3.17 – at 19 weeks or more, 9.7% vs. 3.7%, RR 2.63, 95% CI 1.75 to 3.94		CH	2a
Goldenberg et al., 1996	545	2929 women from 10 centres in the USA from 1992 to 1994	Measurement of fetal fibronectin in the cervix and vagina every two weeks from 22 to 24 weeks of gestation to 30 weeks of gestation as a screening test for preterm birth	Sensitivity and specificity (positive test defined as fetal fibronectin greater than or equal to 50 ng/mL)	Sensitivity and specificity for birth at 34 weeks or earlier for fetal fibronection measurement at: 24 weeks, 23% (95% CI 16 to 31) and 97% 26 weeks, 22% (95% CI 14 to 32) and 97% 28 weeks 20% (95% CI 11 to 30) and 97% 30 weeks, 29% (95% CI 18 to 41) and 96% Sensitivity of fibronectin at 22 to 24 weeks for preterm birth occurring at: 24 to 27 weeks, 63% (95% CI 38 to 84) 24 to 29 weeks, 54% (95% CI 28 to 66) 24 to 31 weeks, 38% (95% CI 25 to 53) 24 to 34 weeks, 21% (95% CI 14 to 29) 24 to 36 weeks, 10% (95% CI 7 to 14)		CH	2a
Mercer et al., 1996	546	2929 women from 10 centres in the USA from 1992 to 1994	Risk assessment for the prediction of preterm birth using clinical information collected at 23 to 24 weeks	Sensitivity and specificity	For a predicted probability of 20% or greater for preterm birth, sensitivity and specificity for multiparous women was 24.2% and 92.1% For a predicted probability of 20% or greater for preterm birth, sensitivity and specificity for nulliparous women was 18.2% and 95.4%	Factors assessed included demographics, socioeconomic status, home and work environment, drug or alcohol use, medical history, height, weight, body mass index, speculum examination, and pelvic examination	CH	2a

11.4 Placenta praevia

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Leerentveld et al., 1990	549	100 women with second or third trimester haemorrhage, suspected placenta praevia, fetal malpresentaion or nonengaged presenting part from 1988 to 1990	In group with suspected placenta praevia (n = 15), transvaginal scan performed at 31 weeks (median). In the rest of the women (n = 85), transvaginal ultrasound performed at 29 weeks (median) Findings at delivery used as gold standard	Sensitivity and specificity of transvaginal placental localisation Cases of vaginal bleeding Sensitivity: 87.5%, 95% CI 61.7 to 98.4 Specificity: 98.8%, 95% CI 93.4 to 100 No cases of vaginal bleeding and no woman who presented with vaginal haemorrhage (n = 76) displayed aggravated bleeding after sonography.			CS	3
Oppenheimer et al., 2001	550	36 pregnant women with a placenta lying within 30mm of the internal cervical os or overlapping it at or after 26 weeks	Eligible women identified by transvaginal ultrasound and repeated every 4 weeks until leading edge migrated beyond 30 mm or delivery	Cases of vaginal bleeding from transvaginal ultrasound	No case of vaginal bleeding Procedure also reported to be well tolerated by all women		CS	3
Sherman et al., 1991	551	38 women with suspected placenta praevia at 26 weeks or more	Group 1 (n = 20): abdominal ultrasound Group 2 (n = 18): abdominal ultrasound followed by vaginal ultrasound All women rescanned at 4 week intervals	Diagnosis of placenta praevia Cases of vaginal bleeding	Group 1, on initial transabdominal scan: 9 complete praevias, 3 partial praevias, 4 marginal praevias, and 4 low lying Group 2, on initial transabdominal scan: 5 complete praevias, 5 partial praevias, 2 marginal praevias, and 6 low lying Group 2, on transvaginal scan: 4 complete praevias, 3 partial praevias, 5 marginal praevias, and 6 low lying In subset of women who gave birth within two weeks of last scan (n = 19), in both groups, transabdominal and transvaginal scans correctly identified all cases of complete praevia. For partial praevia, 2 women in group 1 were identified at delivery but the tranabdominal scan had identified 3 women. In group 2, 2 women with partial praevia at delivery were identified, concording with results from the tranvaginal scan, but not with the transabdominal scan which identified only 1 woman. No patient experienced increased vaginal bleeding within 24 hours after transvaginal scan	Method of randomisation not specified	RCT	1b

11.4 Placenta praevia (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Farine et al., 1990	552	77 women with second or third trimester bleeding or previous diagnosis of placenta praevia	Transabdominal ultrasound followed by transvaginal ultrasound within 24 hours Findings at delivery used as 'gold standard'	Sensitivity and specificity False positives and false negatives Cases of vaginal bleeding	Transvaginal sensitivity and specificity: 100% and 81% Transabdominal sensitivity and specificity: 79% and 39% Transvaginal false positive and false negative rate: 29% and 0% (all false positive cases were marginal placenta praevia) Transabdominal false positive and false negative rate: 62% and 20% None had vaginal bleeding in 12 hours following scan		CS	3
Taipale et al., 1997	553	6428 women with singleton pregnancies from an obstetric clinic in Finland from 1993 to 1994	Transvaginal ultrasound performed at 12 to 16 weeks. Placenta that extended over the internal cervical os was measured with electronic calipers	Number of women with placenta at or over internal cervical os at 12 to 16 weeks Number of women with placenta praevia at birth Sensitivity	287/6428 (4.5%) had placenta at or over internal os 10/6428 (0.16%) had placenta praevia at time of birth 8/10 women with placenta praevia were identified with transvaginal scan: sensitivity 80%, 95% CI 44 to 98 In all 8 of these women, the placenta extended 15mm or more over the internal os at 12 to 16 weeks		CH	2b
Taipale et al., 1998	554	3696 women with singleton pregnancies in Finland from 1995 to 1996	Transvaginal ultrasound performed at 18 to 23 weeks. Distance from edge of placenta to internal cervical os was measured with electronic calipers	Number of women with placenta at or over internal cervical os at 18 to 23 weeks Number of women with placenta praevia at birth Sensitivity and specificity Positive predictive value (PPV) with 15-mm cutoff	57/3696 (1.5%) had placenta at or over internal os 5/3696 (0.14%) had placenta praevia at time of birth Sensitivity: 100%, 95% CI 48 to 100 Specificity: 99.4%, 95% CI 99.1 to 99.6 In all 5 women, placenta extended 15mm or more over the internal os at 18 to 23 weeks PPV: 19%, 95% CI 6 to 38		CH	2b

11.4 Placenta praevia (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hill et al., 1995	555	1252 pregnant women from a women's hospital in the USA	Transvaginal ultrasound performed between 9 and 13 weeks of gestation. The distance from the edge of the placenta to the internal cervical os was measured with electronic calipers	Number of women with placenta at or over internal cervical os between 9 and 13 weeks Number of women with placenta praevia at birth	77/1252 (6.2%) had placenta at or over internal os 4/1252 (0.32%) had placenta praevia at time of birth In all 4 women, the placenta extended more than 1.6 cm over the internal os by transvaginal ultrasound at 9 to 13 weeks.		CSS	3
Dasche et al., 2002	556	714 women with singleton pregnancies and suspected placenta praevia from 1991 to 2000	Retrospective analysis of women who had transvaginal or transabdominal ultrasound between 15 and 36 weeks of gestation	Persistence of placenta praevia to delivery from gestational age at detection	From 15 to 19 weeks: 12% From 20 to 23 weeks: 34% From 24 to 27 weeks: 49% From 28 to 31 weeks: 62% From 32 to 35 weeks: 73%		CS	3

12.2 Measurement of symphysis–fundal distance

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Gardosi and Francis, 1999	567	1272 consecutive women with singleton pregnancies booked before 22 weeks from 1995 to 1995	Fundal height measurement plotted on customised charts (n = 734) vs. fundal height assessment by abdominal palpation and recorded on standard co-operation card (n = 605)	Detection of small- and large-for-gestational-age babies (SGA and LGA) Number of referrals for investigations	SGA: 47.9% vs. 29.2%, OR 2.23, 95% CI 1.12 to 4.45 LGA: 45.7% vs. 24.2%, OR 2.63, 95% CI 1.27 to 5.45 Referrals for investigations in pregnancy assessment centre: 0.33 vs. 0.56 visits per pregnancy, p < 0.005		CT	2a

12.5 Cardiotocography

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Pattison and McCowan, 2001	573	4 RCTs, 1588 pregnancies	Antenatal cardiotocography vs. control for fetal assessment	Perinatal outcomes Methods of delivery Hospital admissions	Perinatal deaths: 3 RCTs, n = 127, Peto OR 2.85, 95% CI 0.99 to 7.12 Neonatal admissions: 2 RCTs, n = 883, Peto OR 1.11, 95% CI 0.80 to 1.54 Elective caesarean section: 3 RCTs, n = 1047, Peto OR 1.01, 95% CI 0.68 to 1.51 Emergency caesarean section: 3 RCTs, n = 1049, Peto OR 1.27 95% CI 0.83 to 1.92 Induction of labour: 3 RCTs, n = 1049, Peto OR 1.09 95% CI 0.85 to 1.40 Hospital admissions: 1 RCT, n = 300, Peto OR 0.37 95% CI 0.17 to 0.83		SR	1a

12.7 Umbilical and uterine artery Doppler ultrasound

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Bricker and Neilson, 2001	575	5 RCTs, 14,388 pregnant women	Routine Doppler ultrasound vs. no/concealed/selective Doppler ultrasound	Antenatal admission Further Doppler ultrasound Birthweight Apgar score Admission to special care baby unit Preterm delivery Perinatal mortality Caesarean section	Antenatal admission: (3 RCTs, n = 9359) Peto OR 1.05, 95% CI 0.95 to 1.15 Further Doppler ultrasound: (1 RCT, n = 3898) Peto OR 1.57 95% CI 1.30 to 1.90 Birthweight: (mean, SD) (1 RCT, n = 2016) WMD –27.000 95% CI –74.235 to 20.235 Apgar score < 7 at 5 minutes: (4 RCTs, n = 11375) Peto OR 0.88 95% CI 0.56 to 1.40 Special care admission: (3 RCTs, n = 7477) Peto OR 0.99 95% CI 0.82 to 1.19 Preterm delivery < 37 weeks of gestation: (3 RCTs, n = 9359) Peto OR 1.09, 95% CI 0.89 to 1.33 Perinatal mortality (excluding congenital abnormalities): (3 RCTs, n = 9359) Peto OR 1.10 95% CI 0.59 to 2.07 Emergency caesarean section: (2 RCTs, n = 5461) Peto OR 1.02, 95% CI 0.84 to 1.23		SR	1a
			Serial ultrasound and Doppler ultrasound vs. selective ultrasound	Caesarean section Gestation at delivery Birthweight Apgar score Admission to neonatal unit Perinatal mortality	Emergency caesarean section: (1 RCT, n = 2834) Peto OR 0.80 95% CI 0.62 to 1.05 Gestation at delivery: (mean, SD) (1 RCT, n = 2834) –WMD 0.100, 95% CI –1.205 to 1.005 Birthweight (mean, SD) (1 RCT, n = 2834): – WMD –25.000 95% CI –67.526 to 17.526 Apgar score < 5 at 7 minutes (1 RCT, n = 2834) Peto OR 0.76 95% CI 0.46 to 1.27 Admission to neonatal unit (1 RCT, n = 2834) Peto OR 0.94 95% CI 0.67 to 1.33 Perinatal mortality: (1 RCT, n = 2834) Peto OR 0.60, 95% CI 0.31 to 1.16			

13.1 Pregnancy after 41 weeks

13.1.1 How is pregnancy after 41 weeks determined and what is it its incidence in the UK?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hilder et al., 1998	577	171,527 births from maternity units in North East Thames region, London, in 1989 to 1991	Retrospective analysis of regional database of birth notifications	Number of deliveries by week of gestation	At 40 weeks, 58% of women delivered At 41 weeks, 74% of women delivered At 42 weeks, 82% of women delivered	Gestational age based on maternal history or ultrasound data Gestations of more than 45 weeks were excluded	CH	2a

13.1.2 What are the maternal and perinatal outcomes associated with pregnancy after 41 weeks?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hilder et al., 1998	577	171,527 notified births from maternity units in North East Thames region, London, in 1989 to 1991	Retrospective analysis of regional database of birth notifications linked to stillbirth and infant death registration	Rates of stillbirth and neonatal mortality/1000 ongoing pregnancies	At 37 weeks, risk of stillbirth was 0.35/1000 and risk of neonatal death was 0.14/1000 ongoing pregnancies At 42 weeks, risk of stillbirth was 1.5/1000 and risk of neonatal death was 1.45/1000 ongoing pregnancies At 43 weeks, risk of stillbirth was 2.12/1000 and risk of neonatal death was 1.59/1000 ongoing pregnancies	Gestational age based on maternal history or ultrasound data Post-term deliveries were defined as those occurring at 42 weeks (294 days) of gestation or later Term deliveries defined as those born at 37 to 41 completed weeks of gestation Gestations of more than 45 weeks were excluded	CH	2a

13.1.3 & 13.1.4 Does induction of labour versus conservative management decrease the risk of adverse perinatal and maternal outcomes and do these interventions improve maternal and perinatal outcomes?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Crowley, 2003	578	26 RCTs	Routine versus selective induction of labour for post-term pregnancy (after 41 weeks)	Induction of labour for post-term pregnancy (after 41 weeks gestation) Perinatal death Caesarean section Instrumental delivery (overall) Use of epidural analgesia (overall) Meconium-stained amniotic fluid Fetal heart rate abnormalities Maternal satisfaction with birth (overall)	Induction of labour: (4 trials) Peto OR 0.68 (95% CI 0.57 to 0.82) Perinatal death: (13 trials, n = 6073): Peto OR 0.23 (95% CI 0.06 to 0.90) Caesarean section: (12 trials, n = 5954): Peto OR 0.87 (95% CI 0.77, 0.99) Instrumental delivery: (14 trials, n = 6591): Peto OR 0.96 (95% CI 0.85 to 1.08) Use of epidural: (5 trials, n = 1543): Peto OR 1.15 (95% CI 0.91 to 1.45) Meconium-stained amniotic fluid: (9 trials, n = 5662): Peto OR 0.74 (95% CI 0.65 to 0.84) Fetal heart rate abnormalities: (6 trials, n = 1745): Peto OR 0.91 (95% CI 0.66 to 1.24) Maternal satisfaction: (1 trial, n = 402): Peto OR 0.84 (95% CI 0.57 to 1.24)		SR	1a

13.1.5 In women with an uncomplicated singleton pregnancy whose pregnancies progress beyond 41 weeks, does serial antenatal monitoring result in worse maternal and perinatal outcomes than induction of labour?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Crowley, 2003	578	26 RCTs	Complex versus simple fetal monitoring of post-term pregnancy (from 42 weeks)	Induction of labour Perinatal death Caesarean section	Induction of labour: (1 trial, n = 145): Peto OR 2.10 (95% CI 1.10 to 4.01) Perinatal death: Peto OR 7.49 (95% CI 0.15 to 377.66) Caesarean section: Peto OR 2.03 (95% CI 0.79 to 5.20)		SR	1a

13.2 Breech presentation at term

13.2.1 What is the prevalence of breech presentation at term and what are the outcomes associated with it?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Danielian et al., 1996	623	1645 infants delivered alive at term > 37 weeks after breech presentation in a Scottish region from 1981 to 1990 269 had handicap	Observational study	Long-term outcome of infants delivered in breech presentation at term by intended mode of delivery Included: handicap, developmental delay, neurological deficit, psychiatric referral	Handicap occurred in 269/1387 (16.9%) of infants Handicap by mode of delivery: Elective CS: 100/482 (20.7%) Planned vaginal delivery: 169/905 (18.7%)	There were no significant differences in the frequency of handicap by intended mode of delivery	CH	2b
Krebs et al., 1999	624	345 infants with cerebral palsy born in East Denmark from 1979 and 1986 Total of 233,764 infants	Observational study	Presentation	Rates of cerebral palsy in term infants according to presentation at birth: CP / All / OR (95% CI) Breech 5.2% / 3.5% / 1.56 (0.9 to 2.4) Vertex 90.7% / 93.4% / 0.7 (0.5 to 1.0) Other 14% / 3.1% / 1.3 (0.7 to 2.2)		CCS	3
Milsom et al., 2002	625	225 deliveries at 37 weeks in 3 hospitals in Sweden from 1985 to 1991	Observational study	Birth asphyxia defined as Apgar score < 7 at 5 minutes	Association of breech delivery with birth asphyxia: OR (95% CI) 20.3 (3.0 to 416.5) (adjusted)		CCS	3

13.2.2 Does external cephalic version (ECV) at term reduce the likelihood of breech presentation?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hofmeyr and Kulier, 1999	597	6 RCTs, 612 women with a breech presentation at term (36 or more weeks) and no contraindication to external cephalic version: 1in South Africa, 1 in Zimbabwe, 2 in the Netherlands, 1 in Denmark, 1 in the USA Cochrane review, updated 1999	ECV at term (36 or more weeks) (with or without the use of tocolysis) vs. no ECV	Noncephalic births	ECV: 99/303 (32.7%) No ECV: 242/309 (78.3%) RR: 0.42 (95% CI 0.35 to 0.50)	Results were consistent from study to study	SR	1a

13.2.3 When should ECV be performed?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hofmeyr, 1994	589	3 RCTs, 889 women with singleton breech presentation in Sweden, Zimbabwe and the Netherlands Cochrane systematic review, updated 1994	ECV before 37 weeks of gestation vs. no ECV attempt	Noncephalic births	ECV: 197/434 (38.5%) No ECV: 204/455 (44.8%) RR: 1.02 (95% CI 0.89 to 1.17)	Results were consistent from study to study	SR	1a

13.2.4 Does tocolysis increase the chance of successful version?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Hofmeyr, 2002	594	6 RCTs, 617 women with breech presentation at term and no contraindication to ECV Cochrane review, updated 2001	Routine betamimetic tocolysis for ECV at term vs. no tocolysis	Failed ECV	Tocolysis: 136/317 (42.9%) No tocolysis: 176/300 (58.7%) RR: 0.74 (95% CI 0.64 to 0.87)	Results were consistent from study to study	SR of RCT & QR	1a

13.2.5 Does pelvimetry predict who will deliver vaginally compared with clinical examination?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
van Loon et al., 1990	626	235 women with singleton breech presentation at term Term defined as duration 37 weeks of gestation or more Randomised between January 1993 and April 1996 US hospital	Pelvimetry results revealed to obstetricians vs. pelvimetry results not disclosed to obstetricians (mode of delivery decided clinically)	Vaginal delivery Overall caesarean section rate Emergency caesarean section rate	Vaginal delivery: Pelvimetry results revealed: 68/118 (57.6% caesarean) Pelvimetry results not disclosed: 58/117 (49.6% caesarean) Absolute risk reduction: 8.0% (95% CI –3.8% to –19.8%) Overall caesarean section rate: Pelvimetry results revealed: 50/118 (42.2% caesarean) Pelvimetry results not disclosed: 59/117 (50.4% caesarean) Absolute risk reduction: 8.2% (95% CI –3.8% to –19.8%) Emergency caesarean section rate: Pelvimetry results revealed: 22/118 (18.6% caesarean) Pelvimetry results not disclosed: 41/117 (35.0% caesarean) Risk reduction: 16.4 % (95% CI 6.6% to 22.6%) NNT: 6	Computer-generated randomisation No description of allocation concealment Women were analysed by intention to treat	RCT	1b

13.2.6 What is the effect of planned caesarean section compared with planned vaginal birth for mother and baby outcomes or singleton term breech presentation?

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Mother outcomes								
Hofmeyr and Hannah, 2000	627	3 RCTs, 2396 women with a breech presentation at term suitable for vaginal delivery Cochrane systematic review, updated 2000	Planned caesarean section vs. planned vaginal delivery	Maternal morbidity (pooled) Maternal morbidity measures included: postpartum bleeding (including blood transfusion), genital tract injury, wound infection, dehiscence or breakdown, maternal systemic infection, early postpartum depression, time in hospital after delivery	Planned caesarean section: 107/1169 (9.2%) Planned vaginal delivery: 106/1227 (8.6%) RR: 1.29 (95% CI 1.03 to 1.61)	Results generally consistent from study to study	SR of RCT	1b
Hannah et al., 2000	628	2088 women with a singleton fetus in a frank or complete breech presentation at term International randomised trial at 121 centres in 26 countries (high and low perinatal mortality rates)	Planned caesarean section vs. planned vaginal delivery	Maternal mortality	Planned caesarean section: 0/1041 Planned vaginal delivery: 1/1041	Centrally-controlled randomisation Analysis was by intention to treat	RCT	1b
Gimovsky et al., 1983	629	105 women with non-frank breech presentations at term US hospital	Trial of labour vs. elective caesarean section	Maternal mortality	No report of maternal deaths	Method of randomisation not indicated	RCT	1b
Collea et al., 1980	630	208 women with frank breech presentation at term US hospital	Trial of labour vs. elective caesarean section	Maternal mortality	No report of maternal deaths	Method of randomisation not indicated	RCT	1b

13.2.6 What is the effect of planned caesarean section compared with planned vaginal birth for mother and baby outcomes or singleton term breech presentation? (continued)

Study	Ref.	Population	Intervention	Outcomes	Results	Comments	Study type	EL
Baby outcomes								
Hofmeyr and Hannah, 2000	627	3 RCTs, 2396 women with a breech presentation at term suitable for vaginal delivery Cochrane systematic review, updated 2000	Planned caesarean section vs. planned vaginal delivery	Perinatal and neonatal death (excluding fatal anomalies)	Planned caesarean section: 3/1166 (0.26%) Planned vaginal delivery: 14/1222 (1.15%) RR: 0.29 (95% CI 0.10 to 0.86) Countries with low (20/1000 or less) perinatal mortality rate was 0.26 (95% CI 0.03 to 2.00)	Planned caesarean section is associated with a 70% decrease in mortality compared with planned vaginal delivery for breech delivery at term	SR of RCT	1a
Hofmeyr and Hannah, 2000	627	3 RCTs involving 2396 women with a breech presentation at term suitable for vaginal delivery Cochrane systematic review, updated 2000	Planned caesarean section vs. planned vaginal delivery	Perinatal death or neonatal morbidity Events included: birth trauma, seizures occurring at less than 24 hours of age or requiring two or more drugs to control them, Apgar score of < 4 at 5 minutes, cord blood base deficit of at least 15, hypotonia for at least 2 hours, stupor (decreased response to pain or coma), intubation and ventilation for at least 24 hours, tube feeding for 4 days or more, admission to neonatal unit for longer than 4 days	Planned caesarean section: 20/1132 (0.18%) Planned vaginal delivery: 66/1152 (5.73%) RR: 0.31 (95% CI 0.19 to 0.52) Countries with low (20/1000 or less) perinatal mortality rate was 0.13 (95%CI 0.05 to 0.31)	Planned caesarean section is associated with a 70% decrease in death or morbidity compared to planned vaginal delivery for breech delivery at term	SR of RCT	1a
Hofmeyr and Hannah, 2000	627	3 RCTs involving 2396 women with a breech presentation at term suitable for vaginal delivery Cochrane systematic review, updated 2000	Planned caesarean section vs. planned vaginal delivery	5-minute Apgar < 7	Planned caesarean section: 11/1164 (0.94%) Planned vaginal delivery: 38/1211 (3.14%) RR: 0.32 (95% CI 0.17 to 0.61)		SR of RCT	1a

References

1. Expert Maternity Group. Woman centred care. In: Department of Health. *Changing Childbirth. Report of the Expert Maternity Group*. London: HMSO; 1993. p.5–8.
2. Garcia J, Loftus-Hills A (National Perinatal Epidemiology Unit: Oxford University). An overview of research on women's views of antenatal care. Personal communication 2001.
3. Singh D, Newburn M, editors. *Access to Maternity Information and Support; the Experiences and Needs of Women Before and After Giving Support*. London: National Childbirth Trust; 2000.
4. Cochrane AL. *Effectiveness and efficiency. Random reflections on health services*. London: Nuffield Provincial Hospitals Trust; 1972.
5. Department of Health. Screening for infectious diseases in pregnancy: standards to support the UK antenatal screening programme. [In preparation]. 2003.
6. National Institute for Clinical Excellence. *Information for national collaborating centres and guideline development groups.* Guideline development process series 3. London: Oaktree Press; 2001.
7. Henderson J, McCandlish R, Kumiega L, Petrou S. Systematic review of economic aspects of alternative modes of delivery. *BJOG* 2001;108:149–57.
8. Bekker H, Thornton JG, Airey CM, Connelly JB, Hewison J, Robinson MB, *et al*. Informed decision making: An annotated bibliography and systematic review. *Health Technology Assessment* 1999;3(1):1–156.
9. Department of Health. *Changing childbirth. Report of the Expert Maternity Group*. London: HMSO; 1993.
10. Audit Commission for Local Authorities, NHS in England and Wales. *First class delivery: improving maternity services in England and Wales*. London: Audit Commission Publications; 1997. p. 1–98.
11. Murray J, Cuckle H, Sehmi I, Wilson C, Ellis A. Quality of written information used in Down syndrome screening. *Prenatal Diagnosis* 2001;21:138–42.
12. Thornton JG, Hewison J, Lilford RJ, Vail A. A randomised trial of three methods of giving information about prenatal testing. *British Medical Journal* 1995;311:1127–30.
13. O'Cathain A, Walters SJ, Nicholl JP, Thomas KJ, Kirkham M. Use of evidence based leaflets to promote informed choice in maternity care: randomised controlled trial in everyday practice. [comment]. *British Medical Journal* 2002;324:643.
14. Stapleton H. Qualitative study of evidence based leaflets in maternity care. *British Medical Journal* 2002;324:639.
15. Dodds R, Newburn M. Support during screening: an NCT report. *Modern Midwife* 1997;7:23–6.
16. Carroll JC, Brown JB, Reid AJ, Pugh P. Women's experience of maternal serum screening. *Canadian Family Physician* 2000;46:614–20.
17. Marteau TM, Slack J, Kidd J, Shaw, RW. Presenting a routine screening test in antenatal care: practice observed. *Public Health* 1992;106(2):131–41.
18. Smith D, Shaw RW, Marteau T. Lack of knowledge in health professionals: a barrier to providing information to patients. *Quality in Health Care* 1994;3:75–8.
19. Smith DK, Shaw RW, Slack J, Marteau TM. Training obstetricians and midwives to present screening tests: evaluation of two brief interventions. *Prenatal Diagnosis* 1995;15:317–24.
20. Green JM. Serum screening for Down's syndrome: experiences of obstetricians in England and Wales. *British Medical Journal* 1994;309:769–72.
21. Michie S, Marteau TM. Non-response bias in prospective studies of patients and health care professionals. *International Journal of Social Research Methodology* 1999;2:203–12.
22. Marteau TM. Towards informed decisions about prenatal testing: a review. *Prenatal Diagnosis* 1995;15(13):1215–26.
23. National Health Service. *The Pregnancy Book*. London: Health Promotion England; 2001.
24. Bro Taf Health Authority. *Tests for you and your baby during pregnancy*. Cardiff, Wales: Bro Taf Health Authority; 2000.
25. Nolan ML, Hicks C. Aims, processes and problems of antenatal education as identified by three groups of childbirth teachers. *Midwifery* 1997;13:179–88.
26. Johnson R, Slade P. Does fear of childbirth during pregnancy predict emergency caesarean section? *BJOG* 2002;109:1213–21.
27. Gagnon AJ. Individual or group antenatal education for childbirth/parenthood. *Cochrane Database of Systematic Reviews* 2001;(3).
28. Hibbard BM, Robinson JO, Pearson JF, Rosen M, Taylor A. The effectiveness of antenatal education. *Health Education Journal* 1979;38:39–46.
29. Rautauva P, Erkkola R, Sillanpaa M. The outcome and experiences of first pregnancy in relation to the mother's childbirth knowledge: The Finnish Family Competence Study. *Journal of Advanced Nursing* 1991;16:1226–32.
30. Lumley J, Brown S. Attenders and nonattenders at childbirth education classes in Australia: how do they and their births differ? *Birth* 1993;20:123–30.
31. Sullivan P. Felt learning needs of pregnant women. *Canadian Nurse* 1993;89:42.
32. Villar J, Khan-Neelofur D. Patterns of routine antenatal care for low – risk pregnancy. *Cochrane Database of Systematic Reviews* 2003;(1).

33. Hodnett ED. Continuity of caregivers for care during pregnancy and childbirth. *Cochrane Database of Systematic Reviews* 2001;(3).
34. Waldenstrom U, Turnbull D. A systematic review comparing continuity of midwifery care with standard maternity services. *British Journal of Obstetrics and Gynaecology* 1998;105:1160–70.
35. North Staffordshire Changing Childbirth Research Team. A randomised study of midwifery caseload care and traditional 'shared care'. *Midwifery* 2000;16:295–302.
36. Homer CS, Davis GK, Brodie PM, Sheehan A, Barclay LM, Wills J, *et al*. Collaboration in maternity care: a randomised controlled trial comparing community-based continuity of care with standard hospital care. *BJOG* 2001;108:16–22.
37. Homer CS, Davis GK, Brodie PM. What do women feel about community-based antenatal care? *Australian and New Zealand Journal of Public Health* 2000;24:590–5.
38. Biro MA, Waldenstrom U. Team midwifery care in a tertiary level obstetric service: a randomized controlled trial. *Birth* 2000;27:168–73.
39. Waldenstrom U. Does team midwife care increase satisfaction with antenatal, intrapartum, and postpartum care? A randomized controlled trial. [see comments.]. *Birth* 2000;27:156–67.
40. Blondel B, Breart G. Home visits for pregnancy complications and management of antenatal care: an overview of three randomized controlled trials. *British Journal of Obstetrics and Gynaecology* 1992;99:283–6.
41. Lilford RJ, Kelly M, Baines A, Cameron S, Cave M, Guthrie K, *et al*. Effect of using protocols on medical care: randomised trial of three methods of taking an antenatal history. *British Medical Journal* 1992;305:1181–4.
42. Elbourne D, Richardson M, Chalmers I, Waterhouse I, Holt E. The Newbury Maternity Care Study: a randomized controlled trial to assess a policy of women holding their own obstetric records. *British Journal of Obstetrics and Gynaecology* 1987;94:612–19.
43. Homer CS, Davis GK, Everitt LS. The introduction of a woman-held record into a hospital antenatal clinic: the bring your own records study. *Australian and New Zealand Journal of Public Health* 1999;39:54–7.
44. Lovell A, Zander LI, James CE, Foot S, Swan AV, Reynolds A. The St. Thomas's Hospital maternity case notes study: a randomised controlled trial to assess the effects of giving expectant mothers their own maternity case notes. *Paediatric and Perinatal Epidemiology* 1987;1:57–66.
45. Petrou S, Kupek E, Vause S, Maresh M. Antenatal visits and adverse perinatal outcomes: results from a British population-based study. *European Journal of Obstetrics Gynecology and Reproductive Biology* 2003;106:40–9.
46. Carroli G, Villar J, Piaggio G, Khan-Neelofur D, Gulmezoglu M, Mugford M, *et al*. WHO systematic review of randomised controlled trials of routine antenatal care. *Lancet* 2001;357:1565–70.
47. Clement S, Sikorski J, Wilson J, Das S, Smeeton N. Women's satisfaction with traditional and reduced antenatal visit schedules. *Midwifery* 1996;12:120–8.
48. Hildingsson I, Waldenstrom U, Radestad I. Women's expectations on antenatal care as assessed in early pregnancy: Number of visits, continuity of caregiver and general content. *Acta Obstetricia et Gynecologica Scandinavica* 2002;81:118–25.
49. Henderson J, Roberts T, Sikorski J, Wilson J, Clement S. An economic evaluation comparing two schedules of antenatal visits. *Journal of Health Services and Research Policy* 2000;5:69–75.
50. Kaminski M, Blondel B, Breart G. Management of pregnancy and childbirth in England and Wales and in France. *Paediatric and Perinatal Epidemiology* 1988;2:13–24.
51. Ryan, M, Ratcliffe, J, Tucker, J. Using willingness to pay to value alternative models of antenatal care. *Social Science and Medicine* 1997;44(3):371–80.
52. Crowther CA, Kornman L, O'Callaghan S, George K, Furness M, Willson K. Is an ultrasound assessment of gestational age at the first antenatal visit of value? A randomised clinical trial. [see comments]. *British Journal of Obstetrics and Gynaecology* 1999;106:1273–9.
53. Savitz DA, Terry JW Jr, Dole N, Thorp JM Jr, Siega-Riz AM, Herring AH. Comparison of pregnancy dating by last menstrual period, ultrasound scanning, and their combination. *American Journal of Obstetrics and Gynecology* 2002;187:1660–6.
54. Backe B, Nakling J. Term prediction in routine ultrasound practice. *Acta Obstetricia et Gynecologica Scandinavica* 1994;73:113–8.
55. Tunon K, Eik-Nes SH, Grottum P. A comparison between ultrasound and a reliable last menstrual period as predictors of the day of delivery in 15000 examinations. *Ultrasound in Obstetrics and Gynecology* 1996;8:178–85.
56. Blondel B, Morin I, Platt RW, Kramer MS, Usher R, Breart G. Algorithms for combining menstrual and ultrasound estimates of gestational age: consequences for rates of preterm and post-term birth. *BJOG* 2002;109:718–20.
57. Neilson JP. Ultrasound for fetal assessment in early pregnancy. *Cochrane Database of Systematic Reviews* 1999;(2).
58. Moutquin J-M, Gagnon R, Rainville C, Giroux L, Amyot G, Bilodeau R, *et al*. Maternal and neonatal outcome in pregnancies with no risk factors. *Canadian Medical Association Journal* 1987;137:728–32.
59. Mohamed H, Martin C, Haloob R. Can the New Zealand antenatal scoring system be applied in the United Kingdom? *Journal of Obstetrics and Gynaecology* 2002;22:389–91.
60. Doyle P, Roman E, Beral V, Brookes M. Spontaneous abortion in dry cleaning workers potentially exposed to perchloroethylene. *Occupational and Environmental Medicine* 1997;54:848–53.
61. Kolstad HA, Brandt LP, Rasmussen K. [Chlorinated solvents and fetal damage. Spontaneous abortions, low birth weight and malformations among women employed in the dry – cleaning industry]. [Danish]. *Ugeskrift for Laeger* 1990;152:2481–2.
62. Kyyronen P, Taskinen H, Lindbohm ML, Hemminki K, Heinonen OP. Spontaneous abortions and congenital malformations among women exposed to tetrachloroethylene in dry cleaning. *Journal of Epidemiology and Community Health* 1989;43:346–51.
63. Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: A meta-analysis. *Obstetrics and Gynecology* 2000;95:623–35.
64. Hanke W, Kalinka J, Makowiec-Dabrowska T, Sobala W. Heavy physical work during pregnancy: a risk factor for small-for-gestational-age babies in Poland. *American Journal of Industrial Medicine* 1999;36:200–5.

65. Kramer, MS. Nutritional advice in pregnancy. *Cochrane Database of Systematic Reviews* 2003;(1):1–10.
66. Abramsky L, Botting B, Chapple J, Stone D. Has advice on periconceptional folate supplementation reduced neural-tube defects? *Lancet* 1999;354:998–9.
67. Lumley J, Watson L, Watson M, Bower C. Periconceptional supplementation with folate and/or multivitamins for preventing neural tube defects. *Cochrane Database of Systematic Reviews* 2002;(1).
68. Li Z, Gindler J, Wang H, Berry RJ, Li S, Correa A, *et al*. Folic acid supplements during early pregnancy and likelihood of multiple births: a population-based cohort study. *Lancet* 2003;361:380–4.
69. Royal College of Obstetricians and Gynaecologists. *Periconceptual folic acid and food fortification in the prevention of neural tube defects*. Scientific Advisory Committee Opinion Paper No. 4, London: RCOG; 2003.
70. Daly LE, Kirke PN, Molloy A, Weir DG, Scott JM. Folate levels and neural tube defects. Implications for prevention. *JAMA* 1995;274:1698–702.
71. Expert Advisory Group. Department of Health, Scottish office Home and Health Department, Welsh Office, and Department of Health and Social Services, Northern Ireland. *Folic acid and the prevention of neural tube defects*. London: HMSO; 1992.
72. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. MRC Vitamin Study Research Group [see comments]. *Lancet* 1991;338:131–7.
73. Wald NJ, Law MR, Morris JK, Wald DS. Quantifying the effect of folic acid. *Lancet* 2001;358:2069–73.
74. Mahomed K. Iron and folate supplementation in pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).
75. Hemminki E, Rimpela U. A randomized comparison of routine versus selective iron supplementation during pregnancy. *Journal of the American College of Nutrition* 1991;10:3–10.
76. Mahomed K. Iron supplementation in pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).
77. British Medical Association, Royal Pharmaceutical Society of Great Britain. *British National Formulary*. London: March 2003. p. 439–40.
78. van den Broek N, Kulier R, Gulmezoglu AM, Villar J. Vitamin A supplementation during pregnancy. *Cochrane Database of Systematic Reviews* 2003;(1):1–21.
79. Dolk HM, Nau H, Hummler H, Barlow SM. Dietary vitamin A and teratogenic risk: European Teratology Society discussion paper. *European Journal Obstetrics and Gynecology Reproductive Biology* 1999;83:31–6.
80. Oakley GP Jr, Erickson JD. Vitamin A and birth defects. Continuing caution is needed. *New England Journal of Medicine* 1995;333:1414–15.
81. Rothman KJ, Moore LL, Singer MR, Nguyen US, Mannino S, Milunsky A. Teratogenicity of high vitamin A intake. *New England Journal of Medicine* 1995;333:1369–73.
82. Mahomed K, Gulmezoglu, A. M. Vitamin D supplementation in pregnancy. *Cochrane Database of Systematic Reviews* 2000;(1).
83. Southwick FS, Purich DL. Intracellular pathogenesis of listeriosis. *New England Journal of Medicine* 1996;334:770–6.
84. Public Health Laboratory Service Press Release. Disease Facts: Salmonella. 2001.
85. British Nutrition Foundation. BNF Information. Diet through Life: Pregnancy. 2003. [www.nutrition.org.uk/] Accessed 20 August 2003.
86. Ledward RS. Drugs in pregnancy. In: Studd J, editor *Progress in Obstetrics and Gynaecology*. Edinburgh: Churchill Livingstone; 1998. p. 19–46.
87. Fugh-Berman A, Kronenberg F. Complementary and alternative medicine (CAM) in reproductive-age women: a review of randomized controlled trials. *Reproductive Toxicology* 2003;17:137–52.
88. Moore ML. Complementary and alternative therapies. *Journal of Perinatal Education* 2002;11:39–42.
89. Pinn G, Pallett L. Herbal medicine in pregnancy. *Complementary Therapies in Nursing and Midwifery* 2002;8:77–80.
90. Leung K-Y, Lee Y-P, Chan H-Y, Lee C-P, Tang MHY. Are herbal medicinal products less teratogenic than Western pharmaceutical products? *Acta Pharmacologica Sinica* 2002;23:1169–72.
91. Hepner DL, Harnett M, Segal S, Camann W, Bader AM, Tsen LC. Herbal medicine use in parturients. *Anesthesia and Analgesia* 2002;94:690–3.
92. Maats FH, Crowther CA. Patterns of vitamin, mineral and herbal supplement use prior to and during pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2002;42:494–6.
93. Tsui B, Dennehy CE, Tsourounis C. A survey of dietary supplement use during pregnancy at an academic medical center. *American Journal of Obstetrics and Gynecology* 2001;185:433–7.
94. Medicines Control Agency. *Safety of Herbal Medicinal Products*. London; 2002. p. 22–23.
95. Ernst E. Herbal medicinal products during pregnancy: are they safe? *BJOG* 2002;109:227–35.
96. Dove D, Johnson P. Oral evening primrose oil: Its effect on length of pregnancy and selected intrapartum outcomes in low-risk nulliparous women. *Journal of Nurse-Midwifery* 1999;44:320–4.
97. Simpson M. Raspberry leaf in pregnancy; its safety and efficacy in labor. *Journal of Midwifery and Women's Health* 2001;46(2):51–9.
98. Gallo M, Sarkar M, Au W, Pietrzak K, Comas B, Smith M, *et al*. Pregnancy outcome following gestational exposure to Echinacea: a prospective controlled study. *Archives of Internal Medicine* 2000;160:3141–3.
99. Goldman RD, Koren G, Motherisk Team. Taking St John's wort during pregnancy. *Canadian Family Physician* 2003;49:29–30.
100. Clapp JF III, Simonian S, Lopez B, Appleby-Wineberg S, Harcar-Sevcik R. The one-year morphometric and neurodevelopmental outcome of the offspring of women who continued to exercise regularly throughout pregnancy. *American Journal of Obstetrics and Gynecology* 1998;178:594–9.
101. Kramer MS. Aerobic exercise for women during pregnancy. *Cochrane Database of Systematic Reviews* 2002;(4).

102. Camporesi EM. Diving and pregnancy. *Seminars in Perinatology* 1996;20:292–302.
103. Read JS, Klebanoff MA. Sexual intercourse during pregnancy and preterm delivery: effects of vaginal microorganisms. *American Journal of Obstetrics and Gynecology* 1993;168:514–19.
104. Klebanoff MA, Nugent RP, Rhoads GG. Coitus during pregnancy: is it safe? *Lancet* 1984;2:914–7.
105. Berghella V, Klebanhoff M, McPherson C. Sexual intercourse association with asymptomatic bacterial vaginosis and *Trichomonas vaginalis* treatment in relationship to preterm birth. *American Journal of Obstetrics and Gynecology* 2002;187:1277–82.
106. Walpole I, Zubrick S, Pontre J. Is there a fetal effect with low to moderate alcohol use before or during pregnancy? *Journal of Epidemiology and Community Health* 1990;44:297–301.
107. Borges G, Lopez-Cervantes M, Medina-Mora ME, Tapia-Conyer R, Garrido F. Alcohol consumption, low birth weight, and preterm delivery in the national addiction survey (Mexico). *International Journal of the Addictions* 1993;28(4):355–68.
108. Holzman C, Paneth N, Little R, Pinto-Martin J. Perinatal brain injury in premature infants born to mothers using alcohol in pregnancy. *Pediatrics* 1995;95:66–73.
109. Aronson M, Hagberg B, Gillberg C. Attention deficits and autistic spectrum problems in children exposed to alcohol during gestation: A follow-up study. *Developmental Medicine and Child Neurology* 1997;39:583–7.
110. Abel EL. Fetal alcohol syndrome: the 'American Paradox'. *Alcohol and Alcoholism* 1998;33:195–201.
111. Royal College of Obstetricians and Gynaecologists. *Alcohol consumption in pregnancy*. Guideline No. 9. London: RCOG; 1999.
112. Lumley J, Oliver S, Waters E. Interventions for promoting smoking cessation during pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2). 2001.
113. Owen L, McNeill A, Callum C. Trends in smoking during pregnancy in England, 1992–7: quota sampling surveys. *British Medical Journal* 1998;317:728.
114. DiFranza JR, Lew, RA. Effect of maternal cigarette smoking on pregnancy complications and sudden infant death syndrome. *Journal of Family Practice* 1995;40(4):385–394.
115. Ananth CV, Smulian JC, Vintzileos AM. Incidence of placental abruption in relation to cigarette smoking and hypertensive disorders during pregnancy: A meta-analysis of observational studies. *Obstetrics and Gynecology* 1999;93:622–8.
116. Castles A, Adams EK, Melvin CL, Kelsch C, Boulton ML. Effects of smoking during pregnancy: Five meta-analyses. *American Journal of Preventive Medicine* 1999;16:208–15.
117. Shah NR, Bracken MB. A systematic review and meta-analysis of prospective studies on the association between maternal cigarette smoking and preterm delivery. *American Journal of Obstetrics and Gynecology* 2000;182:465–72.
118. Wyszynski DF, Duffy DL, Beaty TH. Maternal cigarette smoking and oral clefts: a meta – analysis. *Cleft Palate-Craniofacial Journal* 1997;34:206–10.
119. Conde-Agudelo A, Althabe F, Belizan JM, Kafury-Goeta AC. Cigarette smoking during pregnancy and risk of preeclampsia: a systematic review. *American Journal of Obstetrics and Gynecology* 1999;181:1026–35.
120. Clausson B, Cnattingius S, Axelsson O. Preterm and term births of small for gestational age infants: A population-based study of risk factors among nulliparous women. *British Journal of Obstetrics and Gynaecology* 1998;105:1011–7.
121. Raymond EG, Cnattingius S, Kiely JL. Effects of maternal age, parity and smoking on the risk of stillbirth. *British Journal of Obstetrics and Gynaecology* 1994;101:301–6.
122. Kleinman JC, Pierre MB Jr, Madans JH, Land GH, Schramm WF. The effects of maternal smoking on fetal and infant mortality. *American Journal of Epidemiology* 1988;127:274–82.
123. Lumley J. Stopping smoking. *British Journal of Obstetrics and Gynaecology* 1987;94:289–92.
124. MacArthur C, Knox EG, Lancashire RJ. Effects at age nine of maternal smoking in pregnancy: experimental and observational findings. *BJOG* 2001;108:67–73.
125. von Kries R, Toschke AM, Koletzko B, Slikker W Jr. Maternal smoking during pregnancy and childhood obesity. *American Journal of Epidemiology* 2002;156:954–61.
126. Faden VB, Graubard BI. Maternal substance use during pregnancy and developmental outcome at age three. *Journal of Substance Abuse* 2000;12:329–40.
127. Thorogood M, Hillsdon M, Summerbell C. Changing behaviour: cardiovascular disorders. *Clinical Evidence* 2002;8:37–59.
128. Law M, Tang JL. An analysis of the effectiveness of interventions intended to help people stop smoking. *Archives of Internal Medicine* 1995;155:1933–41.
129. Wisborg K, Henriksen TB, Jespersen LB, Secher NJ. Nicotine patches for pregnant smokers. *Obstetrics and Gynecology* 2000;96:967–71.
130. Hajek P, West R, Lee A, Foulds J, Owen L, Eiser JR, *et al*. Randomized controlled trial of a midwife-delivered brief smoking cessation intervention in pregnancy. *Addiction* 2001;96:485–94.
131. Stotts A, DiClemente CC, Dolan-Mullen P. One-to-one. A motivational intervention for resistant pregnant smokers. *Addictive Behaviors* 2002;27:275–92.
132. Moore L, Campbell R, Whelan A, Mills N, Lupton P, Misselbrook E, *et al*. Self help smoking cessation in pregnancy: cluster randomised controlled trial. *British Medical Journal* 2002;325:1383–6.
133. Li C, Windsor R, Perkins L, Lowe J, Goldenberg R. The impact on birthweight and gestational age of cotinine validated smoking reduction during pregnancy. *JAMA* 1993;269:1519–24.
134. Windsor R, Li C, Boyd N, Hartmann K. The use of significant reduction rates to evaluate health education methods for pregnant smokers: a new harm reduction – behavioral indicator. *Health Education and Behavior* 1999;26:648–62.
135. Fergusson DM, Horwood LJ, Northstone K, ALSPAC Study Team, Avon Longitudinal Study of Pregnancy and Childhood. Maternal use of cannabis and pregnancy outcome. *BJOG* 2002;109:21–7.

136. English DR, Hulse GK, Milne E, Holman CD, Bower CI. Maternal cannabis use and birth weight: a meta-analysis. *Addiction* 1997;92:1553–60.
137. Royal College of Obstetricians and Gynaecologists. Advice on preventing deep vein thrombosis for pregnant women travelling by air. Scientific Advisory Committee Opinion paper No. 1. London: RCOG; 2001.
138. James KV, Lohr JM, Deshmukh RM, Cranley JJ. Venous thrombotic complications of pregnancy. *Cardiovascular Surgery* 1996;4:777–82.
139. McColl MD, Ramsay JE, Tait RC, Walker ID, McCall F, Conkie JA, *et al*. Risk factors for pregnancy associated venous thromboembolism. *Thrombosis and Haemostasis* 1997;78:1183–8.
140. Kierkegaard A. Incidence and diagnosis of deep vein thrombosis associated with pregnancy. *Acta Obstetricia et Gynecologica Scandinavica* 1983;62:239–43.
141. Scurr JH, Machin SJ, Bailey-King S, Mackie IJ, McDonald S, Coleridge Smith PD. Frequency and prevention of symptomless deep-vein thrombosis in long-haul flights: a randomised trial. *Lancet* 2001;357:1485–9.
142. World Health Organization. Travellers with special needs. In: Martinez L, editor. *International Travel and Health*. Geneva: World Health Organization; 2002.
143. Lewis G, Drife J, editors. *Why mothers die 1997–1999: The fifth report of the Confidential Enquiries into Maternal Deaths in the United Kingdom*. London: RCOG Press; 2001.
144. Johnson HC, Pring DW. Car seatbelts in pregnancy: the practice and knowledge of pregnant women remain causes for concern. *BJOG* 2000;107:644–7.
145. Chang A, Magwene K, Frand E. Increased safety belt use following education in childbirth classes. *Birth* 1987;14:148–52.
146. Klinich KD, Schneider LW, Moore JL, Pearlman MD. Investigations of crashes involving pregnant occupants. *Annual Proceedings, Association for the Advancement of Automotive Medicine* 2000;44:37–55.
147. Crosby WM, Costiloe JP. Safety of lap-belt restraint for pregnant victims of automobile collisions. *New England Journal of Medicine* 1971;284:632–6.
148. Crosby WM, King AI, Stout LC. Fetal survival following impact: improvement with shoulder harness restraint. *American Journal of Obstetrics and Gynecology* 1972;112:1101–6.
149. Wolf ME, Alexander BH, Rivara FP, Hickok DE, Maier RV, Starzyk PM. A retrospective cohort study of seatbelt use and pregnancy outcome after a motor vehicle crash. *Journal of Trauma-Injury Infection and Critical Care* 1993;34:116–19.
150. World Health Organization. Special groups. In: Martinez L, editor. *International Travel and Health*. Geneva: World Health Organization; 2002.
151. Hurley PA. International travel and the pregnant women. In: Studd J, editor. *Progress in Obstetrics and Gynaecology*. Edinburgh: Churchill Livingstone; 2003. p. 45–55.
152. Hurley P. Vaccination in pregnancy. *Current Obstetrics and Gynaecology* 1998;8:169–75.
153. Jothivijayarani A. Travel considerations during pregnancy. *Primary Care Update for Ob/Gyns* 2002;9:36–40.
154. World Health Organization. Treatment of P. vivax, P. ovale and P. malariae infections. In: Martinez L, editor. *International Travel and Health*. Geneva: World Health Organization; 2002. [www.who.int/ith/chapter07_04.html] Accessed 4 September 2003.
155. Luxemburger C, McGready R, Kham A, Morison L, Cho T, Chongsuphajaisiddhi T, *et al*. Effects of malaria during pregnancy on infant mortality in an area of low malaria transition. *American Journal of Epidemiology* 2001;154:459–65.
156. World Health Organization. World malaria situation in 1993, Part 1. *Weekly Epidemiological Record* 1996;71:17–24.
157. Linday S, Ansell J, Selman C, Cox V, Hamilton K, Walraven G. Effect of pregnancy on exposure to malaria mosquitoes. *Lancet* 2000;355:1972.
158. Schaefer C, Peters PW. Intrauterine diethyltoluamide exposure and fetal outcome. *Reproductive Toxicology* 1992;6:175–6.
159. Dolan G, ter Kuile FO, Jacoutot V. Bed nets for the prevention of malaria and anaemia in pregnancy. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 1993;87:620–6.
160. Pearce G. Travel insurance and the pregnant woman. *MIDIRS Midwifery Digest* 1997;7:164.
161. Brown H, Campbell H. Special considerations for pregnant travellers. *Modern Medicine of Australia* 1999;42:17–20.
162. Tucker R. Ensure pregnant travellers know the risks. *Practice Nurse* 1999;18:458–66.
163. Rose SR. Pregnancy and travel. *Emergency Medicine Clinics of North America* 1997;15:93–111.
164. Baron TH, Ramirez B, Richter JE. Gastrointestinal motility disorders during pregnancy. *Annals of Internal Medicine* 1993;118:366–75.
165. Weigel RM, Weigel MM. Nausea and vomiting of early pregnancy and pregnancy outcome. A meta-analytical review. *British Journal of Obstetrics and Gynaecology* 1989;96:1312–8.
166. Whitehead SA, Andrews PL, Chamberlain GV. Characterisation of nausea and vomiting in early pregnancy: a survey of 1000 women. *Journal of Obstetrics and Gynaecology* 1992;12:364–9.
167. Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy. *British Journal of General Practice* 1993;43:245–8.
168. Feldman M. Nausea and vomiting. In: Sleisenger MH, Fordtran JS, editors. *Gastrointestinal disease*. Philadelphia: WB Saunders; 1989. p. 229–31.
169. Klebanoff MA, Mills JL. Is vomiting during pregnancy teratogenic? *British Medical Journal* 1986;292:724–6.
170. Smith C, Crowther C, Beilby J, Dandeaux J. The impact of nausea and vomiting on women: a burden of early pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2000;40:397–401.
171. Attard CL, Kohli MA, Coleman S, Bradley C, Hux M, Atanackovic G, *et al*. The burden of illness of severe nausea and vomiting of pregnancy in the United States. *American Journal of Obstetrics and Gynecology* 2002;186:S220–7.
172. Vutyavanich T, Kraisarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. *Obstetrics and Gynecology* 2001;97:577–82.

173. Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).
174. Murphy PA. Alternative therapies for nausea and vomiting of pregnancy. *Obstetrics and Gynecology* 1998;91:149–55.
175. Keating A, Chez RA. Ginger syrup as an antiemetic in early pregnancy. *Alternative Therapies in Health and Medicine* 2002;8:89–91.
176. Vickers AJ. Can acupuncture have specific effects on health? A systematic review of acupuncture antiemesis trials. *Journal of the Royal Society of Medicine* 1996;89:303–11.
177. Norheim AJ, Pedersen EJ, Fonnebo V, Berge L. Acupressure treatment of morning sickness in pregnancy. A randomised, double-blind, placebo-controlled study. *Scandinavian Journal of Primary Health Care* 2001;19:43–7.
178. Knight B, Mudge C, Openshaw S, White A, Hart A. Effect of acupuncture on nausea of pregnancy: a randomized, controlled trial. *Obstetrics and Gynecology* 2001;97:184–8.
179. Werntoft E, Dykes AK. Effect of acupressure on nausea and vomiting during pregnancy: a randomized, placebo-controlled, pilot study. *Journal of Reproductive Medicine* 2001;46:835–9.
180. Smith C, Crowther C, Beilby J. Acupuncture to treat nausea and vomiting in early pregnancy: a randomized controlled trial. *Birth* 2002;29:1–9.
181. Smith C, Crowther C, Beilby J. Pregnancy outcome following womens' participation in a randomised controlled trial of acupuncture to treat nausea and vomiting in early pregnancy. *Complementary Therapies in Medicine* 2002;10:78–83.
182. Mazzotta P, Magee LA. A risk – benefit assessment of pharmacological and nonpharmacological treatments for nausea and vomiting of pregnancy. *Drugs* 2000;59:781–800.
183. Magee LA, Mazzotta P, Koren G. Evidence-based view of safety and effectiveness of pharmacologic therapy for nausea and vomiting of pregnancy (NVP). *American Journal of Obstetrics and Gynecology* 2002;186:S256–61.
184. Marrero JM, Goggin PM, Caestecker JS. Determinants of pregnancy heartburn. *British Journal of Obstetrics and Gynaecology* 1992;99:731–4.
185. Knudsen A, Lebech M, Hansen M. Upper gastrointestinal symptoms in the third trimester of the normal pregnancy. *European Journal of Obstetrics Gynecology and Reproductive Biology* 1995;60(1):29–33.
186. Bainbridge ET, Temple JG, Nicholas SP, Newton JR, Boriah V. Symptomatic gastro-esophageal reflux in pregnancy. A comparative study of white Europeans and Asians in Birmingham. *British Journal of Clinical Practice* 1983;37:53–7.
187. Shaw RW. Randomized controlled trial of Syn-Ergel and an active placebo in the treatment of heartburn of pregnancy. *Journal of International Medical Research* 1978;6:147–51.
188. Lang GD, Dougall A. Comparative study of Algicon suspension and magnesium trisilicate mixture in the treatment of reflux dyspepsia of pregnancy. *British Journal of Clinical Practice* 1989;66:48–51.
189. Association of the British Pharmaceutical Industry. *ABPI Compendium of Data Sheets and Summaries of Product Characteristics. Medicines Compendium*. London: Datapharm Communications; 2001.
190. Atlay RD, Parkinson DJ, Entwistle GD, Weekes AR. Treating heartburn in pregnancy: comparison of acid and alkali mixtures. *British Medical Journal* 1978;2:919–20.
191. Rayburn W, Liles E, Christensen H, Robinson M. Antacids vs. antacids plus non-prescription ranitidine for heartburn during pregnancy. *International Journal of Gynaecology and Obstetrics* 1999;66:35–7.
192. Larson JD, Patatanian E, Miner PB Jr, Rayburn WF, Robinson MG. Double-blind, placebo-controlled study of ranitidine for gastroesophageal reflux symptoms during pregnancy. *Obstetrics and Gynecology* 1997;90:83–7.
193. Magee LA, Inocencion G, Kamboj L, Rosetti F, Koren G. Safety of first trimester exposure to histamine H2 blockers. A prospective cohort study. *Digestive Diseases and Sciences* 1996;41:1145–9.
194. Nikfar S, Abdollahi M, Moretti ME, Magee LA, Koren G. Use of proton pump inhibitors during pregnancy and rates of major malformations: a meta-analysis. *Digestive Diseases and Sciences* 2002;47:1526–9.
195. Meyer LC, Peacock JL, Bland JM, Anderson HR. Symptoms and health problems in pregnancy: their association with social factors, smoking, alcohol, caffeine and attitude to pregnancy. *Paediatric and Perinatal Epidemiology* 1994;8:145–55.
196. Jewell DJ, Young G. Interventions for treating constipation in pregnancy. *Cochrane Database of Systematic Reviews* 2003;(1).
197. Abramowitz L, Sobhani I, Benifla JL, Vuagnat A, Darai E, Mignon M, *et al*. Anal fissure and thrombosed external hemorrhoids before and after delivery. *Diseases of the Colon and Rectum* 2002;45:650–5.
198. Wijayanegara H, Mose JC, Achmad L, Sobarna R, Permadi W. A clinical trial of hydroxyethylrutosides in the treatment of haemorrhoids of pregnancy. *Journal of International Medical Research* 1992;20:54–60.
199. Buckshee K, Takkar D, Aggarwal N. Micronized flavonoid therapy in internal hemorrhoids of pregnancy. *International Journal of Gynecology and Obstetrics* 1997;57:145–51.
200. Saleeby RG Jr, Rosen L, Stasik JJ, Riether RD, Sheets J, Khubchandani IT. Hemorrhoidectomy during pregnancy: risk or relief? *Diseases of the Colon and Rectum* 1991;3445:260–1.
201. Thaler E, Huch R, Huch A, Zimmermann R. Compression stockings prophylaxis of emergent varicose veins in pregnancy: A prospective randomised controlled study. *Swiss Medical Weekly* 2001;131:659–62.
202. Gulmezoglu, AM. Interventions for trichomoniasis in pregnancy. *Cochrane Database of Systematic Reviews* 2002;(3). CD000220.
203. French JI, McGregor JA, Draper D, Parker R, McFee J. Gestational bleeding, bacterial vaginosis, and common reproductive tract infections: risk for preterm birth and benefit of treatment. *Obstetrics and Gynecology* 1999;93:715–24.
204. Young GL, Jewell MD. Topical treatment for vaginal candidiasis in pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).
205. Greenwood CJ, Stainton MC. Back pain/discomfort in pregnancy: invisible and forgotten. *Journal of Perinatal Education* 2001;10:1–12.
206. Kristiansson P, Svardsudd K, von Schoultz B. Back pain during pregnancy: A prospective study. *Spine* 1996;21:702–9.
207. Ostgaard HC, Andersson GBJ, Karlsson K. Prevalence of back pain in pregnancy. *Spine* 1991;16:549–52.

208. Fast A, Shapiro D, Ducommun EJ, Friedman LW, Bouklas T, Floman Y. Low-back pain in pregnancy. *Spine* 1987;12:368–71.
209. Stapleton DB, MacLennan AH, Kristiansson P. The prevalence of recalled low back pain during and after pregnancy: A South Australian population survey. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 2002;42:482–5.
210. Mantle MJ, Greenwood RM, Currey HL. Backache in pregnancy. *Rheumatology and Rehabilitation* 1977;16:95–101.
211. Young G, Jewell, D. Interventions for preventing and treating pelvic and back pain in pregnancy. *Cochrane Database of Systematic Reviews* 2003;(1).
212. Field T, Hernandez-Reif M, Hart S, Theakston H, Schanberg S, Kuhn C. Pregnant women benefit from massage therapy. *Journal of Psychosomatic Obstetrics and Gynecology* 1999;20:31–8.
213. Ostgaard HC, Zetherstrom G, Roos-Hansson E, Svanberg B. Reduction of back and posterior pelvic pain in pregnancy. *Spine* 1994;19:894–900.
214. Noren L, Ostgaard S, Nielsen TF, Ostgaard HC. Reduction of sick leave for lumbar back and posterior pelvic pain in pregnancy. *Spine* 1997;22:2157–60.
215. Tesio L, Raschi A, Meroni M. Autotraction treatment for low-back pain in pregnancy: A pilot study. *Clinical Rehabilitation* 1994;8:314–19.
216. Guadagnino MR III. Spinal manipulative therapy for 12 pregnant patients suffering from low back pain. *Chiropractic Technique* 1999;11:108–11.
217. McIntyre IN, Broadhurst NA. Effective treatment of low back pain in pregnancy. *Australian Family Physician* 1996;25:S65–7.
218. Requejo SM, Barnes R, Kulig K, Landel R, Gonzalez S. The use of a modified classification system in the treatment of low back pain during pregnancy: A case report. *Journal of Orthopaedic and Sports Physical Therapy* 2002;32:318–26.
219. Owens K, Pearson A, Mason G. Symphysis pubis dysfunction: a cause of significant obstetric morbidity. *European Journal of Obstetrics Gynecology and Reproductive Biology* 2002;105:143–6.
220. Fry D, Hay-Smith J, Hough J, McIntosh J, Polden M, Shepherd J, *et al*. National clinic guideline for the care of women with symphysis pubis dysfunction. *Midwives* 1997;110:172–3.
221. Gould JS, Wissinger HA. Carpal tunnel syndrome in pregnancy. *Southern Medical Journal* 1978;71:144–5,154.
222. Voitk AJ, Mueller JC, Farlinger DE, Johnston RU. Carpal tunnel syndrome in pregnancy. *Canadian Medical Association Journal* 1983;128:277–81.
223. Padua L, Aprile I, Caliandro P, Carboni T, Meloni A, Massi S, *et al*. Symptoms and neurophysiological picture of carpal tunnel syndrome in pregnancy. *Clinical Neurophysiology* 2001;112:1946–51.
224. Courts RB. Splinting for symptoms of carpal tunnel syndrome during pregnancy. *Journal of Hand Therapy* 1995;8:31–4.
225. Ekman-Ordeberg G, Salgeback S, Ordeberg G. Carpal tunnel syndrome in pregnancy. A prospective study. *Acta Obstetricia et Gynecologica Scandinavica* 1987;66:233–5.
226. Stahl S, Blumenfeld Z, Yarnitsky D. Carpal tunnel syndrome in pregnancy: Indications for early surgery. *Journal of the Neurological Sciences* 1996;136:182–4.
227. Dawes MG, Grudzinskas JG. Repeated measurement of maternal weight during pregnancy. Is this a useful practice? *British Journal of Obstetrics and Gynaecology* 1991;98:189–94.
228. National Academy of Sciences, Institute of Medicine, Food and Nutrition Board, Committee on Nutritional Status During Pregnancy and Lactation, Subcommittee on Dietary Intake and Nutrient Supplements During Pregnancy, Subcommittee on Nutritional Status and Weight Gain During Pregnancy. *Nutrition during pregnancy*. Washington DC: National Academy Press; 1990.
229. Siega-Riz AM, Adair LS, Hobel CJ. Maternal underweight status and inadequate rate of weight gain during the third trimester of pregnancy increases the risk of preterm delivery. *Journal of Nutrition* 1996;126:146–53.
230. Bergmann MM, Flagg EW, Miracle-McMahill HL, Boeing H. Energy intake and net weight gain in pregnant women according to body mass index (BMI) status. *International Journal of Obesity and Related Metabolic Disorders* 1997;21:1010–7.
231. Alexander JM, Grant AM, Campbell MJ. Randomised controlled trial of breast shells and Hoffman's exercises for inverted and non-protractile nipples. *British Medical Journal* 1992;304:1030–2.
232. Pattinson RE. Pelvimetry for fetal cephalic presentations at term. *Cochrane Database of Systematic Reviews* 2001;(3). 2001.
233. Lenihan JP Jr. Relationship of antepartum pelvic examinations to premature rupture of the membranes. *Obstetrics and Gynecology* 1984;83:33–7.
234. Goffinet F. [Ovarian cyst and pregnancy]. [French]. *Journal de Gynecologie, Obstetrique et Biologie de la Reproduction* 2001;30:4S100–8.
235. O'Donovan P, Gupta JK, Savage J, Thornton JG, Lilford RJ. Is routine antenatal booking vaginal examination necessary for reasons other than cervical cytology if ultrasound examination is planned? *British Journal of Obstetrics and Gynaecology* 1988;95:556–9.
236. World Health Organization. *Female genital mutilation*. WHO Information Fact Sheet No. 241. Geneva: World Health Organization; 2000.
237. British Medical Association. *Female genital mutilation: caring for patients and child protection*. London: BMA; 2001.
238. Momoh C, Ladhani S, Lochrie DP, Rymer J. Female genital mutilation: Analysis of the first twelve months of a southeast London specialist clinic. *BJOG* 2001;108:186–91.
239. World Health Organization. *A systematic review of the health complications of female genital mutilation including sequelae in childbirth*. Geneva: WHO; 2000.
240. McCaffrey M, Jankowska A, Gordon H. Management of female genital mutilation: The Northwick Park Hospital experience. *British Journal of Obstetrics and Gynaecology* 1995;102:787–90.
241. Jordan JA. Female genital mutilation (female circumcision). *British Journal of Obstetrics and Gynaecology* 1994;101:94–5.
242. British Medical Association. *Domestic violence: a health care issue?* London: BMA; 1998.

243. Tjaden P, Thoennes N. *Full report of the prevalence, incidence, and consequences of violence against women. Findings from the National Violence Against Women Survey. NCJ 183781, 1–61.* Washington DC: US Department of Justice, National Institute of Justice; 2000.

244. Canadian Centre for Justice Statistics. *Family violence in Canada: A statistical profile 2002.* 85-224-XIE. Ottawa: Statistics Canada; 2002. [www.statcan.ca/english/IPS/Data/85-224-XIE.htm] Accessed 20 August 2003.

245. Jones AS, Carlson Gielen A, Campbell JC. Annual and lifetimes prevalence of partner abuse in a sample of female HMO enrollees. *Women's Health Issues* 1999;9:295–305.

246. Ballard TJ, Saltzman LE, Gazmararian JA, Spitz AM, Lazorick S, Marks JS. Violence during pregnancy: measurement issues. *American Journal of Public Health* 1998;88:274–6.

247. Royal College of Obstetricians and Gynaecologists. *Violence against women*. London: RCOG Press; 1997.

248. Johnson JK, Haider F, Ellis K, Hay DM, Lindow SW. The prevalence of domestic violence in pregnant women. *BJOG* 2003;110:272–5.

249. Newberger EH, Barkan SE, Lieberman ES, McCormick MC, Yllo K, Gary LT, *et al*. Abuse of pregnant women and adverse birth outcome: current knowledge and implications for practice. *Journal of the American Medical Association* 1992;267:2370–2.

250. Murphy CC, Schei B, Myhr TL, Du MJ. Abuse: a risk factor for low birth weight? A systematic review and meta-analysis. [see comments]. *Canadian Medical Association Journal* 2001;164:1567–72.

251. Cokkinides VE, Coker AL, Sanderson M, Addy C, Bethea L. Physical violence during pregnancy: maternal complications and birth outcomes. *Obstetrics and Gynecology* 1999;93:661–6.

252. Janssen PA, Holt VL, Sugg NK, Emanuel I, Critchlow CM, Henderson AD. Intimate partner violence and adverse pregnancy outcomes: A population-based study. *American Journal of Obstetrics and Gynecology* 2003;188:1341–7.

253. Royal College of Midwives. *Domestic abuse in pregnancy*. London: RCM; 1999.

254. Royal College of Psychiatrists. *Domestic violence*. CR102. London: RCPsych; 2002.

255. Wathen CN, MacMillan HL. Interventions for violence against women. Scientific review. *JAMA* 2003;289:589–600.

256. Ramsay J, Richardson J, Carter YH, Davidson LL, Feder G. Should health professionals screen women for domestic violence? Systematic review. *British Medical Journal* 2002;325:314–18.

257. Cann K, Withnell S, Shakespeare J, Doll H, Thomas J. Domestic violence: a comparative survey of levels of detection, knowledge, and attitudes in healthcare workers. *Public Health* 2001;115:89–95.

258. Department of Health. *Domestic violence: A resource manual for health care professionals*. London: Department of Health; 2000.

259. Wilson LM, Reid AJ, Midmer DK, Biringer A, Carroll JC, Stewart DE. Antenatal psychosocial risk factors associated with adverse postpartum family outcomes. *Canadian Medical Association Journal* 1996;154:785–99.

260. Perkin MR, Bland JM. The effect of anxiety and depression during pregnancy on obstetric complications. *British Journal of Obstetrics and Gynaecology* 1993;100:629–34.

261. Dayan J, Creveuil C, Herlicoviez M. Role of anxiety and depression in the onset of spontaneous preterm labor. *American Journal of Epidemiology* 2002;155:293–301.

262. Lundy BL, Jones NA, Field T. Prenatal depression effects on neonates. *Infant Behavior and Development* 1999;22:119–29.

263. Murray D, Cox JL. Screening for depression during pregnancy with the Edinburgh Depression Scale (EPDS). *Journal of Reproductive and Infant Psychology* 1990;8:99–107.

264. Bolton HL, Hughes PM, Turton P. Incidence and demographic correlates of depressive symptoms during pregnancy in an inner London population. *Journal of Psychosomatic Obstetrics and Gynecology* 1998;19:202–9.

265. Evans J, Heron J, Francomb H, Oke S, Golding J. Cohort study of depressed mood during pregnancy and after childbirth. *British Medical Journal* 2001;323:257–60.

266. Austin M-P, Lumley J. Antenatal screening for postnatal depression: a systematic review. *Acta Psychiatrica Scandinavica* 2003;107:10–17.

267. Hayes BA, Muller R, Bradley BS. Perinatal depression: a randomized controlled trial of an antenatal education intervention for primiparas. *Birth* 2001;28:28–35.

268. Brugha TS, Wheatly S, Taub NA, Culverwell A, Friedman T, Kirwan P. Pragmatic randomized trial of an antenatal intervention to prevent post-natal depression by reducing psychosocial risk factors. *Psychological Medicine* 2000;30:1273–81.

269. Hytten F. Blood volume changes in normal pregnancy. *Clinical Haematology* 1985;14:601–12.

270. Ramsey M, James D, Steer P, Weiner C, Gornik B. *Normal values in pregnancy*. 2nd ed. London: WB Saunders; 2000.

271. Steer P, Alam MA, Wadsworth J, Welch A. Relation between maternal haemoglobin concentration and birth weight in different ethnic groups. *British Medical Journal* 1995;310:489–91.

272. Zhou LM, Yang WW, Hua JZ, Deng CQ, Tao X, Stoltzfus RJ. Relation of hemoglobin measured at different times in pregnancy to preterm birth and low birth weight in Shanghai, China. *American Journal of Epidemiology* 1998;148:998–1006.

273. Breymann C. Iron supplementation during pregnancy. *Fetal and Maternal Medicine Review* 2002;13:1–29.

274. Cuervo LG, Mahomed K. Treatments for iron deficiency anaemia during pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).

275. Davies SC, Cronin E, Gill M, Greengross P, Hickman M, Normand C. Screening for sickle cell disease and thalassaemia: a systematic review with supplementary research. *Health Technology Assessment* 2000;4:1–119.

276. Modell B, Harris R, Lane B, Khan M, Darlison M, Petrou M, *et al*. Informed choice in genetic screening for thalassaemia during pregnancy: audit from a national confidential inquiry. *British Medical Journal* 2000;320:337–41.

277. Modell B, Petrou M, Layton M, Varnavides L, Slater C, Ward RH, *et al*. Audit of prenatal diagnosis for haemoglobin disorders in the United Kingdom: the first 20 years. [see comments]. *British Medical Journal* 1997;315:779–84.

278. Department of Health. *Sickle cell, thalassaemia and other haemoglobinopathies. Report of a Working Party of the Standing Medical Advisory Committee*. London: DoH; 1999.

279. Zeuner D, Ades AE, Karnon J, Brown JE, Dezateux C, Anionwu EN. Antenatal and neonatal haemoglobinopathy screening in the UK: review and economic analysis. *Health Technology Assessment* 1999;3(11):1–186.

280. Streetly A. A national screening policy for sickle cell disease and thalassaemia major for the United Kingdom. Questions are left after two evidence based reports. *British Medical Journal* 2000;320:1353–4.

281. Aspinall PJ, Dyson SM, Anionwu EN. The feasibility of using ethnicity as a primary tool for antenatal selective screening for sickle cell disorders: pointers from the research evidence. *Social Science and Medicine* 2003;56:285–97.

282. Petrou M, Brugiatelli M, Ward RHT, Modell B. Factors affecting the uptake of prenatal diagnosis for sickle cell disease. *Journal of Medical Genetics* 1992;29:820–3.

283. Modell B, Ward RH, Fairweather DV. Effect of introducing antenatal diagnosis on reproductive behaviour of families at risk for thalassaemia major. *British Medical Journal* 1980;280:1347–50.

284. Ahmed S, Saleem M, Sultana N, Raashid Y, Waqar A, Anwar M, *et al*. Prenatal diagnosis of beta-thalassaemia in Pakistan: experience in a Muslim country. *Prenatal Diagnosis* 2000;20:378–83.

285. UK Blood Transfusion Services. Guidelines for the Blood Transfusion Service. 6th ed. London; TSO; 2002. [www.transfusionguidelines.org.uk/uk_guidelines/ukbts6_$01.html] Accessed 20 August 2003.

286. Whittle MJ. Antenatal serology testing in pregnancy. *British Journal of Obstetrics and Gynaecology* 1996;103:195–6.

287. Brouwers HA, Overbeeke MA, van E, I, Schaasberg W, Alsbach GP, van der HC, *et al*. What is the best predictor of the severity of ABO-haemolytic disease of the newborn? *Lancet* 1988;2:641–4.

288. Mollison PL, Engelfriet CP, Contreras M. *Haemolytic disease of the fetus and newborn. Blood transfusion in clinical medicine*. Oxford: Blackwell Science. 1997. p. 390–424.

289. Shanwell A, Sallander S, Bremme K, Westgren M. Clinical evaluation of a solid-phase test for red cell antibody screening of pregnant women. *Transfusion* 1999;39:26–31.

290. Filbey D, Hanson U, Wesstrom G. The prevalence of red cell antibodies in pregnancy correlated to the outcome of the newborn: a 12 year study in central Sweden. *Acta Obstetrica et Gynecologica Scandinavica* 1995;74:687–92.

291. British Committee for Standards in Haematology, Blood Transfusion Task Force. Guidelines for blood grouping and red cell antibody testing during pregnancy. *Transfusion Medicine* 1996;6:71–4.

292. National Institute for Clinical Excellence. *Guidance on the use of routine antenatal anti-D prophylaxis for RhD-negative women*. Technology Appraisal Guidance, No. 41. London: National Institute for Clinical Excellence; 2002. [www.nice.org.uk/pdf/prophylaxisFinalguidance.pdf] Accessed 20 August 2003.

293. Royal College of Obstetricians and Gynaecologists. *Ultrasound screening for fetal abnormalities: report of the RCOG working party*. London: RCOG Press; 1997.

294. Jepsen RG, Forbes CA, Sowden AJ, Lewis RA. Increasing informed uptake and non-uptake of screening: evidence from a systematic review. *Health Expectations* 2001;4:116–26.

295. Department of Health, social Services and Public Safety, Northern Ireland, National Assembly for Wales, Scottish Executive, Department of Health. *Second report of the UK National Screening Committee*. London: DoH; 2000. [www.nsc.nhs.uk/pdfs/secondreport.pdf] Accessed 21 August 2003.

296. Royal College of Obstetricians and Gynaecologists. *Report of the RCOG working party on biochemical markers and the detection of Down's syndrome*. London: Royal College of Obstetricians and Gynaecologists; 1993.

297. Bricker L, Garcia J, Henderson J, Mugford M, Neilson J, Roberts T, *et al*. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technology Assessment* 2000;4:1–193.

298. Williamson P, Alberman E, Rodeck C, Fiddler M, Church S, Harris R. Antecedent circumstances surrounding neural tube defect births in 1990–1991. *British Journal of Obstetrics and Gynaecology* 1997;104:51–6.

299. Saari-Kemppainen A, Karjalainen O, Ylostalo P, Heinonen OP. Fetal anomalies in a controlled one-stage ultrasound screening trial. A report from the Helsinki Ultrasound Trial. *Journal of Perinatal Medicine* 1994;22(4):279–289.

300. Whitlow BJ, Chatzipapas IK, Lazanakis ML, Kadir RA, Economides DL. The value of sonography in early pregnancy for the detection of fetal abnormalities in an unselected population. *British Journal of Obstetrics and Gynaecology* 1999;106:929–36.

301. National Assembly for Wales/Velindre NHS Trust Antenatal Project Team Steering Board. *Choices: Recommendations for the provision and management of antenatal screening in Wales*. Cardiff: Velindre NHS Trust; March 2002. [www.velindre-tr.wales.nhs.uk/antenatal/consult_doc/choices.pdf] Accessed 21 August 2003.

302. Royal College of Obstetricians and Gynaecologists. *Routine ultrasound screening in pregnancy, protocols, standards and training. Supplement to ultrasound screening for fetal abnormalities. Report of the RCOG Working Party*. London: RCOG Press; 2000.

303. Office for National Statistics. *Child health statistics*. London: National Statistics; 2000. p. 1–26.

304. Noble J. Natural history of Down's syndrome: a brief review for those involved in antenatal screening. *Journal of Medical Screening* 1998;5:172–7.

305. Marteau TM, Dormandy E. Facilitating informed choice in prenatal testing: how well are we doing? *American Journal of Medical Genetics* 2001;106:185–90.

306. Smith DK, Shaw RW, Marteau TM. Informed consent to undergo serum screening for Down's syndrome: the gap between policy and practice. *British Medical Journal* 1994;309:776.

307. Royal College of Obstetricians and Gynaecologists. *Amniocentesis*. Guideline No. 8. London: Royal College of Obstetricians and Gynaecologists; 2000.

308. Deeks JJ. Systematic reviews of evaluations of diagnostic and screening tests. *British Medical Journal* 2001;323:157–62.

309. Lijmer JG, Mol BW, Heisterkamp S, Bonsel GJ, Prins MH, van der Meulen JH, *et al*. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA* 1999;282:1061–6.

310. Hook EB. Spontaneous deaths of fetuses with chromosomal abnormalities diagnosed prenatally. *New England Journal of Medicine* 1978;299:1036–8.

311. Morris JK, Mutton DE, Alberman E. Revised estimates of the maternal age specific live birth prevalence of Down's syndrome. *Journal of Medical Screening* 2002;9:2–6.

312. Paranjothy S, Thomas J. National Sentinel Caesarean Section Audit. *MIDIRS Midwifery Digest* 2001;11:S13–15.

313. Wald NJ, Huttly WJ, Hennessy CF. Down's syndrome screening in the UK in 1998. *Lancet* 1999;354:1264.

314. Youings S, Gregson N, Jacobs P. The efficacy of maternal age screening for Down's syndrome in Wessex. *Prenatal Diagnosis* 1991;11:419–25.

315. Smith-Bindman R, Hosmer W, Feldstein VA, Deeks JJ, Goldberg JD. Second-trimester ultrasound to detect fetuses with Down's syndrome. *JAMA* 2001;285:1044–55.

316. Wald NJ, Rodeck C, Hackshaw AK, Walters J, Chitty L, Mackinson AM. First and second trimester antenatal screening for Down's syndrome: the results of the serum, urine and ultrasound screening study (SURUSS). *Health Technology Assessment* 2003;7:1–88.

317. Bindra R, Heath V, Nicolaides KH. Screening for chromosomal defects by fetal nuchal translucency at 11 to 14 weeks. *Clinical Obstetrics and Gynecology* 2002;45:661–70.

318. Niemimaa M, Suonpaa M, Perheentupa A, Seppala M, Heinonen S, Laitinen P, *et al*. Evaluation of first trimester maternal serum and ultrasound screening for Down's syndrome in Eastern and Northern Finland. *European Journal of Human Genetics* 2001;9:404–8.

319. Wald NJ, Kennard A, Hackshaw A, McGuire A. Antenatal screening for Down's syndrome. *Health Technology Assessment* 1998;2:1–112.

320. Conde-Agudelo A, Kafury-Goeta AC. Triple-marker test as screening for Down syndrome: a meta-analysis. *Obstetrical and Gynecological Survey* 1998;53:369–76.

321. Wald NJ, Huttly WJ, Hackshaw AK. Antenatal screening for Down's syndrome with the quadruple test. *Lancet* 2003;361:835–6.

322. Spencer K, Spencer CE, Power M, Dawson C, Nicolaides KH. Screening for chromosomal abnormalities in the first trimester using ultrasound and maternal serum biochemistry in a one-stop clinic: a review of three years prospective experience. *BJOG* 2003;110:281–6.

323. Alfirevic Z, Gosden C, Neilson, JP. Chorion villus sampling versus amniocentesis for prenatal diagnosis. *Cochrane Database of Systematic Reviews* 1998;(4):1–8.

324. Alfirevic, Z. Early amniocentesis versus transabdominal chorion villus sampling. *Cochrane Database of Systematic Reviews* 2000;(1), 1.

325. Tercyak KP, Johnson SB, Roberts SF, Cruz AC. Psychological response to prenatal genetic counseling and amniocentesis. *Patient Education and Counseling* 2001;43:73–84.

326. Green JM. Women's experiences of prenatal screening and diagnosis. In: Abramsky L, Chapple J, editors. Prenatal diagnosis: the human side. London: Chapman and Hall; 1994. p. 37–53.

327. Liu S, Joseph KS, Kramer MS, Allen AC, Sauve R, Rusen ID, *et al*. Relationship of prenatal diagnosis and pregnancy termination to overall infant mortality in Canada. *JAMA* 2002;287:1561–7.

328. Whalley P. Bacteriuria of pregnancy. *American Journal of Obstetrics and Gynecology* 1967;97:723–38.

329. Little PJ. The incidence of urinary infection in 5000 pregnant women. *Lancet* 1966;2:925–8.

330. Campbell-Brown M, McFadyen IR, Seal DV, Stephenson ML. Is screening for bacteriuria in pregnancy worth while? *British Medical Journal* 1987;294:1579–82.

331. Foley ME, Farquharson R, Stronge JM. Is screening for bacteriuria in pregnancy worthwhile? *British Medical Journal* 1987;295:270.

332. LeBlanc AL, McGanity WJ. The impact of bacteriuria in pregnancy: a survey of 1300 pregnant patients. *Biologie Medicale* 1964;22:336–47.

333. Kincaid-Smith P, Bullen M. Bacteriuria in pregnancy. *Lancet* 1965;395–9.

334. Thomsen AC, Morup L, Hansen KB. Antibiotic elimination of group-B streptococci in urine in prevention of preterm labour. *Lancet* 1987;591–3.

335. Elder HA, Santamarina BAG, Smith S, Kass EH. The natural history of asymptomatic bacteriuria during pregnancy: the effect of tetracycline on the clinical course and the outcome of pregnancy. *American Journal of Obstetrics and Gynecology* 1971;111:441–62.

336. Gold EM, Traub FB, Daichman I, Terris M. Asymptomatic bacteriuria during pregnancy. *Obstetrics and Gynecology* 1966;27:206–9.

337. Mulla N. Bacteriuria in Pregnancy. *Obstetrics and Gynecology* 1960;16:89–92.

338. Savage WE, Hajj SN, Kass EH. Demographic and prognostic characteristics of bacteriuria in pregnancy. *Medicine* 1967;46:385–407.

339. Mittendorf R, Williams MA, Kass EH. Prevention of preterm delivery and low birth weight associated with asymptomatic bacteriuria. *Clinical Infectious Diseases* 1992;14:927–32.

340. Patterson TF, Andriole VT. Bacteriuria in pregnancy. *Infectious Disease Clinics of North America* 1987;1:807–22.

341. Screening for asymptomatic bacteriuria, hematuria and proteinuria. The US Preventive Services Task Force. *American Family Physician* 1990;42:389–95.

342. Etherington IJ, James DK. Reagent strip testing of antenatal urine specimens for infection. *British Journal of Obstetrics and Gynaecology* 1993;100:806–8.

343. Shelton SD, Boggess KA, Kirvan K, Sedor F, Herbert WN. Urinary interleukin-8 with asymptomatic bacteriuria in pregnancy. *Obstetrics and Gynecology* 2001;97:583–6.

344. Millar L, Debuque L, Leialoha C, Grandinetti A, Killeen J. Rapid enzymatic urine screening test to detect bacteriuria in pregnancy. *Obstetrics and Gynecology* 2000;95:601–4.

345. McNair RD, MacDonald SR, Dooley SL, Peterson LR. Evaluation of the centrifuged and Gram-stained smear, urinalysis, and

reagent strip testing to detect asymptomatic bacteriuria in obstetric patients. *American Journal of Obstetrics and Gynecology* 2000;182:1076–9.

346. Robertson AW, Duff P. The nitrite and leukocyte esterase tests for the evaluation of asymptomatic bacteriuria in obstetric patients. *Obstetrics and Gynecology* 1988;71:878–81.
347. Bachman JW, Heise RH, Naessens JM, Timmerman MG. A study of various tests to detect asymptomatic urinary tract infections in an obstetric population. *JAMA* 1993;270:1971–4.
348. Tincello DG, Richmond DH. Evaluation of reagent strips in detecting asymptomatic bacteriuria in early pregnancy: prospective case series. *British Medical Journal* 1998;316:435–7.
349. Abyad A. Screening for asymptomatic bacteriuria in pregnancy: urinalysis vs. urine culture. *Journal of Family Practice* 1991;33:471–4.
350. Graninger W, Fleischmann D, Schneeweiss B, Aram L, Stockenhuber F. Rapid screening for bacteriuria in pregnancy. *Infection* 1992;20:9–11.
351. Smaill, F. Antibiotic treatment for symptomatic bacteriuria: antibiotic vs. no treatment for asymptomatic bacteriuria in pregnancy. *Cochrane Database of Systematic Reviews* 2002;(3):1–5.
352. Villar J, Lydon-Rochelle MT, Gulmezoglu AM. Duration of treatment for asymptomatic bacteriuria during pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).
353. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines 2002. *Morbidity and Mortality Weekly Report* 2002;51:1–80.
354. Joesoef M, Schmid G. Bacterial vaginosis. *Clinical Evidence* 2002;7:1400–8.
355. Goldenberg RL, Klebanoff MA, Nugent R, Krohn MA, Hilliers S, Andrews WW. Bacterial colonization of the vagina during pregnancy in four ethnic groups. Vaginal Infections and Prematurity Study Group. *American Journal of Obstetrics and Gynecology* 1996;174:1618–21.
356. Hay PE, Morgan DJ, Ison CA, Bhide SA, Romney M, McKenzie P, *et al*. A longitudinal study of bacterial vaginosis during pregnancy. *British Journal of Obstetrics and Gynaecology* 1994;101:1048–53.
357. Flynn CA, Helwig AL, Meurer LN. Bacterial vaginosis in pregnancy and the risk of prematurity: a meta-analysis. *Journal of Family Practice* 1999;48:885–92.
358. Gratacos E, Figueras F, Barranco M, Vila J, Cararach V, Alonso PL, *et al*. Spontaneous recovery of bacterial vaginosis during pregnancy is not associated with an improved perinatal outcome. *Acta Obstetricia et Gynecologica Scandinavica* 1998;77:37–40.
359. Amsel R, Totten PA, Spiegel CA. Nonspecific vaginitis: diagnostic criteria and microbial and epidemiological associations. *American Journal of Medicine* 1983;74:14–22.
360. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardised methods of Gram stain interpretation. *Journal of Clinical Microbiology* 1991;29:297–301.
361. Thiagarajan M. Evaluation of the use of yogurt in treating bacterial vaginosis in pregnancy. *Journal of Clinical Epidemiology* 1998;51:22S.
362. McDonald H, Brocklehurst P, Parsons J, Vigneswaran R. Interventions for treating bacterial vaginosis in pregnancy. *Cochrane Database of Systematic Reviews* 2003;(2):1–30.
363. Ugwumadu A, Manyonda I, Reid F, Hay P. Effect of early oral clindamycin on late miscarriage and preterm delivery in asymptomatic women with abnormal vaginal flora and bacterial vaginosis: a randomised controlled trial. *Lancet* 2003;361:983–8.
364. Stary A. European guideline for the management of chlamydial infection. *International Journal of STD and AIDS* 2001;12:30–3.
365. Preece PM, Ades A, Thompson RG, Brooks JH. Chlamydia trachomatis infection in late pregnancy: A prospective study. *Paediatric and Perinatal Epidemiology* 1989;3:268–77.
366. Goh BT, Morgan-Capner P, Lim KS. Chlamydial screening of pregnant women in a sexually transmitted diseases clinic. *British Journal of Venereal Diseases* 1982;58:327–9.
367. Association of chlamydia trachomatis and mycoplasma hominis with intrauterine growth restriction and preterm delivery. The John Hopkins Study of Cervicitis and Adverse Pregnancy Outcome. *American Journal of Epidemiology* 1989;129:1247–51.
368. Ryan GM, Jr, Abdella TN, McNeeley SG, Baselski VS, Drummond DE. Chlamydia trachomatis infection in pregnancy and effect of treatment on outcome. [see comments.]. *American Journal of Obstetrics and Gynecology* 1990;162:34–9.
369. Brocklehurst P, Rooney G. Interventions for treating genital chlamydia trachomatis infection in pregnancy. *Cochrane Database of Systematic Reviews* 2002;(3).
370. Preece PM, Anderson JM, Thompson RG. Chlamydia trachomatis infection in infants: A prospective study. *Archives of Disease in Childhood* 1989;64:525–9.
371. Schachter J, Grossman M, Sweet RL, Holt J, Jordan C, Bishop E. Prospective study of perinatal transmission of Chlamydia trachomatis. *JAMA* 1986;255:3374–7.
372. FitzGerald MR, Welch J, Robinson AJ, Ahmed-Jushuf IH. Clinical guidelines and standards for the management of uncomplicated genital chlamydial infection. *International Journal of STD and AIDS* 1998;9:253–62.
373. Scottish Intercollegiate Guidelines Network. *Management of genital Chlamydia trachomatis* Infection. SIGN Publication No. 42. Edinburgh: Scottish Intercollegiate Guideline Network; 2000.
374. Ryan M, Miller E, Waight P. Cytomegalovirus infection in England and Wales: 1992 and 1993. *Communicable Diseases Report* 1995;5:R74–6.
375. Preece PM, Tookey P, Ades A, Peckham CS. Congenital cytomegalovirus infection: predisposing maternal factors. *Journal of Epidemiology and Community Health* 1986;40:205–9.
376. Peckham CS, Coleman JC, Hurley R, Chin KS, Henderson K, Preece PM. Cytomegalovirus infection in pregnancy: preliminary findings from a prospective study. *Lancet* 1983;1352–5.

377. Bolyard EA, Tablan OC, Williams WW, Pearson ML, Shapiro CN, Deitchmann SD. Guideline for infection control in health care personnel. Centers for Disease Control and Prevention. *Infection Control and Hospital Epidemiology* 1998;19:407–63. Erratum 1998;19:493

378. Stagno S, Whitley RJ. Herpesvirus infections of pregnancy. Part 1: Cytomegalovirus and Epstein-Barr virus infections. *New England Journal of Medicine* 1985;313:1270–4.

379. Boxall E, Skidmore S, Evans C, Nightingale S. The prevalence of hepatitis B and C in an antenatal population of various ethnic origins. *Epidemiology and Infection* 1994;113:523–8.

380. Brook MG, Lever AM, Kelly D, Rutter D, Trompeter RS, Griffiths P, *et al*. Antenatal screening for hepatitis B is medically and economically effective in the prevention of vertical transmission: three years experience in a London hospital. *Quarterly Journal of Medicine* 1989;71:313–7.

381. Chrystie I, Sumner D, Palmer S, Kenney A, Banatvala J. Screening of pregnant women for evidence of current hepatitis B infection: selective or universal? *Health Trends* 1992;24:13–5.

382. Derso A, Boxall EH, Tarlow MJ, Flewett TH. Transmission of HBsAg from mother to infant in four ethnic groups. *British Medical Journal* 1978;15(6118):949–952.

383. Beasley RP, Trepo C, Stevens CE, Szmuness W. The e antigen and vertical transmission of hepatitis B surface antigen. *American Journal of Epidemiology* 1977;105:94–8.

384. Beasley RP, Hwang L-Y. Epidemiology of hepatocellular carcinoma. In: Vyas GN, Dienstag JL, Hoofnagle JH, editors. *Viral hepatitis and liver disease*. Orlando, FL: Grune and Stratton; 1984. p. 209–24.

385. Ramsay M, Gay N, Balogun K, Collins M. Control of hepatitis B in the United Kingdom. *Vaccine* 1998;16 Suppl:S52–5.

386. Sehgal A, Sehgal R, Gupta I, Bhakoo ON, Ganguly NK. Use of hepatitis B vaccine alone or in combination with hepatitis B immunoglobulin for immunoprophylaxis of perinatal hepatitis B infection. *Journal of Tropical Pediatrics* 1992;38:247–51.

387. Wong VC, Ip HM, Reesink HW, Lelie PN, Reerink-Brongers EE, Yeung CY, *et al*. Prevention of the HBsAg carrier state in newborn infants of mothers who are chronic carriers of HBsAg and HBeAg by administration of hepatitis-B vaccine and hepatitis-B immunoglobulin. Double-blind randomised placebo – controlled study. *Lancet* 1984;1:921–6.

388. Zhu Q. A preliminary study on interruption of HBV transmission in uterus. *Chinese Medical Journal* 1997;110:145–7.

389. Lo K, Tsai Y, Lee S, Yeh C, Wang J, Chiang BN, *et al*. Combined passive and active immunization for interruption of perinatal transmission of hepatitis B virus in Taiwan. *Hepato-gastroenterology* 1985;32:65–8.

390. Beasley RP, Hwang LY, Lee GC, Lan CC, Roan CH, Huang FY, *et al*. Prevention of perinatally transmitted hepatitis B virus infections with hepatitis B virus infections with hepatitis B immune globulin and hepatitis B vaccine. *Lancet* 1983;2:1099–102.

391. Nair PV, Weissman JY, Tong MJ, Thursby MW, Paul RH, Henneman CE. Efficacy of hepatitis B immune globulin in prevention of perinatal transmission of the hepatitis B virus. *Gastroenterology* 1984;87:293–8.

392. Xu Z-Y, Liu C-B, Francis DP. Prevention of perinatal acquisition of hepatitis B virus carriage using vaccine: preliminary report of a randomized, double-blind placebo-controlled and comparative trial. *Pediatrics* 1985;76:713–18.

393. Balmer S, Bowens A, Bruce E, Farrar H, Jenkins C, Williams R. *Quality management for screening: report to the National Screening Committee*. Leeds: Nuffield Institute for Health; 2000.

394. Summers PR, Biswas MK, Pastorek JG, Pernoll ML, Smith LG, Bean BE. The pregnant hepatitis B carrier: evidence favoring comprehensive antepartum screening. *Obstetrics and Gynecology* 1987;69:701–4.

395. Chaita TM, Graham SM, Maxwell SM, Sirivasin W, Sabchareon A, Beeching NJ. Salivary sampling for hepatitis B surface antigen carriage: a sensitive technique suitable for epidemiological studies. *Annals of Tropical Paediatrics* 1995;15:135–9.

396. Pembrey L, Newell ML, Tovo PA. Hepatitis C virus infection in pregnant women and their children. *Italian Journal of Gynaecology and Obstetrics* 2000;12:21–8.

397. Whittle M, Peckham C, Anionwu E, *et al*. Antenatal screening for hepatitis C. Working party report on screening for hepatitis C in the UK. January 2002. [www.nelh.nhs.uk/screening/antenatal_pps/Hep_C_NSC.pdf] Accessed 4 September 2003.

398. Ades AE, Parker S, Walker J, Cubitt WD, Jones R. HCV prevalence in pregnant women in the UK. *Epidemiology and Infection* 2000;125:399–405.

399. Okamoto M, Nagata I, Murakami J, Kaji S, Iitsuka T, Hoshika T, *et al*. Prospective reevaluation of risk factors in mother-to-child transmission of hepatitis C virus: high virus load, vaginal delivery, and negative anti-NS4 antibody. *Journal of Infectious Diseases* 2000;182:1511–4.

400. Tajiri H, Miyoshi Y, Funada S, Etani Y, Abe J, Onodera T, *et al*. Prospective study of mother-to-infant transmission of hepatitis C virus. *Pediatric Infectious Disease Journal* 2001;20:10–4.

401. Paccagnini S, Principi N, Massironi E, Tanzi E, Romano L, Muggiasca ML, *et al*. Perinatal transmission and manifestation of hepatitis C virus infection in a high risk population. *Pediatric Infectious Disease Journal* 1995;14:195–9.

402. Tovo PA, Pembrey L, Newell M-L. Persistence rate and progression of vertically acquired hepatitis C infection. *Journal of Infectious Diseases* 2001;181:419–24.

403. Ketzinel-Gilad M, Colodner SL, Hadary R, Granot E, Shouval D, Galun E. Transient transmission of hepatitis C virus from mothers to newborns. *European Journal of Clinical Microbiology and Infectious Diseases* 2000;19:267–74.

404. Lin HH, Kao J-H. Effectiveness of second- and third-generation immunoassays for the detection of hepatitis C virus infection in pregnant women. *Journal of Obstetrics and Gynaecology Research* 2000;26:265–70.

405. Vrielink H, Reesink HW, van den Burg PJ. Performance of three generations of anti-hepatitis C virus enzyme-linked immunosorbent assays in donors and patients. *Vox Sanguinis* 1997;72:67–70.

406. Zaaijer HL, Vrielink H, Van Exel-Oehlers PJ, Cuypers HT, Lelie PN. Confirmation of hepatitis C infection: a comparison of five immunoblot assays. *Transfusion* 1993;33:634–8.

407. Unlinked Anonymous Surveys Steering Group. *Prevalence of HIV and hepatitis infections in the United Kingdom 2001. Annual report of the Unlinked Anonymous Prevalence Monitoring Programme*. London: Department of Health; 2002. [www.doh.gov.uk/hivhepatitis/hivhepatitis2001.pdf] Accessed 21 August 2003.

408. Unlinked Anonymous Surveys Steering Group. *Prevalence of HIV and hepatitis infections in the United Kingdom 2000. Annual report of the Unlinked Anonymous Prevalence Monitoring Programme*. London: Department of Health; 2001. p. 5, 7, 24–30.

409. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, *et al*. Reduction of maternal – infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *New England Journal of Medicine* 1994;331:1173–80.

410. Mandelbrot L, Le Chenadec J, Berrebi A, Bongain A, Benifla J-L, Delfraissy JF, *et al*. Perinatal HIV-1 transmission. Interaction between zidovudine prophylaxis and mode of delivery in the French perinatal cohort. *JAMA* 1998;280:55–60.

411. Duong T, Ades AE, Gibb DM, Tookey PA, Masters J. Vertical transmission rates for HIV in the British Isles: estimates based on surveillance data. *British Medical Journal* 1999;319:1227–9.

412. AIDS and HIV infection in the United Kingdom: monthly report. *CDR Weekly* 2001;11(17):10–15. [www.phls.org.uk/publications/cdr/PDFfiles/2001/cdr1701.pdf] Accessed 4 September 2003.

413. Samson L, King S. Evidence-based guidelines for universal counselling and offering of HIV testing in pregnancy in Canada. *Canadian Medical Association Journal* 1998;158:1449–57 [erratum appears in *CMAJ* 1999;159(1):22.

414. Van Doornum GJJ, Buimer M, Gobbers E, Bindels PJ, Coutinho RA. Evaluation of an expanded two-ELISA approach for confirmation of reactive serum samples in an HIV-screening programme for pregnant women. *Journal of Medical Virology* 1998;54:285–90.

415. Public Health Laboratory Service AIDS Diagnosis Working Group. Towards error free HIV diagnosis: notes on laboratory practice. *PHLS Microbiology Digest* 1992;9:61–4.

416. Brocklehurst P, Volmink J. Antiretrovirals for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database of Systematic Reviews* 2002;(3).

417. European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. The European Mode of Delivery Collaboration. *Lancet* 1999;353:1035–9. [published erratum appears in *Lancet* 1999;353:1714].

418. Ricci E, Parazzini F. Caesarean section and antiretroviral treatment. *Lancet* 2000;355:496.

419. Cunningham CK, Chaix ML, Rekacewicz C, Britto P, Rouzioux C, Gelber RD, *et al*. Development of resistance mutations in women receiving standard antiretroviral therapy who received intrapartum nevirapine to prevent perinatal human immunodeficiency virus type 1 transmission: a substudy of pediatric AIDS clinical trials group protocol 316. *Journal of Infectious Diseases* 2002;186:181–8.

420. Palumbo P, Holland B, Dobbs T, Pau CP, Luo CC, Abrams EJ, *et al*. Antiretroviral resistance mutations among pregnant human immunodeficiency virus type 1-infected women and their newborns in the United States: vertical transmission and clades. *Journal of Infectious Diseases* 2001;184:1120–6.

421. Control and prevention of rubella: evaluation and management of suspected outbreaks, rubella in pregnant women, and surveillance for congenital rubella syndrome. *Morbidity and Mortality Weekly Report* 2001; 50:1–23.

422. Tookey P. Antenatal screening for rubella. Personal communication; 2002.

423. Miller E, Waight P, Gay N, Ramsay M, Vurdien J, Morgan-Capner P, *et al*. The epidemiology of rubella in England and Wales before and after the 1994 measles and rubella vaccination campaign: fourth joint report from the PHLS and the National Congenital Rubella Surveillance Programme. *Communicable Diseases Report* 1997;7:R26–32.

424. Tookey PA, Corina-Borja M, Peckham CS. Rubella susceptibility among pregnant women in North London, 1996–1999. *Journal of Public Health Medicine* 2002;24:211–6.

425. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. *Lancet* 1982;2:781–4.

426. Grangeot-Keros L, Enders G. Evaluation of a new enzyme immunoassay based on recombinant Rubella virus-like particles for detection of immunoglobulin M antibodies to Rubella virus. *Journal of Clinical Microbiology* 1997;35:398–401.

427. Morgan-Capner P, Crowcroft NS. Guidelines on the management of, and exposure to, rash illness in pregnancy (including consideration of relevant antibody screening programmes in pregnancy). On behalf of the PHLS joint working party of the advisory committees of virology and vaccines and immunisation. *Communicable Disease and Public Health/PHLS* 2002;5(1):59–71.

428. Grillner L, Forsgren M, Barr B. Outcome of rubella during pregnancy with special reference to the 17th–24th weeks of gestation. Scandinavian Journal of Infectious Diseases 1983;Vol 15:321–5.

429. Morgan-Capner P, Hodgson J, Hambling MH. Detection of rubella-specific IgM in subclinical rubella reinfection in pregnancy. *Lancet* 1985;1:244–6.

430. Revised ACIP recommendation for avoiding pregnancy after receiving a rubella-containing vaccine. *MMWR–Morbidity and Mortality Weekly Report* 2001;50:1117.

431. Health Protection Agency. Incidence of Group B streptococcal disease in infants aged less than 90 days old. *CDR Weekly* 2002;12(16):3. [http://193.129.245.226/publications/cdr/archive02/News/news1602.html gpB] Accessed 21 August 2003.

432. Merenstein GB, Todd WA, Brown G. Group B beta-hemolytic streptococcus: Randomized controlled treatment study at term. *Obstetrics and Gynecology* 1980;55:315–8.

433. Regan JA, Klebanoff MA, Nugent RP. The epidemiology of Group B streptococcal colonization in pregnancy. *Obstetrics and Gynecology* 1991;77:604–10.

434. Hastings MJ, Easmon CS, Neill J, Bloxham B, Rivers RP. Group B streptococcal colonisation and the outcome of pregnancy. *Journal of Infection* 1986;12:23–9.

435. Oddie S, Embleton ND. Risk factors for early onset neonatal group B streptococcal sepsis: case–control study. *British Medical Journal* 2002;325:308.

436. Centers for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. Revised Guidelines from CDC. *Morbidity and Mortality Weekly Report* 2002;51(RR11):1–25. [www.cdc.gov/mmwr/preview/mmwrhtml/rr5111a1.htm] Accessed 21 August 2003.

437. Fey R, Stuart J, George R. Neonatal group B streptococcal disease in England and Wales 1981–1997. *Archives of Disease in Childhood* 1999;80:A70.

438. Bignardi GE. Surveillance of neonatal group B streptococcal infection in Sunderland. *Communicable Disease and Public Health/PHLS* 1999;2(1):64–5.

439. Yancey MK, Schuchat A, Brown LK, Ventura VL, Markenson GR. The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery. *Obstetrics and Gynecology* 1996;88:811–5.

440. Boyer KM, Gadzala CA, Kelly PD, Burd LI, Gotoff SP. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. II. Predictive value of prenatal cultures. *Journal of Infectious Diseases* 1983;148:802–9.

441. Molnar P, Biringer A, McGeer A, McIsaac W. Can pregnant women obtain their own specimens for group B streptococcus? A comparison of maternal versus physician screening. The Mount Sinai GBS Screening Group. *Family Practice* 1997;14:403–6.

442. Spieker MR, White DG, Quist BK. Self-collection of group B Streptococcus cultures in pregnant women. *Military Medicine* 1999;164:471–4.

443. Schrag SJ, Zell ER, Lynfield R, Roome A, Arnold KE, Craig AS, *et al*. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. *New England Journal of Medicine* 2002;347:233–9.

444. Smaill, F. Intrapartum antibiotics for group B streptococcal colonisation. *Cochrane Database of Systematic Reviews* 1999;(3):1–5.

445. Benitz WE, Gould JB, Druzin ML. Antimicrobial prevention of early-onset group B streptococcal sepsis: estimates of risk reduction based on a critical literature review. *Pediatrics* 1999;103:e78.

446. Gibbs RS, McNabb F. Randomized clinical trial of intrapartum clindamycin cream for reduction of group B streptococcal maternal and neonatal colonization. *Infectious Disease in Obstetrics and Gynecology* 1996;41:25–7.

447. Schrag SJ, Zywicki S, Farley MM, Reingold AL. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. *New England Journal of Medicine* 2000;342:15–20.

448. Jeffery HE, Moses LM. Eight-year outcome of universal screening and intrapartum antibiotics for maternal group B streptococcal carriers. *Pediatrics* 1998;101:E2.

449. Egglestone SI, Turner AJL. Serological diagnosis of syphilis. *Communicable Disease and Public Health/PHLS* 2000;3:158–62.

450. Doherty L, Fenton KA, Jones J, Paine TC, Higgins SP, Williams D, *et al*. Syphilis: old problem, new strategy. *British Medical Journal* 2002;325:153–6.

451. Division of STD/HIV Prevention. *Sexually Transmitted Disease Surveillance 1993*. Atlanta, GA: Centers for Disease Control and Prevention;1994.

452. Flowers J, Camilleri-Ferrante. *Antenatal screening for syphilis in East Anglia: a cost-benefit analysis*. Cambridge: Institute of Public Health; 1996.

453. STD Section, HIV and STD Division, PHLS Communicable Disease Surveillance Centre, with the PHLS Syphilis Working Group. *Report to the National Screening Committee. Antenatal Syphilis Screening in the UK: A Systematic Review and National Options Appraisal with Recommendations*. London: PHLS; 1998.

454. Public Health Laboratory Service, DHSS & PS, Scottish ISD D 5 Collaborative Group. *Sexually transmitted infections in the UK: new episodes seen at Genitourinary Medicine Clinics, 1995–2000*. London: PHLS; 2001.

455. Ingraham NR Jr. The value of penicillin alone in the prevention and treatment of congenital syphilis. *Acta Dermato-Venereologica* 1951;31:60–88.

456. Association of Genitourinary Medicine and the Medical Society for the Study of Venereal Diseases, Clinical Effectiveness Group. *UK national guidelines on the management of early syphilis*. London: Medical Society for the Study of Venereal Diseases; 2002. p. 1–18.

457. Goh BT, van Voorst Vader PC. European guideline for the management of syphilis. *International Journal of STD and AIDS* 2001;12:14–26.

458. Fiumara NJ, Fleming WL, Downing JG, Good FL. The incidence of prenatal syphilis at the Boston City Hospital. *New England Journal of Medicine* 1952;247:48–52.

459. Rotchford K, Lombard C, Zuma K, Wilkinson D. Impact on perinatal mortality of missed opportunities to treat maternal syphilis in rural South Africa: baseline results from a clinic randomized controlled trial. *Tropical Medicine and International Health* 2000;5:800–4.

460. Young H, Moyes A, McMillan A, Patterson J. Enzyme immunoassay for anti-treponemal IgG: Screening of confirmatory test? *Journal of Clinical Pathology* 1992;45:37–41.

461. Young H, Moyes A, McMillan A, Robertson DHH. Screening for treponemal infection by a new enzyme immunoassay. *Genitourinary Medicine* 1989;65:72–8.

462. Walker, GJA. Antibiotics for syphilis diagnosed during pregnancy [protocol]. *Cochrane Database of Systematic Reviews* 2001;(2).

463. Alexander JM, Sheffield JS, Sanchez PJ, Mayfield J, Wendel GD Jr. Efficacy of treatment for syphilis in pregnancy. *Obstetrics and Gynecology* 1999;93:5–8.

464. Watson-Jones D, Gumodoka B, Weiss H, Changalucha J, Todd J, Mugeye K, *et al*. Syphilis in pregnancy in Tanzania. II. The effectiveness of antenatal syphilis screening and single-dose benzathine penicillin treatment for the prevention of adverse pregnancy outcomes. *Journal of Infectious Diseases* 2002;186:948–57.

465. Hashisaki P, Wertzberger GG, Conrad GL, Nicholes CR. Erythromycin failure in the treatment of syphilis in a pregnant woman. *Sexually Transmitted Diseases* 1983;10:36–8.

466. Eskild A, Oxman A, Magnus P, Bjorndal A, Bakketeig LS. Screening for toxoplasmosis in pregnancy: what is the evidence of reducing a health problem? *Journal of Medical Screening* 1996;3:188–94.

467. Ades AE, Parker S, Gilbert R, Tookey PA, Berry T, Hjelm M, *et al*. Maternal prevalence of toxoplasma antibody based on anonymous neonatal serosurvey: a geographical analysis. *Epidemiology and Infection* 1993;110:127–33.

468. Allain JP, Palmer CR, Pearson G. Epidemiological study of latent and recent infection by toxoplasma gondii in pregnant women from a regional population in the UK. *Journal of Infection* 1998;36:189–96.

469. Lebech M, Andersen O, Christensen NC, Hertel J, Nielsen HE, Peitersen B, *et al*. Feasibility of neonatal screening for toxoplasma infection in the absence of prenatal treatment. *Lancet* 1999;353:1834–7.

470. Cook AJ, Gilbert RE, Buffolano W, Zufferey J, Petersen E, Jenum PA, *et al*. Sources of toxoplasma infection in pregnant women: European multicentre case–control study. European Research Network on Congenital Toxoplasmosis. *British Medical Journal* 2000;321:142–7.

471. Pratlong F, Boulot P, Villena I, Issert E, Tamby I, Cazenave J *et al*. Antenatal diagnosis of congenital toxoplasmosis: evaluation of the biological parameters in a cohort of 286 patients. *British Journal of Obstetrics and Gynaecology* 1996;103:552–7.

472. Dunn D, Wallon M, Peyron F, Petersen E, Peckham C, Gilbert R. Mother-to-child transmission of toxoplasmosis: risk estimates for clinical counselling. *Lancet* 1999;353:1829–33.

473. Foulon W, Villena I, Stray-Pedersen B, Decoster A, Lappalainen M, Pinon JM, *et al*. Treatment of toxoplasmosis during pregnancy: a multicenter study of impact on fetal transmission and children's sequelae at age 1 year. *American Journal of Obstetrics and Gynecology* 1999;180:410–5.

474. Cubitt WD, Ades AE, Peckham CS. Evaluation of five commercial assays for screening antenatal sera for antibodies to Toxoplasma gondii. *Journal of Clinical Pathology* 1992;45:435–8.

475. Gilbert RE, Peckham CS. Congenital toxoplasmosis in the United Kingdom: to screen or not to screen? *Journal of Medical Screening* 2002;9:135–41.

476. Peyron, F, Wallon, M, Liou, C, and Garner, P. Treatments for toxoplasmosis in pregnancy. *Cochrane Database of Systematic Reviews* 2002;(3).

477. Wallon M, Liou C, Garner P, Peyron F. Congenital toxoplasmosis: systematic review of evidence of efficacy of treatment in pregnancy. *British Medical Journal* 1999;318:1511–14.

478. Garland SM, O'Reilly MA. The risks and benefits of antimicrobial therapy in pregnancy. *Drug Safety* 1995;13:188–205.

479. Bader TJ, Macones GA, Asch DA. Prenatal screening for toxoplasmosis. *Obstetrics and Gynecology* 1997;90:457–64.

480. Scottish Intercollegiate Guidelines Network. Management of diabetes: a national clinical guideline. SIGN Publication No. 55Edinburgh: SIGN; 2001. [www.sign.ac.uk/guidelines/fulltext/55/index.html] Accessed 21 August 2003.

481. World Health Organization, Department of Noncommunicable Disease Surveillance. *Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consultation. Part 1: diagnosis and classification of diabetes mellitus*. Geneva: World Health Organization; 1999.

482. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabetic Medicine* 1998;15:539–53.

483. Scott DA, Loveman E, McIntyre L, Waugh N. Screening for gestational diabetes: a systematic review and economic evaluation. *Health Technology Assessment* 2002;6:1–172.

484. World Health Organization. *Prevention of diabetes mellitus: report of a WHO study group*. WHO Technical Report Series No. 844. Geneva: WHO; 1994.

485. Mestman JH, Anderson GV, Guadalupe V. Follow-up study of 360 subjects with abnormal carbohydrate metabolism during pregnancy. *Obstetrics and Gynecology* 1972;39:421–5.

486. Jensen DM, Sorensen B, Feilberg-Jorgensen N, Westergaard JG, Beck-Neilsen H. Maternal and perinatal outcomes in 143 Danish women with gestational diabetes mellitus and 143 controls with a similar risk profile. *Diabetic Medicine* 2000;17:281–6.

487. O'Sullivan JB, Charles D, Mahan CM, Dandrow RV. Gestational diabetes and perinatal mortality rate. *American Journal of Obstetrics and Gynecology* 1973;116:901–4.

488. Essel JK, Opai-Tetteh ET. Macrosomia: maternal and fetal risk factors. *South African Medical Journal* 1995;85(1):43–6.

489. Vogel N, Burnand B, Vial Y, Ruiz J, Paccaud F, Hohlfeld P. Screening for gestational diabetes: variation in guidelines. *European Journal Obstetrics, Gynecology and Reproductive Biology* 2000;91:29–36.

490. Marquette GP, Klein VR, Niebyl JR. Efficacy of screening for gestational diabetes. *American Journal of Perinatology* 1985;2:7–9.

491. O'Sullivan JB, Mahan CM, Charles D, Dandrow RV. Screening criteria for high-risk gestational diabetic patients. *American Journal of Obstetrics and Gynecology* 1973;116:895–900.

492. Wen SW, Liu S, Kramer MS, Joseph KS, Levitt C, Marcoux S, *et al*. Impact of prenatal glucose screening on the diagnosis of gestational diabetes and on pregnancy outcomes. *American Journal of Epidemiology* 2000;152:1009–14.

493. Watson WJ. Screening for glycosuria during pregnancy. *Southern Medical Journal* 1990;83:156–8.

494. Gribble RK, Meier PR, Berg RL. The value of urine screening for glucose at each prenatal visit. *Obstetrics and Gynecology* 1995;86:405–10.

495. Hooper DE. Detecting GD and preeclampsia. Effectiveness of routine urine screening for glucose and protein. *Journal of Reproductive Medicine* 1996;41:885–8.

496. McElduff A, Goldring J, Gordon P, Wyndham L. A direct comparison of the measurement of a random plasma glucose and a post-50 g glucose load glucose, in the detection of gestational diabetes. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 1994;34:28–30.

497. Jowett NI, Samanta AK, Burden AC. Screening for diabetes in pregnancy: is a random blood glucose enough? *Diabetic Medicine* 1987;4:160–3.

498. Reichelt AJ, Spichler ER, Branchtein L, Nucci LB, Franco LJ, Schmidt MI. Fasting plasma glucose is a useful test for the detection of gestational diabetes. Brazilian Study of Gestational Diabetes (EBDG) Working Group. *Diabetes Care* 1998;21:1246–9.

499. Perucchini D, Fischer U, Spinas GA, Huch R, Huch A, Lehmann R. Using fasting plasma glucose concentrations to screen for gestational diabetes mellitus: prospective population based study. *British Medical Journal* 1999;319:812–5.

500. Lewis GF, McNally C, Blackman JD, Polonsky KS, Barron WM. Prior feeding alters the response to the 50-g glucose challenge test in pregnancy. The Staub-Traugott Effect revisited. *Diabetes Care* 1993;16:1551–6.

501. Watson WJ. Serial changes in the 50-g oral glucose test in pregnancy: implications for screening. *Obstetrics and Gynecology* 1989;74:40–3.

502. Jovanovic L, Peterson CM. Screening for gestational diabetes. Optimum timing and criteria for retesting. *Diabetes* 1985;34:21–3.

503. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care 2000*;26 Supplement 1:S5–S20.

504. Walkinshaw SA. Dietary regulation for 'gestational diabetes'. *Cochrane Database of Systematic Reviews* 2000;(2).

505. Persson B, Stangenberg M, Hansson U, Nordlander E. Gestational diabetes mellitus (GDM). Comparative evaluation of two treatment regimens, diet versus insulin and diet. *Diabetes* 1985;34:101–4.

506. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance. Pathophysiology or practice style? *JAMA* 1996;275:1165–70.

507. Avery MD, Leon AS, Kopher RA. Effects of a partially home-based exercise program for women with gestational diabetes. *Obstetrics and Gynecology* 1997;89:10–5.

508. Goldberg JD, Franklin B, Lasser D, Jornsay DL, Hausknecht RU, Ginsberg-Fellner F, *et al*. Gestational diabetes: impact of home glucose monitoring on neonatal birth weight. *American Journal of Obstetrics and Gynecology* 1986;154:546–50.

509. Roberts JM, Redman CW. Pre-eclampsia: more than pregnancy-induced hypertension. *Lancet* 1993;341:1447–51.

510. Douglas KA, Redman CW. Eclampsia in the United Kingdom. *British Medical Journal* 1994;309:1395–400.

511a. National High Blood Pressure Education Programme. *Working Group Report on high blood pressure in pregnancy*. NIH Publication 00-3029. Bethesda, MD: National Institutes of Health, National Heart, Lung and Blood Institute; 2000.

511b. National High Blood Pressure Education Program Working Group. Report on high blood pressure in pregnancy. *American Journal of Obstetrics and Gynecology* 1990;163:1691–712.

512. Duckitt, K. Risk factors for pre-eclampsia that can be assessed at the antenatal booking visit: a systematic review. Presented at the International Society for the Study of Hypertension in Pregnancy Conference, 24–25 July 2003, Glasgow. 2003.

513. Friedman EA. *Blood pressure, edema and proteinuria in pregnancy*. Oxford: Elsevier Scientific; 1976.

514. Redman CW. Hypertension in pregnancy. pp 182–225. 1995.

515. Barton JR, O'Brien JM, Bergauer NK, Jacques DL, Sibai BM. Mild gestational hypertension remote from term: progression and outcome. American Journal of *Obstetrics and Gynaecology* 2001;184:979–83.

516a. Page EW, Christianson R. The impact of mean arterial pressure in the middle trimester upon the outcome of pregnancy. *American Journal of Obstetrics and Gynecology* 1976;125:740–6.

516b. Page EW, Christianson R. Influence of blood pressure changes with and without proteinuria upon outcome of pregnancy. *American Journal of Obstetrics and Gynecology* 1976;126:821–33.

517. Greer IA. Hypertension. In Dunlop W, Calder AA, editors. *High risk pregnancy*. Oxford: Butterworth Heinemann; 1992. p. 30–93.

518. Redman CW, Jefferies M. Revised definition of pre-eclampsia. *Lancet* 1988;1:809–12.

519. North RA, Taylor RS, Schellenberg JC. Evaluation of a definition of pre-eclampsia. *British Journal of Obstetrics and Gynaecology* 1999;106:767–73.

520. Levine RJ. Should the definition of preeclampsia include a rise in diastolic blood pressure > 15 mmHg to a level < 90 mmHg in association with proteinuria? *American Journal of Obstetrics and Gynecology* 2000;183:787–92.

521. Perry IJ, Wilkinson LS, Shinton RA, Beevers DG. Conflicting views on the measurement of blood pressure in pregnancy. *British Journal of Obstetrics and Gynaecology* 1991;98:241–3.

522. Frohlich ED, Grim C, Labarthe DR, Maxwell MH, Perloff D, Weidman WH. Recommendations for human blood pressure determination by sphygmomanometers: Report of a special task force appointed by the Steering Committee, American Heart Association. *Hypertension* 1988;11:210A–22A.

523. Petrie JC, O'Brien ET, Littler WA, de Swiet M. Recommendations on blood pressure measurement. *British Medical Journal* 1986;293:611–5.

524. Shennan AH, Halligan AWF. Measuring blood pressure in normal and hypertensive pregnancy. *Baillieres Clinical Obstetrics and Gynaecology* 1999;13(1):1–26.

525. Cuckson AC, Golara M, Reinders A, Shennan AH. Accuracy of automated devices in pregnancy and pre-eclampsia: a meta-analysis. *Journal of Obstetrics and Gynaecology* 2002;22:S43.

526. Mattoo TK. Arm cuff in the measurement of blood pressure. *American Journal of Hypertension* 2002;15:675–85.

527. Brown MA, Buddle ML, Farrell T, Davis G, Jones M. Randomised trial of management of hypertensive pregnancies by Korotkoff phase IV or phase V. *Lancet* 1998;352:777–81.

528. Shennan A, Gupta M, Halligan A, Taylor DJ, de Swiet M. Lack of reproducibility in pregnancy of Korotkoff phase IV as measured by mercury sphygmomanometry. *Lancet* 1996;347:139–42.

529. MacGillivray I. *Pre-eclampsia. The hypertensive disease of pregnancy*. London: WB Saunders; 1983.

530. Stamilio DM, Sehdev HM, Morgan MA, Propert K, Macones GA. Can antenatal clinical and biochemical markers predict the development of severe preeclampsia? *American Journal of Obstetrics and Gynecology* 2000;182:589–94.

531. Skjaerven R, Wilcox AJ, Lie RT. The interval between pregnancies and the risk of preeclampsia. *New England Journal of Medicine* 2002;346:33–8.

532. Taylor DJ. The epidemiology of hypertension during pregnancy. In: Rubin PC, editor. *Hypertension in pregnancy*. Amsterdam: Elsevier Science; 1988. p. 223–40.

533. Salonen-Ros H, Lichtenstein P, Lipworth W. Genetic effects on the liability of developing pre-eclampsia and gestational hypertension. *American Journal of Medical Genetics* 2000;91:256–60.

534. Sibai BM, Caritis S, Hauth J. Risks of preeclampsia and adverse neonatal outcomes among women with progestational diabetes mellitus. *American Journal of Obstetrics and Gynecology* 2000;182:364–9.

535. Davey DA, MacGillivray I. The classification and definition of the hypertensive disorders of pregnancy. *American Journal of Obstetrics and Gynecology* 1988;158(4):892–898.

536. Murray N, Homer LS, Davis GK, Curtis J, Manzos G, Brown MA. The clinical utility of routine urinalysis in pregnancy: a prospective study. *Medical Journal of Australia* 2002;177:477–80.

537. Shennan AH, Waugh JJS. The measurement of blood pressure and proteinuria. In: Critchley H, MacLean AB, Poston L, Walker JJ, editors. *Pre-eclampsia*. London: RCOG Press; 2003. p. 305–24.

538. Rodriguez-Thompson D, Lieberman ES. Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy. *American Journal of Obstetrics and Gynecology* 2001;185:808–11.

539. Ferrazzani S, Caruso A, De Carolis S, Martino IV, Mancuso S. Proteinuria and outcome of 444 pregnancies complicated by hypertension. *American Journal of Obstetrics and Gynecology* 1990;162:366–71.

540. Waugh JJS, Clark TJ, Divakaran TG, Khan KS, Kilby MD. A systematic review and meta-analysis comparing protein/creatinine ratio measurements and dipstick urinalysis in predicting significant proteinuria in pregnancy. Presented at the British Maternal and Fetal Medicine Society, University of York, 20–21 March 2003.

541. Chamberlain G, Morgan M. *ABC of Antenatal Care*. London: BMJ Publishing; 2002.

542. Buekens P, Alexander S, Boutsen M, Blondel B, Kaminski M, Reid M. Randomised controlled trial of routine cervical examinations in pregnancy. European Community Collaborative Study Group on Prenatal Screening. *Lancet* 1994;344:841–4.

543. Iams JD, Goldenberg RL, Meis PJ. The length of the cervix and the risk of spontaneous premature delivery. *New England Journal of Medicine* 1996;334:567–72.

544. Goldenberg RL, Klebanoff M, Carey JC. Vaginal fetal fibronectin measurements from 8 to 22 weeks' gestation and subsequent spontaneous preterm birth. *American Journal of Obstetrics and Gynecology* 2000;183:469–75.

545. Goldenberg RL, Mercer BM, Meis PJ, Copper RL, Das A, McNellis D. The preterm prediction study: fetal fibronectin testing predicts early spontaneous birth. *Obstetrics and Gynecology* 1996;87:643–8.

546. Mercer BM, Goldenberg RL, Das A. The preterm prediction study: a clinical risk assessment system. *American Journal of Obstetrics and Gynecology* 1996;174:1885–95.

547. Newton ER, Barss V, Cetrulo CL. The epidemiology and clinical history of asymptomatic midtrimester placenta previa. *American Journal of Obstetrics and Gynecology* 1984;148:743–8.

548. Lauria MR, Smith RS, Treadwell MC, Comstock CH, Kirk JS, Lee W, *et al*. The use of second-trimester transvaginal sonography to predict placenta previa. *Ultrasound in Obstetrics and Gynecology* 1996;8:337–40.

549. Leerentveld RA, Gilberts EC, Arnold MJ, Wladimiroff JW. Accuracy and safety of transvaginal sonographic placental localization. *Obstetrics and Gynecology* 1990;76:759–62.

550. Oppenheimer L, Holmes P, Simpson N, Dabrowski A. Diagnosis of low-lying placenta: can migration in the third trimester predict outcome? *Ultrasound in Obstetrics and Gynecology* 2001;18:100–2.

551. Sherman SJ, Carlson DE, Platt LD, Medearis AL. Transvaginal ultrasound: does it help in the diagnosis of placenta previa? *American Journal of Obstetrics and Gynecology* 1991;164:344.

552. Farine D, Peisner DB, Timor-Tritsch IE. Placenta previa: is the traditional diagnostic approach satisfactory? *Journal of Clinical Ultrasound* 1990;18:328–30.

553. Taipale P, Hiilesmaa V, Ylostalo P. Diagnosis of placenta previa by transvaginal sonographic screening at 12–16 weeks in a nonselected population. *Obstetrics and Gynecology* 1997;89:364–7.

554. Taipale P, Hiilesmaa V, Ylostalo P. Transvaginal ultrasonography at 18–23 weeks in predicting placenta previa at delivery. *Ultrasound in Obstetrics and Gynecology* 1998;12:422–5.

555. Hill LM, DiNofrio DM, Chenevey P. Transvaginal sonographic evaluation of first-trimester placenta previa. *Ultrasound in Obstetrics and Gynecology* 1995;5:301–3.

556. Dashe JS, McIntire DD, Ramus RM. Persistence of placenta previa according to gestational age at ultrasound detection. *Obstetrics and Gynecology* 2002;99:692–7.

557. Groo KM, Paterson-Brown S. Placenta praevia and placenta praevia accreta: A review of aetiology, diagnosis and management. *Fetal and Maternal Medicine Review* 2001;12:41–66.

558. Ananth CV, Smulian JC, Vintzileos AM. The association of placenta previa with history of cesarean delivery and abortion: a metaanalysis. *American Journal of Obstetrics and Gynecology* 1997;177:1071–8.

559. Ananth CV, Demissie K, Smulian JC. Placenta previa in singleton and twin births in the United States, 1989 through 1998: a comparison of risk factor profiles and associated conditions. *American Journal of Obstetrics and Gynecology* 2003;188:275–81.

560. Royal College of Obstetricians and Gynaecologists. *Placenta praevia: diagnosis and management*. Guideline No. 27. London: RCOG; 2001.

561. Neilson JP. Interventions for suspected placenta praevia. *Cochrane Database of Systematic Reviews* 2003;(1):1–19.

562. McFarlin BL, Engstrom JL, Sampson MB, Cattledge F. Concurrent validity of Leopold's maneuvers in determining fetal presentation and position. *Journal of Nurse-Midwifery* 1985;30:280–4.

563. Vause S, Hornbuckle J, Thornton JG. Palpation or ultrasound for detecting breech babies? *British Journal of Midwifery* 1997;5:318–9.

564. Thorp JM Jr, Jenkins T, Watson W. Utility of Leopold maneuvers in screening for malpresentation. *Obstetrics and Gynecology* 1991;78:394–6.

565. Olsen K. Midwife to midwife. 'Now just pop up here, dear...' revisiting the art of antenatal abdominal palpation. *Practising Midwife* 1999;2:13–5.

566. Neilson JP. Symphysis-fundal height measurement in pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).

567. Gardosi J, Francis A. Controlled trial of fundal height measurement plotted on customised antenatal growth charts. *British Journal of Obstetrics and Gynaecology* 1999;106:309–317.

568. Macones GA, Depp R. Fetal monitoring. In: Wildschut HIJ, Weiner CP, Peters TJ, editors. *When to screen in obstetrics and gynaecology*. London: WB Saunders; 1996. p. 202–18.

569. Grant A, Elbourne D, Valentin L, Alexander S. Routine formal fetal movement counting and risk of antepartum late death in normally formed singletons. *Lancet* 1989;ii:345–9.

570. Divanovic E, Buchmann EJ. Routine heart and lung auscultation in prenatal care. *International Journal of Gynecology and Obstetrics* 1999;64:247–51.

571. Sharif K, Whittle M. Routine antenatal fetal heart rate auscultation: is it necessary? *Journal of Obstetrics and Gynaecology* 1993;13:111–3.

572. Garcia J, Corry M, MacDonald D, Elbourne D, Grant A. Mothers' views of continuous electronic fetal heart monitoring and intermittent auscultation in a randomized controlled trial. *Birth* 1985;12:79–86.

573. Pattison N, McCowan L. Cardiotocography for antepartum fetal assessment. *Cochrane Database of Systematic Reviews* 2001;(2).

574. Bricker L, Neilson JP. Routine ultrasound in late pregnancy (> 24 weeks gestation). *Cochrane Database of Systematic Reviews* 2001;(2).

575. Bricker L, Neilson JP. Routine Doppler ultrasound in pregnancy. *Cochrane Database of Systematic Reviews* 2001;(2).

576. Chien PF, Arnott N, Gordon A, Owen P, Khan KS. How useful is uterine artery Doppler flow velocimetry in the prediction of pre-eclampsia, intrauterine growth retardation and perinatal death? An overview. *BJOG* 2000;107:196–208.

577. Hilder L, Costeloe K, Thilaganathan B. Prolonged pregnancy: evaluating gestation-specific risks of fetal and infant mortality. *British Journal of Obstetrics and Gynaecology* 1998;105:169–73.

578. Crowley, P. Interventions for preventing or improving the outcome of delivery at or beyond term. *Cochrane Database of Systematic Reviews* 2003;(1).

579. Boulvain M, Fraser WD, Marcoux S, Fontaine JY, Bazin S, Pinault JJ, Blouin D. Does sweeping of the membranes reduce the need for formal induction of labour? A randomised controlled trial. *British Journal of Obstetrics and Gynaecology* 1998;105:34–40.

580. Melzack R. The short-form McGill pain questionnaire. *Pain* 1987;30:191–7.

581. Royal College of Obstetricians and Gynaecologists, Clinical Effectiveness Support Unit. *National Sentinel Caesarean Section Audit Report*. London: RCOG Press; 2001.

582. Nelson KB, Ellenberg JH. Antecedents of cerebral palsy. Multivariate analysis of risk. *New England Journal of Medicine* 1986;315:81–6.

583. Kitchen WH, Yu VY, Orgill AA, Ford G, Rickards A, Astbury J, *et al*. Infants born before 29 weeks gestation: survival and morbidity at 2 years of age. *British Journal of Obstetrics and Gynaecology* 1982;89:887–91.

584. Lau TK, Lo KW, Rogers M. Pregnancy outcome after successful external cephalic version for breech presentation at term. *American Journal of Obstetrics and Gynecology* 1997;176:218–23.

585. Brocks V, Philipsen T, Secher NJ. A randomized trial of external cephalic version with tocolysis in late pregnancy. *British Journal of Obstetrics and Gynaecology* 1984;91:653–6.

586. Van Veelan AJ, Van Cappellen AW, Flu PK, Straub MJPF, Wallenburg HC. Effect of external cephalic version in late pregnancy on presentation at delivery: a randomized controlled trial. *British Journal of Obstetrics and Gynaecology* 1989;96:916–21.

587. Dugoff L, Stamm CA, Jones OW, Mohling SI, Hawkins JL. The effect of spinal anesthesia on the success rate of external cephalic version: a randomized trial. *Obstetrics and Gynecology* 1999;93:345–9.

588. Van Dorsten JP, Schifrin BS, Wallace RL. Randomized control trial of external cephalic version with tocolysis in late pregnancy. *American Journal of Obstetrics and Gynecology* 1981;141:417–24.

589. Hofmeyer GJ. External cephalic version for breech presentation before term. *Cochrane Database of Systematic Reviews* 2001;(2).

590. Hofmeyer GJ. External cephalic version facilitation for breech presentation at term. *Cochrane Database of Systematic Reviews* 2001;(2).

591. Mahomed K, Seeras R, Coulson R. External cephalic version at term. A randomized controlled trial using tocolysis. *British Journal of Obstetrics and Gynaecology* 1991;98:8–13.

592. Hofmeyr GJ. Effect of external cephalic version in late pregnancy on breech presentation and caesarean section rate: a controlled trial. *British Journal of Obstetrics and Gynaecology* 1983;90:392–9.

593. Mushambi M. External cephalic version: new interest and old concerns. *International Journal of Obstetric Anesthesia* 2001;10:263–6.

594. Hofmeyer GJ. Interventions to help external cephalic version for breech presentation at term. *Cochrane Database of Systematic Reviews* 2002;(4).

595. van Loon AJ, Mantingh A, Serlier EK, Kroon G, Mooyaart EL, Huisjes HJ. Randomised controlled trial of magnetic-resonance pelvimetry in breech presentation at term. *Lancet* 1997;350:1799–804.

596. Walkinshaw SA. Pelvimetry and breech at term. *Lancet* 2002;350:1791–2.

597. Hofmeyr GJ, Kulier, R. Cephalic version by postural management for breech presentation. *Cochrane Database of Systematic Reviews* 2003;(1).

598. Cardini F, Weixin H. Moxibustion for correction of breech presentation: a randomized controlled trial. *JAMA* 1998;280:1580–4.

599. Li Q. Clinical observation on correcting malposition of fetus by electro-acupuncture. *Journal of Traditional Chinese Medicine* 1996;16:260–2.

600. Rouse DJ, Andrews WW, Goldenberg RL, Owen J. Screening and treatment of asymptomatic bacteriuria of pregnancy to prevent pyelonephritis: a cost-effectiveness and cost-benefit analysis. *Obstetrics and Gynecology* 1995;86:119–23.

601. Petrou S, Sach T, Davidson L. The long-term costs of preterm birth and low birth weight: results of a systematic review. *Child: Care, Health and Development* 2001;27:97–115.

602. Connor N, Roberts J, Nicoll A. Strategic options for antenatal screening for syphilis in the United Kingdom: a cost effectiveness analysis. *Journal of Medical Screening* 2000;7:7–13.

603. Read JS, Klebanoff MA. Sexual intercourse during pregnancy and preterm delivery: effects of vaginal microorganisms. *American Journal of Obstetrics and Gynecology* 1993;168:514–19.

604. Raymond EG, Cnattingius S, Kiely JL. Effects of maternal age, parity, and smoking on the risk of stillbirth. *British Journal of Obstetrics and Gynaecology* 1994;101:301–6.

605. Ho KY, Kang JY, Viegas OA. Symptomatic gastro-oesophageal reflux in pregnancy: a prospective study among Singaporean women. *Journal of Gastroenterology and Hepatology* 1998;13:1020–6.

606. Kovacs GT, Campbell J, Francis D, Hill D, Adena A. Is Mucaine an appropriate medication for the relief of heartburn during pregnancy? *Asia-Oceania Journal of Obstetrics and Gynaecology* 1990;16:357–62.

607. Briggs DW, Hart DM. Heartburn of pregnancy. A continuation study. *British Journal of Clinical Practice* 1972;26:167–9.

608. Dick PT, with the Canadian Task Force on the Periodic Health Examination. Prenatal screening and diagnosis of Down Syndrome. 84–98. 1994. [www.ctfphc.org/Full_Text/Ch08full.htm] Accessed 4 September 2003.

609. Bindra R, Heath V, Liao A, Spencer K, Nicolaides KH. One-stop clinic for assessment of risk for trisomy 21 at 11–14 weeks: a prospective study of 15030 pregnancies. *Ultrasound in Obstetrics and Gynecology* 2002;20:219–25.

610. Mastrobattista JM, Bishop KD, Newton ER. Wet smear compared with gram stain diagnosis of bacterial vaginosis in asymptomatic pregnant women. *Obstetrics and Gynecology* 2000;96:504–6.

611. Krohn MA, Hillier SL, Eschenbach DA. Comparison of methods of diagnosing bacterial vaginosis among pregnant women. *Journal of Clinical Microbiology* 1990;27:1266–71.

612. Royal College of Obstetricians and Gynaecologists. *Induction of labour*. Evidence-based Clinical Guideline No. 9. London: RCOG Press; 2001.

613. Department of Health. Unlinked Anonymous Prevalence Monitoring Programme in the United Kingdom. *Summary Report from the Unlinked Anonymous Surveys Steering Group. Data to the end of 1998*. London: DoH; 1999.

614. Balano K, Beckerman K, Ng V. Rapid HIV screening during labor. *JAMA* 1998;280:1664.

615. Postma MJ, Beck EJ, Mandalia S, Sherr L, Walters MDS, Houweling H, *et al*. Universal HIV screening of pregnant women in England: cost effectiveness analysis. *British Medical Journal* 1999;318:1656–60.

616. Shey Wiysonge CU, Brocklehurst P, Sterne JAC. Vaginal disinfection during labor for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database of Systematic Reviews* 2002;(3).

617. Kind C, Rudin C, Siegrist C, Wyler C, Biedermann K, Lauper U, *et al*. Prevention of vertical HIV transmission: additive protective effect of elective cesarean section and zidovudine prophylaxis. *AIDS* 1998;12:205–10.

618. Shey Wiysonge CU, Brocklehurst P, Sterne, JAC. Vitamin A supplementation for reducing the risk of mother-to-child transmission of HIV infection. *Cochrane Database of Systematic Reviews* 2002;(3).

619. Stray-Pedersen B. Economic evaluation of different vaccination programmes to prevent congenital rubella. *NIPH Annals* 1982;5:69–83.

620. Hurtig AK, Nicoll A, Carne C, Lissauer T, Connor N, Webster JP, *et al*. Syphilis in pregnant women and their children in the United Kingdom: results from national clinician reporting surveys 1994–97. *British Medical Journal* 1998;317:1617–19.

621. Ryan M, Hall SM, Barrett NJ, Balfour AH, Holliman RE, Joynson DH. Toxoplasmosis in England and Wales 1981 to 1992. *CDR Review* 1995;5:R13–21.

622. Lappalainen M, Koskiniemi M, Hiilesmaa V, Ammala P, Teramo K, Koskela P, *et al*. Outcome of children after maternal primary Toxoplasma infection during pregnancy with emphasis on avidity of specific IgG. *Pediatric Infectious Disease Journal* 1995;14:354–61.

623. Danielian PJ, Wang J, Hall MH. Long-term outcome by method of delivery of fetuses in breech presentation at term: population based follow up. *British Medical Journal* 1996;312:1451–3.

624. Krebs L, Topp M, Langhoff-Roos, J. The relation of breech presentation at term to cerebral palsy. *British Journal of Obstetrics and Gynaecology* 1999;106:943–7.

625. Milsom I, Ladfors L, Thiringer K, Niklasson A, Odeback A, Thornberg E. Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. *Acta Obstetricia et Gynecologica Scandinavica* 2002;81:907–17.

626. van Loon AJ, Mantingh A, Thijn CJP, Mooyaart EL. Pelvimetry by magnetic resonance imaging in breech presentation. *American Journal of Obstetrics and Gynecology* 1990;163:1256–60.

627. Hofmeyr GJ, Hannah ME. Planned caesarean section for term breech delivery. *Cochrane Database of Systematic Reviews* 2000;(2).

628. Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. *Lancet* 2000;356:1375–83.

629. Gimovsky ML, Wallace RL, Schifrin BS, Paul RH. Randomized management of the nonfrank breech presentation at term: a preliminary report. *American Journal of Obstetrics and Gynecology* 1983;146:34–40.

630. Collea JV, Chein C, Quilligan EJ. The randomized management of term frank breech presentation: a study of 208 cases. *American Journal of Obstetrics and Gynecology* 1980;137:235–44.

631. Royal College of Obstetricians and Gynaecologists. *The Management of Breech Presentation*. Guideline No. 20. London: RCOG; April 2001. [www.rcog.org.uk/guidelines.asp?PageID=106&GuidelineID=19] Accessed 8 September 2003.