National Institute for Health and Care Excellence

Surveillance programme

Surveillance proposal consultation document

Intravenous fluid therapy in adults in hospital NICE guideline CG174 – 4-year surveillance review

Background information

Guideline issue date: December 2013

This guideline has not undergone previous surveillance.

Surveillance proposal for consultation

We will not update the guideline at this time.

We also propose to remove the following NICE research recommendations from the NICE version of the guideline and the NICE research recommendations database:

- Are balanced solutions superior to sodium chloride 0.9% for the fluid resuscitation of patients with acute hypovolaemic shock?
- Are balanced crystalloids superior to a combination of a balanced crystalloid and a gelatin suspended in a balanced solution for the fluid resuscitation of patients with acute hypovolaemic shock?
- Does a higher sodium content IV fluid regimen for maintenance reduce the risk of developing hyponatraemia and volume depletion without increasing the risk of volume overload in hospitalised adults?
- Does the introduction of hospital systems that ensure:
  - all hospital healthcare professionals involved in prescribing and delivering IV fluid therapy are appropriately trained in the principles of fluid prescribing; and
  - all IV fluid therapy-related complications are reported;

lead to a reduction in fluid-related complications and associated healthcare costs?

Reason for the proposal

New evidence

We found 89 new studies in a search for systematic reviews and randomised controlled trials published between 12 March 2013 and 24 October 2016. We also considered 1 additional study identified by members of the guideline committee who originally worked on this guideline.

From all sources, 90 studies were considered to be relevant to the guideline.

This included new evidence that is consistent with current recommendations on:

- Principles and protocols for intravenous fluid therapy
- Assessment and monitoring
- Resuscitation
- Replacement and redistribution.

We also identified new evidence in the following areas that was inconsistent with, or not covered by, current recommendations, but the evidence was not considered to impact on the guideline:

- Intravenous fluid therapy for patients in the intensive care unit (ICU)
- Intravenous fluid therapy for patients undergoing surgery.

We did not find any new evidence on routine maintenance and training and education.

None of the new evidence considered in surveillance of this guideline was thought to have an effect on current recommendations. We asked topic experts whether this new evidence would affect current recommendations on Intravenous fluid therapy in adults in hospital. Generally, the topic experts thought that an update was not needed.

No equalities issues were identified during the surveillance process.

Research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. See the research recommendations section for further information.

For this surveillance review we assessed 5 prioritised research recommendations, and proposed that 4 should be removed from the NICE version of the guideline and the NICE database.

Overall decision

After considering all the new evidence and views of topic experts, we decided not to update this guideline.

We also propose to remove 4 NICE research recommendations from the NICE version of the guideline and the NICE research recommendations database.

Further information

See appendix A: summary of new evidence from surveillance below for further information.

For details of the process and update decisions that are available, see ensuring that published guidelines are current and accurate in 'Developing NICE guidelines: the manual'.

Appendix A: summary of evidence from surveillance

Principles and protocols of intravenous fluid therapy

Preamble to the recommendations in this section of the guideline

The assessment and management of patients' fluid and electrolyte needs is fundamental to good patient care.

174 - 1 Fluid prescribing principles

Recommendations derived from this question

1.1.1 Assess and manage patients' fluid and electrolyte needs as part of every ward review. Provide intravenous (IV) fluid therapy only for patients whose needs cannot be met by oral or enteral routes, and stop as soon as possible.

1.1.2 Skilled and competent healthcare professionals should prescribe and administer IV fluids, and assess and monitor patients receiving IV fluids (see recommendations 1.6.1–1.6.3).

1.1.3 When prescribing IV fluids, remember the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and Reassessment.

1.1.5 Include the following information in IV fluid prescriptions:

- The type of fluid to be administered.
- The rate and volume of fluid to be administered.

1.1.6 Patients should have an IV fluid management plan, which should include details of:

- the fluid and electrolyte prescription over the next 24 hours
- the assessment and monitoring plan.

Initially, the IV fluid management plan should be reviewed by an expert daily. IV fluid management plans for patients on longer-term IV fluid therapy whose condition is stable may be reviewed less frequently.

1.1.7 When prescribing IV fluids and electrolytes, take into account all other sources of fluid and electrolyte intake, including any oral or enteral intake, and intake from drugs, IV nutrition, blood and blood products.

1.1.8 Patients have a valuable contribution to make to their fluid balance. If a patient needs IV fluids, explain the decision, and discuss the signs and symptoms they need to look out for if their fluid balance needs adjusting. If possible or when asked, provide written information (for example, NICE's Information for the public), and involve the patient's family members or carers (as appropriate).

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

174 - 2 What is the clinical and cost effectiveness of clinical algorithms or defined protocols for the assessment, monitoring and/or management of intravenous fluid and electrolyte requirement in hospitalised adult patients?

Recommendations derived from this question

1.1.4 Offer IV fluid therapy as part of a protocol (see Algorithms for IV fluid therapy):

- Assess patients' fluid and electrolyte needs following Algorithm 1: Assessment.
- If patients need IV fluids for fluid resuscitation, follow Algorithm 2: Fluid resuscitation.
- If patients need IV fluids for routine maintenance, follow Algorithm 3: Routine maintenance.
- If patients need IV fluids to address existing deficits or excesses, ongoing abnormal losses or abnormal fluid distribution, follow Algorithm 4: Replacement and redistribution.

Surveillance decision

This review question should not be updated.

Early goal-directed therapy

4-year surveillance summary

Early goal-directed therapy (EGDT) was compared with usual care for resuscitation of patients with severe sepsis and septic shock in a meta-analysis of randomised controlled trials (RCTs)[1] (6 trials, n=4,336 participants). There was no significant difference in mortality and incidence of adverse events between the two groups and there was significant heterogeneity in the included trials. EGDT might equivalent to usual care for resuscitation of patients with severe sepsis and septic shock.

A meta-analysis of RCTs[2] compared EGDT with usual care or lactate-guided therapy for resuscitation of adults with severe sepsis and septic shock (13 trials, n=5,268 participants). EGDT was significantly associated to decreased mortality compared with usual care (8 trials, n=4,664 participants). However, EGDT was also significantly associated with increased mortality compared with lactate clearance-guided therapy (5 trials, n=604 participants).

An RCT[3,4] compared EGDT with usual resuscitation in patients who presented at emergency department with septic shock (n=1,243 participants). There was no significant difference between the groups in 90-day mortality. The probability that EGDT was more cost-effective than usual resuscitation was below 30%.

An RCT[5] compared EGDT with usual care in adults presenting to the emergency department with early septic shock (n=1,600 participants). There was no significant difference in 90-day mortality between the groups. Therefore, the results indicated no evidence of benefit with EGDT compared to usual care for adults with early septic shock at the emergency department.

EGDT for patients with severe sepsis or septic shock was compared with usual care or early lactate clearance in a systematic review and meta-analysis of RCTs[6] (10 trials, n=4,157). Mortality was not significantly different between EGDT and the control group but heterogeneity was substantial. In subgroup analyses, standard EGDT, but not modified EGDT, was associated with lower mortality rate in comparison with usual care. However, EGDT was associated with a higher mortality rate in comparison with early lactate clearance.

An RCT[7] conducted in adults with septic shock at emergency departments undergoing 6 hours of resuscitation. Three groups were compared: protocol-based EGDT (n=439 participants); protocol-based standard therapy that did not require the placement of a central venous catheter, administration of inotropes, or blood transfusions (n=446 participants); and usual care (n=456 participants). There were no significant differences between the groups for the primary end point of 60-day in-hospital

mortality indicating no benefit with protocol-based EGDT compared to standard therapy or usual care.

Topic expert feedback

Topic experts highlighted two of the RCTs[5,7] as evidence ruling out any advantage of EGDT in severe sepsis and septic shock.

Impact statement

New evidence about EGDT for resuscitation of adults with severe sepsis or septic shock was identified through surveillance but results were not consistent between studies. All included studies reported on mortality. Five studies found no significant differences between EGDT and usual care. One of these studies also compared EGDT with standard therapy and reported no significant difference between the groups. Two studies found that mortality was significantly lower with EGDT compared to usual care but significantly higher compared to lactate clearance-guided therapy or early lactate clearance. Due to the inconsistent results on EGDT, further research would be beneficial before considering for inclusion in the guideline.

New evidence is unlikely to impact on the guideline.

Defined protocols for the management of intravenous fluid therapy

4-year surveillance summary

An RCT[8] reported no significant difference in in-hospital mortality between a simplified severe sepsis protocol (up to 4 L of intravenous fluids within 6 hours, guided by jugular venous pressure assessment, and dopamine and/or blood transfusion in selected patients) and usual care in 109 patients with severe sepsis.

A fluid responsiveness protocol (using Non-Invasive Cardiac Output Monitor [NICOM] to assess for fluid responsiveness [>10% increase in stroke volume in response to 5 mL/kg fluid bolus]) was compared with standard clinical care in an RCT[9] (n=64 participants with sepsis). Sepsis-related Organ Failure Assessment (SOFA) score was not significantly different between the groups. However, the trial was initially powered for 600 participants but it was stopped early due to change in funding.

An RCT[10] compared protocol-based intravenous fluid resuscitation for patients with severe sepsis and septic shock (using the non-invasive cardiac output monitor and passive leg-raising manoeuvre) against usual care in the emergency department (n=122 participants). Hospital mortality was not significantly different between the groups.

Liberal fluid resuscitation strategies were compared with restricted fluid resuscitation strategies in trauma patients in a systematic review and meta-analysis[11] of RCTs (3 trials) and observational studies (7 observational studies). Meta-analysis of RCTs showed that liberal fluid resuscitation strategies were significantly associated with higher mortality compared with restricted fluid strategies.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

Different protocols for the management of intravenous fluid therapy were identified as new evidence through surveillance. No evidence was found for reduction of hospital mortality from a simplified severe sepsis protocol and a protocol-based intravenous fluid resuscitation. An RCT was stopped early due to change in funding and it did not have enough participants to provide a conclusion about a fluid responsiveness protocol compared with standard clinical care in patients with sepsis. There was evidence from an RCT suggesting a reduction of mortality with restricted fluid resuscitation strategies in trauma patients compared with liberal fluid resuscitation strategies. However, due to the inconsistency across the new evidence, further research would be beneficial before considering additional protocols in the guideline.

New evidence is unlikely to impact on the guideline.

Assessment and monitoring

174 - 3 What aspects of clinical assessment are required to assess, monitor and re-evaluate fluid and electrolyte status?

Recommendations derived from this question

Initial assessment

1.2.1 Assess whether the patient is hypovolaemic. Indicators that a patient may need urgent fluid resuscitation include:

- systolic blood pressure is less than 100 mmHg
- heart rate is more than 90 beats per minute
- capillary refill time is more than 2 seconds or peripheries are cold to touch
- respiratory rate is more than 20 breaths per minute
- National Early Warning Score (NEWS) is 5 or more
- passive leg raising suggests fluid responsiveness*.

1.2.2 Assess the patient's likely fluid and electrolyte needs from their history, clinical examination, current medications, clinical monitoring and laboratory investigations:

- History should include any previous limited intake, thirst, the quantity and composition of abnormal losses (see Diagram of ongoing losses), and any comorbidities, including patients who are malnourished and at risk of refeeding syndrome (see Nutrition support in adults [NICE clinical guideline 32]).
- Clinical examination should include an assessment of the patient's fluid status, including:
  - pulse, blood pressure, capillary refill and jugular venous pressure
  - presence of pulmonary or peripheral oedema
  - presence of postural hypotension.
- Clinical monitoring should include current status and trends in:
  - NEWS
  - fluid balance charts
  - weight.
- Laboratory investigations should include current status and trends in:
  - full blood count
  - urea, creatinine and electrolytes.

* Passive leg raising is a bedside method to assess fluid responsiveness in a patient. It is best undertaken with the patient initially semi-recumbent and then tilting the entire bed through 45°. Alternatively it can be done by lying the patient flat and passively raising their legs to greater than 45°. If, at 30–90 seconds, the patient shows signs of haemodynamic improvement, it indicates that volume replacement may be required. If the condition of the patient deteriorates, in particular breathlessness, it indicates that the patient may be fluid overloaded.

Surveillance decision

This review question should not be updated.

Passive leg raising

4-year surveillance summary

A systematic review and meta-analysis of clinical trials[12] (23 trials, n=1,013 patients and n=1,034 fluid challenges) reported that passive leg raising had high diagnostic performance predicting fluid responsiveness with high sensitivity, high specificity and high summary area under the receiver operating characteristic curve. The use of passive leg raising induced changes in flow variables (such as cardiac output or its direct derivatives) and had significantly higher sensitivity and specificity compared with the use of changes in pulse pressure on passive leg raising.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

During the 4-year surveillance review, there was evidence showing that passive leg raising had high diagnostic performance and that the use of passive leg raising-induced changes in flow variables might have better diagnostic performance compared with the use of changes in pulse pressure on passive leg raising for the prediction of fluid responsiveness. This evidence supports recommendation 1.2.1 which recommends to assess whether the patient is hypovolaemic with passive leg raising as one of the indicators that a patient may need urgent fluid resuscitation.

New evidence is unlikely to change guideline recommendations.

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174 - 4 In hospitalised patients receiving intravenous fluids, what is the clinical and cost effectiveness of measuring and recording serial body weight?

Recommendations derived from this question

Reassessment

1.2.3 If patients are receiving IV fluids for resuscitation, reassess the patient using the ABCDE approach (Airway, Breathing, Circulation, Disability, Exposure), monitor their respiratory rate, pulse, blood pressure and perfusion continuously, and measure their venous lactate levels and/or arterial pH and base excess according to guidance on advanced life support (Resuscitation Council [UK], 2011).

1.2.4 All patients continuing to receive IV fluids need regular monitoring. This should initially include at least daily reassessments of clinical fluid status, laboratory values (urea, creatinine and electrolytes) and fluid balance charts, along with weight measurement twice weekly. Be aware that:

- Patients receiving IV fluid therapy to address replacement or redistribution problems may need more frequent monitoring.
- Additional monitoring of urinary sodium may be helpful in patients with high-volume gastrointestinal losses. (Reduced urinary sodium excretion [less than 30 mmol/l] may indicate total body sodium depletion even if plasma sodium levels are normal. Urinary sodium may also indicate the cause of hyponatraemia, and guide the achievement of a negative sodium balance in patients with oedema. However, urinary sodium values may be misleading in the presence of renal impairment or diuretic therapy.)
- Patients on longer-term IV fluid therapy whose condition is stable may be monitored less frequently, although decisions to reduce monitoring frequency should be detailed in their IV fluid management plan.

1.2.6 Clear incidents of fluid mismanagement (for example, unnecessarily prolonged dehydration or inadvertent fluid overload due to IV fluid therapy) should be reported through standard critical

incident reporting to encourage improved training and practice (see Consequences of fluid mismanagement to be reported as critical incidents).

1.2.7 If patients are transferred to a different location, reassess their fluid status and IV fluid management plan on arrival in the new setting.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 5 In hospitalised patients receiving intravenous fluids, what is the clinical and cost effectiveness of measuring and recording urine output in addition to recording standard parameters stated in NEWS (National Early Warning Score) to determine the need for intravenous fluid administration?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 4.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 6 In hospitalised patients receiving intravenous fluids, what is the incidence and clinical significance of hyperchloraemia and hypochloraemia?

Recommendations derived from this question

Reassessment

1.2.5 If patients have received IV fluids containing chloride concentrations greater than 120 mmol/l (for example, sodium chloride 0.9%), monitor their serum chloride concentration daily. If patients develop hyperchloraemia or acidaemia, reassess their IV fluid prescription and assess their acid–base status. Consider less frequent monitoring for patients who are stable.

See recommendation 1.1.4 regarding Algorithm 1: Assessment which is relevant to this question.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Resuscitation

174 - 7 What is the most clinically and cost effective intravenous fluid for fluid resuscitation of hospitalised patients?

Recommendations derived from this question

1.3.1 If patients need IV fluid resuscitation, use crystalloids that contain sodium in the range 130–154 mmol/l, with a bolus of 500 ml over less than 15 minutes. (For more information, see the Composition of commonly used crystalloids table.)

1.3.2 Do not use tetrastarch for fluid resuscitation.

1.3.3 Consider human albumin solution 4–5% for fluid resuscitation only in patients with severe sepsis.

Surveillance decision

This review question should not be updated.

Colloids, albumin and crystalloids

4-year surveillance summary

A network meta-analysis of RCTs[13] compared crystalloids, albumin and hydroxyethyl starch (HES) in patients with severe sepsis (13 trials, people in hospital receiving intravenous fluid therapy for resuscitation). It was concluded that albumin was associated with the highest survival benefit and HES with the higher morbidity which might affect mortality.

A systematic review and network meta-analysis of RCTs[14] assessed the effect of different resuscitative fluids in adults with sepsis (14 trials, n=18,916 participants). It was concluded that albumin and balanced crystalloids were associated with reduced mortality compared to other fluids (such as starches and saline fluids) in adults with sepsis. However, the authors highlighted limitations of the included studies such as heterogeneity in terms of case mix, fluids evaluated, duration of fluid exposure, and risk of bias. The network meta-analysis might have also been limited by imprecise estimates for several comparisons.

Resuscitation fluids for adult patients with sepsis or septic shock were compared in a systematic review and network meta-analysis[15] of RCTs (10 trials, n=6,664 participants) which included nine direct comparisons. Network meta-analysis at the four-node level (this represents comparisons between 4 treatments) showed that an increased risk of receiving renal replacement therapy (RRT) was significantly associated with fluid resuscitation with starch compared with crystalloid. RRT was not significantly different between albumin and crystalloid or albumin and starch. The risk of receiving RRT was significantly decreased with balanced crystalloid compared to heavy starch or light starch at the six-node level (this represents comparisons between 6 treatments). There was no significant difference between balanced crystalloid and saline or balanced crystalloid and albumin. It was highlighted that the trials were heterogeneous in terms of case mix, fluids evaluated, duration of fluid exposure and risk of bias. The results suggested that crystalloids and balanced crystalloids might be better than starches (including light and heavy starches), crystalloids and balanced crystalloids might be similar to albumin and saline, and albumin might be similar to starch for the risk of receiving RRT.

A meta-analysis of RCTs[16] compared hypertonic saline (HS) with isotonic saline for fluid resuscitation in patients with traumatic hypovolaemic shock (6 trials). Mortality was not significantly different between hypertonic saline and isotonic saline.

Topic expert feedback

Topic experts highlighted two of the network meta-analyses[13,14] as new evidence for safety of colloids.

Impact statement

During the 4-year surveillance review, new evidence suggested that crystalloids, balanced crystalloids and albumin might be a better choice for fluid resuscitation in patients with sepsis and septic shock compared with starches and saline fluids. This evidence supports recommendations 1.3.1 to 1.3.3 for the use of crystalloids and human albumin for intravenous fluid resuscitation and that tetrastarch should not be used for fluid resuscitation.

New evidence is unlikely to change guideline recommendations.

Colloids compared with crystalloids

4-year surveillance summary

An RCT[17] compared two resuscitation fluid strategies (colloids and crystalloids) in patients with signs of acute hypovolaemia (n=2,857 participants). Use of continuous RRT and 28-day mortality were not significantly different between the groups. Colloids and crystalloids might be similar for fluid resuscitation in patients with signs of acute hypovolaemia.

A systematic review and meta-analysis of trials[18] compared HES with crystalloids for fluid resuscitation in patients with sepsis (10 trials, n=4,624 participants). Resuscitation with HES was significantly associated with increased incidence of acute kidney injury (AKI), need of RRT, increased transfusion of red blood cell, and higher 90-day mortality. Intensive care unit mortality, 28-day mortality, and fresh frozen plasma were no significantly different between HES and crystalloids. It seems that HES and crystalloids might be similar for short term outcomes but crystalloids might be better than HES for longer term outcomes for fluid resuscitation in patients with sepsis.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

During the 4-year surveillance, there was evidence from an RCT showing no significant difference between colloids and crystalloids for fluid resuscitation in patients with signs of acute hypovolaemia. A systematic review and meta-analysis found that HES and crystalloids were similar for 28-day mortality which was regarded as a critical outcome during guideline development. However, 90-day mortality was also considered for decision making during guideline development and it was found to be significantly higher with HES compared to crystalloids in the new evidence. More research on other relevant outcomes such as length of stay in hospital, respiratory complications and morbidity would be useful before considering updating recommendation 1.3.2 do not use tetrastarch for fluid resuscitation.

New evidence is unlikely to change guideline recommendations.

Albumin compared with crystalloid

4-year surveillance summary

A meta-analysis of RCTs[19] compared albumin with crystalloid for resuscitation of adult patients with severe sepsis and septic shock (5 trials, n=3,658 participants with severe sepsis, n=2,180 participants with septic shock). There was a trend, but not significant, in reduction of 90-day mortality with albumin compared with crystalloid in patients with severe sepsis. Albumin significantly reduced 90-day mortality in patients with septic shock. Heterogeneity was not significant.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

During the 4-year surveillance review, new evidence showed that albumin might be better for severe sepsis and septic shock compared with crystalloid. This evidence supports recommendation 1.3.3 which suggests to consider human albumin solution 4–5% for fluid resuscitation only in patients with severe sepsis.

New evidence is unlikely to change guideline recommendations.

Albumin compared with other fluids

4-year surveillance summary

A meta-analysis of RCTs[20] (15 trials) evaluated the use of albumin-containing fluids for resuscitation in patients with sepsis compared with other fluids. The meta-analysis showed that there was no significant effect of albumin-containing fluids on mortality in patients with sepsis of any severity. However, types of other fluids were not mentioned in the abstract.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

During the 4-year surveillance review, new evidence showed no significant differences in mortality between albumin and other fluids for resuscitation in patients with sepsis. It was not possible to assess the impact of this evidence on current recommendations because the abstract did not report the types of fluids compared with albumin and the severity of sepsis was not clear.

New evidence is unlikely to change guideline recommendations.

Colloids compared with other fluids

4-year surveillance summary

A systematic review and meta-analysis of RCTs[21] compared 6% HES with a molecular weight of 130 kD and a molar substitution ratio of approximately 0.4 (6% HES 130) against other intravascular fluids for resuscitation in hospitalised adults (35 trials, n=10,391 participants). The number of deaths and the number of people treated with RRT was reported to be significantly higher in the 6% HES 130 group compared to the control fluid group. It seems that 6% HES 130 compared to other intravascular fluids might increase the risk of mortality and RRT. However, the lower confidence interval crossed the line of no effect (being 1.0) for the outcome on number of deaths.

An updated Cochrane systematic review of RCTs and quasi-RCTs[22] compared HES with other fluid resuscitation therapies in different patient populations (42 trials, n=11,399 participants). Fifteen studies were excluded from the original review (nine retracted from publication due to concerns about integrity of data and six lacking individual patient creatinine data for the calculation of RIFLE criteria). Overall, there was a significant increase in the need for RRT (19 trials, n=9,857 participants), number of people with author-defined kidney failure (15 trials, n=1,361 participants) and risk of AKI based on RIFLE-F and RIFLE-I criteria (15 trials, n=8,402 participants), with HES compared to other fluid therapies. It was noted that methodological quality of the studies was good.

A systematic review of RCTs[23] compared different colloids solutions for fluid resuscitation in patients with sepsis (17 trials, n=1,281 participants). No significant difference in mortality was found in four comparisons: HES compared with albumin, gelatin compared with albumin, HES compared with gelatin, and HES compared with dextran.

A systematic review and meta-analysis of RCTs[24] compared tetrastarch with either crystalloid or albumin in patients with sepsis (9 trials, n=3,456 participants). Tetrastarch lead to a significantly increased use of RRT and red blood cells, and more serious adverse events compared with crystalloid or albumin.

Topic expert feedback

Topic experts highlighted the systematic review and meta-analysis of RCTs[21] as a new reference on interventions since the guideline published. The Cochrane systematic review of RCTs[22] was highlighted as evidence for safety of colloids.

Impact statement

During the 4-year surveillance, a systematic review was identified that showed no significant differences in mortality with comparisons of

different types of colloids in patients with sepsis. Two systematic reviews with meta-analyses showed that mortality and RRT were significantly higher with HES compared to other fluids for resuscitation in hospitalised adults. Overall, this evidence supports recommendation 1.3.2 to not use tetrastarch for fluid resuscitation.

New evidence is unlikely to change guideline recommendations.

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174 - 8 What is clinical and cost effectiveness of different volumes of fluid administration in patients requiring fluid resuscitation?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 7.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 9 What are the most clinically and cost effective timings and rate of administration of intravenous fluids in fluid resuscitation?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 7.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Routine maintenance

174 - 10 What is the most clinically and cost effective fluid to be used for intravenous fluid therapy for routine maintenance in hospitalised patients?

Recommendations derived from this question

1.4.1 If patients need IV fluids for routine maintenance alone, restrict the initial prescription to:

- 25–30 ml/kg/day of water **and**
- approximately 1 mmol/kg/day of potassium, sodium and chloride **and**
- approximately 50–100 g/day of glucose to limit starvation ketosis. (This quantity will not address patients' nutritional needs; see Nutrition support in adults [NICE clinical guideline 32].)

For more information see IV fluid prescription for routine maintenance over a 24-hour period.

1.4.2 For patients who are obese, adjust the IV fluid prescription to their ideal body weight. Use lower range volumes per kg (patients rarely need more than a total of 3 litres of fluid per day) and seek expert help if their BMI is more than 40 kg/m^2.

1.4.3 Consider prescribing less fluid (for example, 20–25 ml/kg/day fluid) for patients who:

- are older or frail
- have renal impairment or cardiac failure
- are malnourished and at risk of refeeding syndrome (see Nutrition support in adults [NICE clinical guideline 32]).

1.4.4 When prescribing for routine maintenance alone, consider using 25–30 ml/kg/day sodium chloride 0.18% in 4% glucose with 27 mmol/l potassium on day 1 (there are other regimens to achieve this). Prescribing more than 2.5 litres per day increases the risk of hyponatraemia. These are initial prescriptions and further prescriptions should be guided by monitoring.

1.4.5 Consider delivering IV fluids for routine maintenance during daytime hours to promote sleep and wellbeing.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 11 What is clinical and cost effectiveness of different volumes of fluid administration in patients requiring intravenous fluids for routine maintenance?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 10.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 12 What are the most clinically and cost effective timings of administration of intravenous fluids in patients requiring intravenous fluids for routine maintenance?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 10.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Replacement and redistribution

174 - 13 What is the most clinically and cost effective fluid to be used for intravenous fluid therapy for replacement of ongoing losses in hospitalised patients?

Recommendations derived from this question

1.5.1 Adjust the IV prescription (add to or subtract from maintenance needs) to account for existing fluid and/or electrolyte deficits or excesses, ongoing losses (see Diagram of ongoing losses) or abnormal distribution.

1.5.2 Seek expert help if patients have a complex fluid and/or electrolyte redistribution issue or imbalance, or significant comorbidity, for example:

- gross oedema
- severe sepsis
- hyponatraemia or hypernatraemia
- renal, liver and/or cardiac impairment
- post-operative fluid retention and redistribution
- malnourished and refeeding issues (see Nutrition support in adults [NICE clinical guideline 32]).

Surveillance decision

This review question should not be updated.

Crystalloids compared with colloids

4-year surveillance summary

A systematic review of RCTs[25] compared crystalloids with colloids as volume replacement solutions in patients with traumatic injuries, undergoing surgery, and in critically ill patients (59 trials, n=16,889 participants). Mortality was not significantly different between crystalloids and colloids (32 trials, n=16,647 participants). Colloids significantly increased the risk of developing AKI requiring RRT (9 trials, n=11,648 participants). It was highlighted that most studies had selection, detection or performance bias.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

During the 4-year surveillance review, new evidence indicated no significant differences in mortality between crystalloids and colloids as replacement solutions in patients with traumatic injuries, undergoing surgery, and in critically ill patients. However, colloids significantly increased the risk of AKI requiring RRT. More research on other relevant outcomes such as length of stay in hospital, quality of life, respiratory complications and morbidity would be useful before considering updating recommendations 1.5.1 and 1.5.2 which do not include specific types of fluids for replacement and distribution.

New evidence is unlikely to change guideline recommendations.

174 - 14 What is clinical and cost effectiveness of different volumes of fluid administration in patients requiring intravenous fluids for replacement for ongoing losses?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 13.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

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174 - 15 What are the most clinically and cost effective timings for the administration of intravenous fluids for replacement for ongoing losses?

Recommendations derived from this question

The same recommendations were derived from this question as in 174 - 13.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Training and education

174 - 16 What are the barriers faced by healthcare professionals in the effective prescription and monitoring of intravenous fluids in hospital settings?

Recommendations derived from this question

1.6.1 Hospitals should establish systems to ensure that all healthcare professionals involved in prescribing and delivering IV fluid therapy are trained on the principles covered in this guideline, and are then formally assessed and reassessed at regular intervals to demonstrate competence in:

- understanding the physiology of fluid and electrolyte balance in patients with normal physiology and during illness
- assessing patients' fluid and electrolyte needs (the 5 Rs: Resuscitation, Routine maintenance, Replacement, Redistribution and Reassessment)
- assessing the risks, benefits and harms of IV fluids
- prescribing and administering IV fluids
- monitoring the patient response
- evaluating and documenting changes **and**
- taking appropriate action as required.

1.6.2 Healthcare professionals should receive training and education about, and be competent in, recognising, assessing and preventing consequences of mismanaged IV fluid therapy, including:

- pulmonary oedema
- peripheral oedema
- volume depletion and shock.

1.6.3 Hospitals should have an IV fluids lead, responsible for training, clinical governance, audit and review of IV fluid prescribing and patient outcomes.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

NQ – 01 What is the most clinically effective intravenous fluid for patients in the intensive care unit (ICU)?

This question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This question should not be added.

Sodium administration in critically ill patients

4-year surveillance summary

A multicentre point prevalence study[26] reported on amount and sources of sodium administered in ICUs (n=365 critically ill patients). It was concluded that sodium administration in excess of recommended daily requirements might be common in studied ICUs with the main sodium source being intravenous fluids for maintenance or replacement.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include critical care. The multicentre point prevalence study[26] was highlighted by topic experts as a new reference since the guideline published.

Impact statement

The new evidence identified through surveillance has limited applicability because it was an observational study. This new question could potentially be answered by an RCT. Therefore, it was considered that further research would be beneficial before considering extending the scope of NICE guideline CG174 to cover the amount and source of sodium administered in ICUs to critically ill patients.

New evidence is unlikely to change guideline recommendations.

Defined protocols for fluid resuscitation

4-year surveillance summary

An RCT[27] compared a protocol restricting resuscitation fluid (fluid boluses were permitted only if signs of severe hypoperfusion occurred) with a standard care protocol (fluid boluses were permitted as long as circulation continued to improve) after initial resuscitation in ICU patients with septic shock (n=151 participants). Ischaemic events and 90-day mortality were not significantly different between the protocol restricting resuscitation fluid and the standard care protocol. Worsening of AKI was significantly less frequent with the restricting resuscitation fluid protocol compared to the standard care protocol.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include critical care.

Impact statement

The evidence identified through surveillance did not provide conclusive evidence that a protocol restricting resuscitation fluid was better than a standard care protocol in ICU patients with septic shock. It was considered that further research would be beneficial before considering extending the scope of NICE guideline CG174 to cover specific protocols for fluid resuscitation in ICU patients with septic shock.

New evidence is unlikely to impact on the guideline.

Albumin compared with crystalloids or colloids

4-year surveillance summary

An RCT[28] compared a 20% albumin and crystalloid solution against crystalloid solution alone (n=1818 adults with severe sepsis in 100 ICUs). Mortality at 28 days was not significantly different between the albumin and crystalloid solution compared to the group of crystalloids alone showing no evidence of a benefit adding albumin to crystalloids in the ICU population.

A systematic review and meta-analysis of RCTs[29] compared human albumin solutions (albumin group) with crystalloids or colloids (control fluid group) as part of fluid volume expansion and resuscitation in adults with sepsis, severe sepsis, or septic shock in critical or intensive care (16 trials, n=4,190 participants). Mortality was not significantly different between albumin groups and control fluid groups, between albumins and crystalloids (n=3,878 participants), and between albumins and colloids (n=299 participants).

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include critical care. The RCT[28] was highlighted by topic experts as a relevant article.

Impact statement

During the 4-year surveillance review, new evidence showed no significant difference in mortality with albumin compared to crystalloids or colloids in adults with sepsis, severe sepsis, or septic shock in critical or intensive care. It was considered that further research would be beneficial before considering extending the scope of NICE guideline CG174 to cover the management of ICU patients with albumin, crystalloids, or colloids.

New evidence is unlikely to impact on the guideline.

Crystalloids compared with other fluids

4-year surveillance summary

An RCT[30] was identified which compared colloids against crystalloids for fluid resuscitation in adults admitted to the ICU with hypovolaemic shock (n=1414 with colloids; n=1443 with crystalloids). There were fewer deaths in the colloids group compared to the crystalloids group within 28 days but the difference was not significant. This difference was significant at 90 days but 90-day mortality was a secondary outcome. The authors concluded that the results for 90-day mortality were exploratory and that more evidence is necessary to confirm the efficacy of colloids

compared to crystalloids in adults admitted to the ICU.

A systematic review and meta-analysis[31] included RCTs, controlled clinical trials, and observational studies. High-chloride (ion concentration >111 mmol/l to 154 mmol/l) was compared to lower-chloride (concentration 111 mmol/l or less) crystalloids for resuscitation in acutely ill or surgical patients in the perioperative or intensive care setting (21 studies, n=6,253 patients). Mortality was not affected by high-chloride fluids but the risk of AKI was significantly higher with high-chloride compare to lower-chloride fluids. Sensitivity analysis excluding heavily weighted studies resulted in non-significant effect of high-chloride fluids on AKI.

An RCT[32] compared a crystalloid with a colloid for resuscitation in patients admitted to ICU (n=7,000 participants). The crystalloid was 0.9% sodium chloride (saline) and the colloid was 6% hydroxyethyl starch with a molecular weight of 130 kDa (HES) and a molar substitution ratio of 0.4 (130/0.4, Voluven) in 0.9% sodium chloride. Mortality was not significantly different between HES and saline. AKI was significantly less frequent in the HES group compared with the saline group. However, RRT and adverse events were significantly more frequent with HES compared to saline.

A systematic review and meta-analysis of RCTs[33] compared colloids against crystalloids in adults with acute respiratory distress syndrome (3 trials, n=206 participants). Mortality was not significantly different between colloids and crystalloids. Overall risk of bias was reported as unclear to high in the included trials.

An RCT[34] compared a buffered crystalloid against saline in patients admitted to the ICU (n=2,262 participants). Four ICUs were included (three were general medical and surgical ICUs and one had predominantly cardiothoracic and vascular surgical patients). There were no significant differences between the groups for AKI and in-hospital mortality showing no superiority between a buffered crystalloid and a saline fluid.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include critical care. Topic experts highlighted three of the studies found from the surveillance search[30,31,34]. Topic experts highlighted that the systematic review and meta-analysis[31] added to the evidence on balanced crystalloids vs. 0.9% saline. The RCT[34] comparing a buffered crystalloid against saline was highlighted as a study investigating the trend to increased mortality in saline treated patients. Topic experts also highlighted that several shortcomings were discussed about the RCT[34] in an editorial[35].

Impact statement

The evidence identified through surveillance showed no significant differences in mortality in patients admitted to the ICU (including patients with hypovolaemic shock, acutely ill patients, surgical patients, and patients with acute respiratory distress syndrome) from four comparisons: HES compared with saline, colloids compared with crystalloids, high-chloride crystalloids compared with lower-chloride crystalloids, and crystalloids compared with saline. More research on other relevant outcomes such as length of stay in ICU, quality of life, respiratory complications and morbidity would be useful before considering extending the scope of NICE guideline CG174 to cover the management of ICU patients with HES, saline, colloids, crystalloids, high-chloride or lower-chloride crystalloids.

New evidence is unlikely to impact on the guideline.

HES compared with other fluids

4-year surveillance summary

A post hoc analysis of an RCT[36] compared HES 130/0.42 with Ringer's acetate for fluid resuscitation in patients with severe sepsis in the ICU (n=798 participants). Bleeding was significantly more frequent with HES compared to Ringer's acetate but not severe bleeding. Mortality was significantly higher in patients with any bleeding and severe bleeding compared to those without bleeding.

An RCT[24] compared 6% HES 130/0.42 (Tetraspan) with Ringer's acetate for fluid resuscitation in patients with severe sepsis in the ICU (n=798 participants). At 90 days, mortality and RRT were significantly higher with HES 130/0.42 compared to Ringer's acetate. At

90 days, dialysis-dependence and severe bleeding were similar between HES 130/0.42 and Ringer's acetate. Post-hoc sensitivity analysis showed a significantly increased risk of any bleeding with HES compared to Ringer's acetate.

A meta-analysis of RCTs[37] compared 6% HES versus other fluids for non-septic ICU patients (22 trials, n=6,064 participants). There were no differences in overall mortality between the comparison groups. However, included studies had small sample sizes.

A post-hoc analysis of an RCT[38] compared HES with Ringer's acetate for fluid resuscitation in a subgroup of patients with severe sepsis (n=798 participants). This post-hoc analysis aimed to detect subgroup heterogeneity of the effects on 90-day mortality. There was no significant heterogeneity in the intervention effect of HES 130/0.42 on increased 90-day mortality in the following subgroups:

- randomisation earlier than 4 h after ICU admission versus later,
- surgery versus no surgery,
- colloids given versus not given,
- <2 l of crystalloids given prior to randomisation vs. >2 l or plasma lactate >4 mmol/l versus <4 mmol/l,
- hypotension versus no hypotension or use of vasopressor or inotropic agents at randomisation versus no use.

Another post-hoc analysis of this RCT[39] reported that the maximal AKI stage was higher in the HES group compared with the Ringer's group. An increase in AKI stage was significantly associated with higher mortality. RRT was significantly more frequent in the HES group compared with the Ringer's group. The results indicated that HES might be less effective than Ringer's acetate for fluid resuscitation in patients with severe sepsis.

An RCT[40] compared 6% HES 130/0.42 with Ringer's acetate in patients with severe sepsis needing fluid resuscitation in general ICUs (n=804 participants). Mortality rates between HES and Ringer's acetate were not significantly different at 6 months, 1 year, and at the time of longest follow-up.

A systematic review and meta-analysis of RCTs[41] compared 6% tetrastarch (of potato or waxy maize origin) against other non-HES fluids for resuscitation in adults with severe sepsis in the critical care setting (6 trials, n=3,033 participants). Ninety-day mortality was significantly higher with tetrastarch compared to crystalloid. It was reported that there was no publication bias or statistical heterogeneity. The study concluded that the use of tetrastarch for initial fluid resuscitation in adults with severe sepsis should be avoided due to the harms associated with it.

A pre-specified cost-effectiveness analysis of a cohort of adults included in an RCT which compared 6% HES (molecular weight of 130 kD and molar substitution ratio of 0·4) with 0·9% sodium chloride (saline) for fluid resuscitation at ICU[42] (n=3,450 adults, around half of the participants enrolled in the RCT). There were no significant differences in mortality at 6 and 24 months between HES and saline groups. The following outcomes were similar between the groups: mean number of life-years gained at 6 months and 24 months, mean health-related quality of life score at 6 months, mean number of quality-adjusted life-years gained at 6 months, and total hospital costs at 24 months. It was concluded that the probability of HES being cost effective was low.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include critical care. They highlighted two studies[37,41] as evidence on safety of colloids. Topic experts highlighted that the systematic review and meta-analysis[37] informed the colloid (HES) and crystalloid debate. Topic experts also highlighted that the recommendations against the use of HES were worthy of review because an RCT[42] found no evidence of long-term harm with HES.

Impact statement

During the 4-year surveillance review, the new evidence on HES compared to other fluids in the ICU reported differing results. Four studies found that HES was worse than Ringer's acetate, crystalloid or albumin for mortality, bleeding, increased use of RRT, red blood cells, and serious adverse events. However, two studies found that HES was similar to Ringer's acetate or other fluids for mortality. As such, further research would be beneficial before considering the inclusion of guidance on HES and other fluids in the ICU.

New evidence is unlikely to impact on the guideline.

NQ – 02 What is the most clinically effective intravenous fluid for patients undergoing surgery?

This question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This question should not be added.

Goal-directed therapy

4-year surveillance summary

An RCT[43] compared stroke volume-guided fluid therapy (goal-directed therapy [GDT]) with standard fluid therapy (control group) in patients scheduled for open radical prostatectomy (n=42 participants). Both groups received a fixed-volume crystalloid regimen supplemented with 1:1 replacement of blood loss with colloid, and in addition, the GDT group received colloid to obtain a maximal stroke volume (oesophageal Doppler). Orthostatic intolerance was not significantly different between GDT and standard fluid therapy. The GDT group significantly received more colloid during surgery and reached a higher stroke volume.

An RCT[44] compared fluid therapy protocol combined with GDT against standard fluid therapy (control group) in American Society of Anaesthesiologists (ASA) II-III patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (n=80 participants). The incidence of major abdominal complications and the median duration of hospitalisation were significantly lower in the GDT group compared with the control group. Although there were no deaths in the GDT group, the difference with the control group was not significant. The amount of fluids received by the GDT group was significantly lower compared with the control group. The volume of crystalloids was significantly lower in the GDT group.

An RCT[45] compared GDT using stroke volume variation as an end point against standard perioperative resuscitation in patients undergoing liver resection (n=135 participants). The GDT group received significantly less intraoperative fluid compared with the standard perioperative resuscitation group. Perioperative transfusions and boluses in the post-anaesthesia care unit were not significantly different between the groups. Two deaths occurred in the GDT group.

An RCT[46] compared GDT targeting stroke volume variation with an arterial pulse contour cardiac output monitor against a control group (fluid therapy was administered at the discretion of the attending anaesthesiologist) in adult patients undergoing elective open repair of their abdominal aortic aneurysm (n=40 participants). Cardiac index and stroke volume index were significantly higher in the GDT group compared with the control group. Complications were significantly fewer in the GDT group compared with the control group.

An RCT[47] compared perioperative goal-directed fluid therapy (GDFT) with arterial-based continuous stroke volume variation (SVV) monitoring against a control group in patients undergoing abdominal surgery excluding patients undergoing laparoscopic surgery, patients with atrial fibrillation and patients with severe mitral/aortal stenosis (n=30 participants). An arterial-line cardiac output monitor was used to measure SVV, and fluid was given after an algorithm in the intervention group. After 1 year, the study was halted due to slow inclusion rate. The study needed 164 participants but only 30 were included after 1 year. The sample size of this RCT was not enough to draw conclusions.

An RCT[48] compared intraoperative SVV-based GDT against standard fluid management (control) in patients scheduled for major orthopaedic surgery under general anaesthesia (n=80 participants). In the GDT group, patients received colloid boluses of 4 ml/kg to maintain an SVV <10% when in the supine position or an SVV <14% if prone. In the control group, fluids were given to maintain a mean arterial pressure >65 mm Hg, a heart rate <100 bpm, a central venous pressure of 8-14 mm Hg, and a urine output >0.5 ml/kg/h. There were significant differences between the groups with GDT showing lower heart rate at the end of surgery, fewer hypotensive episodes, higher arterial and gastric intramucosal pH, lower gastric intramucosal PCO2, lower intraoperative infused colloids and total infused volume, and shorter postoperative time to flatus compared to the control group.

An RCT[49] compared intraoperative GDT guided by an arterial pressure-based cardiac output system against standard fluid therapy in low to moderate risk patients undergoing major abdominal surgery. Fluids were managed to maintain SVV <12%. The GDT group had significantly faster return of gastrointestinal function compared with the standard group.

A systematic review, meta-analysis and trial sequential analysis of RCTs[50] compared perioperative goal directed hemodynamic therapy (GDHT) against other fluid management in adult non-cardiac surgery (15 trials, n=1,368 participants). Overall complications were significantly reduced with GDHT compared to conventional fluid therapy in colorectal, urological and high-risk surgery.

A systematic review and meta-analysis of RCTs[51] compared the use of last-generation colloids (derived from corn) with crystalloids in GDFT for major non-cardiac surgery in adults (6 trials, n=390 participants). Colloids were significantly associated with a higher mortality compared with crystalloids.

A systematic review and meta-analysis of RCTs[52] compared intraoperative goal directed hemodynamic therapy against conventional fluid therapy in adult non-cardiac surgery (29 trials, n=2,654 participants). Goal directed hemodynamic therapy was associated with a significant reduction in postoperative complications. Mortality was not significantly different between goal directed hemodynamic therapy and conventional fluid therapy. Goal directed hemodynamic therapy might be better than conventional fluid therapy for reduction in postoperative complications but not difference was found for the reduction of mortality.

A systematic review and meta-analysis[53] compared perioperative GDT against conventional fluid therapy in adult non-cardiac surgery (10 trials, n=1,527). Mortality was significantly reduced with GDT compared to conventional fluid therapy. There were no significant differences in the number of patients with complications between GDT and conventional fluid therapy.

An RCT[54] compared individualised GDFT based on continuous SVV and stroke volume (SV) monitoring against a control group in patients undergoing high-risk surgery (n=52 participants). During surgery, the GDT group received significantly more colloids compared with the control group. The decrease in SVV and the number of postoperative wound infections was significantly lower with GDT compared to the control.

A meta-analysis and systematic review[55] compared dynamic GDFT based on non-invasive flow based hemodynamic measurement against standard care in non-cardiac surgical patients (n=41 participants). There were no significant differences in postoperative hospital/30-day mortality, length of post-operative hospital stay, and length of ICU stay with the use of GDFT compared to standard care. The number of patients having at least one postoperative complication, abdominal complications, and postoperative hypotension was significantly lower with GDFT compared to standard care. The GDFT group was infused with significantly more colloid compared to the group under standard care.

A meta-analysis of RCTs[56] compared intraoperative GDFT against conventional fluid therapy in adults undergoing elective major abdominal surgery (23 trials n=2,099 participants). The use of enhanced recovery after surgery (ERAS) protocols was also assessed. Hospital length of stay was significantly lower in the GDFT group compared to the conventional fluid therapy group. There was no difference in mortality between the groups. There was a significant reduction in length of stay in intensive care in adults managed with ERAS protocols. A significant reduction was also found in overall morbidity and total hospital length of stay in adults managed in a traditional care setting. The authors concluded that GDFT may not be

beneficial for adults undergoing major abdominal surgery, in particular those managed in an ERAS setting.

An RCT[57] compared perioperative GDFT against conventional intraoperative fluid therapy in elderly patients with gastric cancer and hypertension underwent gastric cancer radical surgery (n=60 participants). The conventional group were infused with crystalloids or colloids according to the methods of Miller's Anaesthesia. The GDFT were infused with 200 mL hydroxyethyl starch over 15 minutes under the FloTrac/Vigileo monitoring system, with stroke volume variation between 8% and 13%. The average intraoperative intravenous infusion quantity was significantly reduced in the GDFT group compared with the conventional group. Average colloid fluid volume was significantly increased in the GDFT group compared with the conventional group.

An RCT[58] compared perioperative GDT against traditional fluid therapy in elderly patients with coronary heart disease scheduled for gastrointestinal surgery (n=60 participants). In the GDT group, fluid management was carried out under guidance of hemodynamic status indicators. Total fluids infused were significantly lower with GDT compared to traditional fluid therapy. Numbers of adverse cardiac events were not significantly different between the groups. Return of GI function was significantly faster with GDT compared to traditional fluid therapy. Median ICU stay and median hospital stay were significantly lower with GDT compared to traditional fluid therapy.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy. They referred to the meta-analysis of RCTs[56] as new evidence since the guideline published. It was highlighted that although on GDFT, this meta-analysis[56] added to the evidence that fluid overload should be avoided in the perioperative period.

Impact statement

During the 4-year surveillance review, there was new evidence on GDT, GDFT and GDHT for perioperative intravenous fluids therapy. However, there was inconsistency between studies regarding relevant outcomes like mortality, complications, and hospital stay. For example, one study reported that GDFT significantly decreased mortality but another study reported no differences in mortality between GDFT and standard care. NICE is developing a guideline on perioperative care and it was considered that goal directed therapies could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow goal-directed fluid therapies to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

Other Protocols

4-year surveillance summary

A systematic review and meta-analysis of RCTs[59] compared restrictive fluid management against a conventional fluid management protocol in adult patients undergoing surgery (15 trials, n=1,594 participants). Restrictive and conventional fluid management were not significantly different in oliguria (5 trials), frequency of acute renal failure (ARF) (15 trials), and ARF occurrence between studies targeting oliguria reversal and not targeting oliguria reversal. Intraoperative fluid intake was significantly lower in restrictive compared to conventional fluid management with or without targeting oliguria reversal (7 trials and 6 trials, respectively).

An RCT[60] compared liberal (LIB) with restricted (RES) perioperative fluid regimen in patients scheduled to undergo pancreatic resection (n=330 participants). Intraoperatively, LIB patients received crystalloid 12 mL/kg/h and RES patients 6 mL/kg/h. Days 0 to 3, cumulative crystalloid was significantly higher in the LIB group compared with the RES group. The difference in grade 3 complications was not significantly different between the LIB and the RES groups. Liberal and restricted perioperative fluid regimens seem to be similar for the reduction of complications.

An RCT[61] evaluated the efficacy and safety of fluid management via SVV in patients who underwent radical cystectomy (n=46 participants). The control group was maintained at <10% SVV and the intervention group was maintained at 10% to 20% SVV. Estimated

blood loss, estimated red cell mass loss, and transfusion requirements of red blood cells were significantly lower in the intervention group compared with the control group. Fluid management via SVV might be better than a control fluid management for estimated blood loss, estimated red cell mass loss, and transfusion requirements of red blood cells.

An RCT[62] compared standard fluid therapy with (intervention group) or without (control group) supplementary blinded intraoperative stroke volume optimisation in patients having major elective rectal resection or cystectomy with ileal conduit (n=220 participants). Interventional fluid challenges used Gelofusine guided by stoke volume variability measured by LiDCOrapid. The prevalence of moderate or severe complications on day 5 after surgery and the hospital length of stay were not significantly different between intervention and control groups. Fluid therapy with stroke volume optimisation might not be better or worse than standard fluid therapy for reduction of complications and hospital length of stay.

A systematic review of RCTs[63] compared perioperative fluid optimisation methods and usual care in adults undergoing surgical repair of hip fracture (5 trials, n=403 participants). Methods of perioperative fluid optimisation included advanced invasive haemodynamic monitoring (such as transoesophageal Doppler and pulse contour analysis) and protocols using standard measures (such as blood pressure, urine output and central venous pressure). Three studies compared advanced haemodynamic monitoring with a protocol using standard measures; three compared advanced haemodynamic monitoring with usual care; and one compared a protocol using standard measures with usual care. Risk of mortality was not significantly different in meta-analyses for the two advanced haemodynamic monitoring comparisons. Length of stay and time to medical fitness were not significantly different between advanced haemodynamic monitoring and usual care (3 trials). There were no significant differences in the number of participants with one or more complications in each of the two advanced haemodynamic monitoring comparisons.

An RCT[64] compared restricted fluid regimen with standard fluid regimen in patients undergoing gastrointestinal surgery for malignancy (n=174 participants). Fluid distribution was determined by Bioelectrical Impedance Analyser. Postoperative complications were significantly lower with restricted fluid regimen compared to standard fluid regimen.

An RCT[65] compared standard fluid administration against reduced fluid administration in patients undergoing abdominal aortic aneurysm repair with elective minilaparotomy (n=60 participants). Total fluid administration and administration of blood products were significantly lower in the reduced fluid administration group compared with the standard fluid administration group. The number of nonlethal complications was significantly lower in reduced fluid administration compared with standard fluid administration but the difference in lethal complications was not significant. The average ICU stay and duration of postoperative hospital stay were significantly shorter in reduced fluid administration compared with standard fluid administration.

An RCT[66] compared two urine output targets guiding perioperative fluid therapy in patients with elective colectomy without significant risk factors for acute kidney injury (n= 40 participants). The low group had a minimum urine output target of 0.2 mL/kg/h and the standard group had an output target of 0.5 mL/kg/h from induction of anaesthesia until 8 AM 2 days after surgery. The amount of intravenous fluids given was significantly lower in the low group compared with the standard group. The low group was not inferior to the standard group in terms of neutrophil gelatinase-associated lipocalin, serum cystatin C, serum creatinine, and measured glomerular filtration. Effective renal plasma flow increased in both groups after surgery, and more in the standard group. The authors concluded that a lower perioperative urine output target was not inferior to a standard target.

A systematic review and meta-analysis of RCTs[67] compared restrictive fluid management against liberal fluid management during elective surgery (n=1,397 participants). Complications were significantly less frequent with restrictive fluid compared to liberal fluid management. The total complication rate, risk of infection, and transfusion rate (were significantly lower with restrictive fluid compared to liberal fluid. Postoperative re-bleeding was not significantly different between the groups.

An RCT[68] compared aggressive hydration with lactated Ringer's solution (3 mL/kg/h during endoscopic retrograde cholangiopancreatography [ERCP], followed by a 20 mL/kg bolus and 3 mL/kg/h for 8 h after the procedure) against standard amount of hydration (1.5 mL/kg/h during and for 8 h after ERCP) in patients undergoing ERCP (n=150 participants). Pancreatitis and pancreatic pain were significantly more frequent in patients receiving standard hydration compared with patients receiving aggressive hydration.

An RCT[69] compared standard (10ml/kg/hr) against restricted (5ml/kg/hr) crystalloid fluid protocols in patients scheduled to undergo pancreatoduodenectomy (n=54 participants). The median gastric emptying time and delayed gastric emptying were not significantly different between standard and restricted protocols.

An RCT[70] compared intravenous fluid therapy guided by Pleth Variability Index (PVI) against intravenous fluid therapy guided by oesophageal Doppler with 250 mL boluses of colloid to maintain a maximal stroke volume, or a PVI of less than 14% in low-risk patients undergoing elective colorectal surgery (n=40 participants). Mean total fluid administered and mean intraoperative fluid balance were not significantly different between the groups.

An RCT[71] compared PVI directed fluid management (PVI group) against non PVI-directed fluid management (control group) in patients scheduled for major abdominal surgeries under combined general and epidural anaesthesia (n=30 participants). Two mL/kg/h crystalloid fluid infusion was maintained in PVI group, once PVI>13%, a 250 mL colloid or crystalloid was rapidly infused. 4-8 mL/kg/h crystalloid fluid infusion was maintained in control group, and quick fluid infusion was initiated if mean arterial blood pressure (BP) <65 mmHg. Small doses of norepinephrine were given to keep mean arterial BP above 65 mmHg as needed in both groups. The total amount of intraoperative fluids, the amount of crystalloid fluid and the first hour blood lactate levels during surgery were significantly lower in the PVI group compared with the control group.

An RCT[72] compared intra-operative intravenous administration of fluid boluses based on stroke volume measured by oesophageal Doppler (probe arm) against intravenous fluid based on clinical indicators (no-probe arm) undergoing bowel surgery (n=91 participants). Physiological and Operative Severity Score for the Enumeration of Morbidity and Mortality (POSSUM)-predicted mortality was significantly higher in the probe arm. There were no significant differences between the groups in epidural analgesia, type of resection, incision length, type of incision, operation time, estimated blood loss, time to ambulation, flatus, diet, removal of the epidural anaesthesia, and length of hospital stay. Septic complication rates were significantly decreased in the probe arm compared with the no-probe-arm.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy.

Impact statement

During the 4-year surveillance review, there was new evidence on different protocols for perioperative intravenous fluids therapy but there was inconsistency between studies regarding relevant outcomes like complications and hospital stay. Studies on perioperative fluid optimisation methods and cardiac output-guided hemodynamic fluid therapy reported no significant differences between these fluid protocols and usual care for mortality. NICE is developing a guideline on perioperative care and it was considered that protocols of fluid therapies could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow protocols of fluid therapies to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

HES compared with other fluids

4-year surveillance summary

An RCT[73] compared 6% HES with hyperosmolar sodium lactate (HSL) in patients undergoing cardiac surgery (n=98 participants). Both HSL and HES 6% were administered at 3 mL/kgBW within 15 min, at the beginning of surgery. The increase in cardiac index was significantly higher with HSL. The systemic

vascular resistance index decreased significantly more in HSL compared with HES. The difference in fluid balance was significant being negative in the HSL group and positive in the HES group. The authors concluded that HSL improved cardiac performance and haemodynamic status better than HES during the cardiac surgery.

A systematic review and meta-analysis of RCTs[74] compared 6% HES solutions against non-starch intravenous fluids in patients undergoing surgery (19 trials, n=1,567). There were no differences in hospital mortality or acute kidney injury between the comparison groups. It was concluded that the included studies were small with low event rates and low risk of heterogeneity. The use of 6% HES solution in surgical patients was not recommended because the data did not show benefits with this solution.

An RCT[75] compared HES 130/0.4 with lactated Ringer's solution (LR) in patients undergoing major abdominal surgery (n=84 participants). The total amount of fluid administered was significantly lower with HES compared to LR. It was concluded that HES 130/0.4 was more efficient than LR.

An RCT[76] compared HES 130/0.4 against modified fluid gelatin for volume expansion during major abdominal surgery guided by transoesophageal Doppler (TED) in adult patients (n=50 participants). All participants received basal fluid requirement plus 200 cc of either 6% HES 130/0.4 (HES group) or 3% modified fluid gel (GEL group) as intraoperative colloid replacement guided by TED. Platelet count showed a significant drop with GEL compared to HES. Prothrombin time and INR were comparable between groups. It was concluded that HES had a more favourable effect on platelet counts than GEL.

A systematic review and meta-analysis of RCTs[77] compared the synthetic colloid HES against any crystalloid in adults undergoing non-cardiac surgery (13 trials including 20 to 202 participants each trial). Mortality and acute kidney injury was not significantly different between the groups. Length of stay in hospital was significantly shorter in adults resuscitated with HES but heterogeneity was high. It was concluded that this data was insufficient to identify a difference in outcomes associated with crystalloids and HES in scheduled or elective non-cardiac surgery.

An RCT[78] compared HES 130/0.4 against lactated Ringer's solution in patients undergoing major surgery (n= 33 participants). Coagulation competence and perioperative blood loss were significantly worse with HES compared to lactated Ringer. The lactated Ringer's group received significantly more fluids compared with the HES group.

An RCT[79] compared balanced 6% HES (130/0.4, Volulyte) against balanced crystalloid (Hartmann's solution) as haemodynamic optimisation fluid in medium to high-risk patients undergoing elective colorectal surgery (n=202 participants). There was no significant difference between the groups in the number of patients with gastrointestinal morbidity on postoperative day 5. Participants in the crystalloid group received significantly more fluid and had a higher 24 h fluid balance compared with the HES group.

A meta-analysis of RCTs[80] compared HES against non-HES control fluid in adult surgical patients (15 trials, n=4,409 participants). It was noted that the Crystalloid versus Hydroxyethyl Starch Trial (CHEST) was the source for two thirds of participants. Recourse to RRT was significantly increased with HES compared to non-HES fluids as well as with HES 130/0.4 compared to crystalloid.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy. They referred to two of the systematic reviews and meta-analyses of RCTs[74,77] as new evidence for the safety of colloids. Topic experts highlighted that one of the systematic reviews[77] informed the colloid (HES) and crystalloid debate.

Impact statement

During the 4-year surveillance review, there was new evidence on intraoperative use of HES compared with other fluids but there was inconsistency between studies regarding the benefit of HES over other fluids. Three studies reported worse outcomes with HES compared to hyperosmolar sodium lactate (cardiac performance and haemodynamic status), lactated Ringer (coagulation competence and perioperative blood loss), and non-HES fluids and crystalloids (recourse to RRT). One study reported that HES was more efficient than lactated Ringer for total amount of fluid administrated and another study reported that HES had more favourable effects on platelet

counts than modified fluid gelatin. NICE is developing a guideline on perioperative care and it was considered that HES and other fluids could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow HES and other fluids to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

Ringer lactate compared with other fluids

4-year surveillance summary

An RCT[81] compared Ringer lactate against 0.45% dextrose normal saline and potassium chloride 20 mmol/L in nondiabetic patients undergoing major non-cardiac surgeries under general anaesthesia (n=100 participants). Both groups were given calculated dosage of IV fluids accordingly 4-2-1 formula. A significant increase of capillary blood glucose level was observed during intraoperative and immediate postoperative period in the group with 0.45% dextrose normal saline and potassium chloride 20 mmol/L. It was concluded that Ringer lactate solution might be the alternative choice of IV fluid for perioperative maintenance and can be used as replacement fluid in nondiabetic patients undergoing major surgeries.

An RCT[82] compared 250 mL lactated Ringer's solution against dextrose 5% in lactated Ringer's solution over 2 hours beginning with surgical closing in adult female ASA physical status I and II nondiabetic patients scheduled for outpatient gynaecologic, urologic, or breast surgery (n= 162 participants). There was no significant difference in postoperative nausea and vomiting (PONV) during the first 2 hours after anaesthesia between the groups. In both groups, patients who developed PONV within 2 hours of anaesthesia were not significantly different in number of severity scores >1 during recovery stay, proportions of PONV onset within 30 minutes of recovery room arrival, dose and class of antiemetic medication.

An RCT[83] compared a restrictive fluid regimen of 3% hypertonic saline (9 mL/kg/hr lactated Ringers [LAR] and 1 mL/kg/hr hypertonic saline [HYS] intraoperation, 1 mL/kg/hr HYS postoperation) against lactated Ringers (15 mL/kg/hr LAR intraoperation, 2 mL/kg/hr LAR postoperation) for pancreaticoduodenectomy (n=264 participants). The overall complication rate and the total number of complications were significantly reduced with the restrictive fluid regimen of 3% hypertonic saline compared to lactated Ringers.

An RCT[84] compared perioperative Ringer's lactate against 5% human albumin or 6% HES 130/0.4 in patients undergoing elective cardiac surgery (n=240 participants). All fluids were infused up to 50 ml kg(-1) day(-1). Requirement of blood products was significantly less frequent with Ringer's lactate compared to human albumin and HES. Total perioperative fluid balance was significantly less positive with human albumin group compared to HES and Ringer's lactate. It was concluded that human albumin and HES interfered with blood coagulation and produced greater haemodilution than Ringer's lactate.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy.

Impact statement

During the 4-year surveillance review, new evidence was identified on intraoperative use of Ringer lactate compared with other fluids in patients undergoing surgery but there was inconsistency between studies regarding the benefit of Ringer lactate over other fluids. Two studies reported that Ringer lactate was better than dextrose normal saline and potassium chloride (as perioperative maintenance and replacement fluid) and human albumin and HES (blood coagulation and haemodilution). Another study reported no differences between lactated Ringer's solution and dextrose 5% in lactated Ringer's solution for PONV. Another study reported that complications were significantly reduced with a restrictive fluid regimen of 3% hypertonic saline compared to lactated Ringers. NICE is developing a guideline on perioperative care and it was considered that lactate Ringer’s solutions and other fluids could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow lactate Ringer’s solutions and other fluids to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

Colloid compared with crystalloid

4-year surveillance summary

An RCT[85] compared colloid (HES) with crystalloid (0.9% NaCl) in adult patients scheduled to undergo orthopaedic surgery under general anaesthesia (n=56 participants). Cardiac preload optimisation directed by oesophageal Doppler was performed after induction with fluid challenges of 250ml of solution until SV no longer increased by 10%. Number of fluid challenges necessary for SV optimisation was not significantly different between 0.9% NaCl and HES.

A systematic review and stratified meta-analysis of RCTs[86] assessed the efficacy and safety of colloids (HES, dextran, or albumin) and crystalloids for fluid administration during major elective surgery (31 trials, n=2,287 participants). HES was stratified to HES 130/0.4 and HES 200/0.5. Thromboelastography maximum amplitude was significantly reduced following HES administration (31 trials). Increased blood loss was significant after administration of HES compared with crystalloids (12 trials). Reduced haemorrhage was significantly associated with albumin administration compared with HES (6 trials). There was no significant reduction in reoperation with crystalloids but it was significantly more frequent with HES compared to albumin.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy.

Impact statement

During the 4-year surveillance review, there was new evidence on intraoperative use of colloids and crystalloids in people undergoing surgery. One study reported no significant differences between HES (colloid) and 0.9% NaCl (crystalloid) for the number of fluid challenges necessary for SV optimisation. Another study reported that blood loss, haemorrhage and reoperation were significantly better with crystalloids and albumin compared to HES. NICE is developing a guideline on perioperative care and it was considered that colloids and crystalloids could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow colloids and crystalloids to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

Isotonic saline compared with other fluids

4-year surveillance summary

An RCT[87] compared 1.4% sodium bicarbonate against normal intravenous saline solutions for deficit fluid therapy during cervical and lumbar laminectomy in adults with American Society of Anaesthesiologists physical status class I-II (n=40 participants). The mean serum lactate increased significantly with sodium bicarbonate and the mean serum chloride increased significantly with normal saline. It was concluded that 1.4% sodium bicarbonate fluid was better than normal saline for controlling acid-base and electrolyte imbalances.

A systematic review of RCTs[88] compared hypertonic salt solutions (HS) against isotonic salt solutions (IS) administered for fluid resuscitation to adults undergoing surgery (18 trials, n=1,087 participants). Most participants were in a positive fluid balance postoperatively (meaning that fluid intake was greater than output), the excess was significantly less in HS compared with IS. The HS group received significantly less fluid compared with the IS group. The maximum serum sodium was significantly higher with HS compared to IS with levels remaining within normal limits. It was noted that included trials were highly heterogeneous and their quality was from high to very low. It was concluded that hypertonic salt solutions reduced the volume of intravenous fluid required for routine

maintenance in people undergoing surgery but transiently increases serum sodium.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy.

Impact statement

During the 4-year surveillance review, there was new evidence on intraoperative use of isotonic saline compared with other fluids. The evidence suggests that isotonic saline might not be better than 1.4% sodium bicarbonate and hypertonic salt solutions for controlling acid-base and electrolyte imbalances, and for the reduction of volume of intravenous fluid required for maintenance. However, the largest study was a systemic review of 18 trials which reported high heterogeneity and variable quality of these trials. NICE is developing a guideline on perioperative care and it was considered that isotonic saline and other fluids could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow isotonic saline and other fluids to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

4-year surveillance summary

Plasmalyte compared with other fluids

An RCT[89] compared 0.9% saline against plasmalyte during operation and until 12 h post operation in patients undergoing multi-level lumbar spinal fusion (n= 50 participants). Urine output was significantly greater with plasmalyte compared to 0.9% saline.

An RCT[90] compared Hartmann's solution (HS) against Plasmalyte-148 (PL) in patients undergoing major liver resection (n=60 participants). At completion of surgery, there were no significant differences in mean standard base excess between HS compared with PL. Hyperchloraemia and hyperlactatemia were significantly more frequent with HS compared to PL. Intraoperatively, median blood loss was significantly lower with PL compared to HS. Total complications were significantly more frequent with HS compared to PL.

Topic expert feedback

Topic experts suggested to extend the scope of NICE guideline CG174 to include intraoperative fluid therapy.

Impact statement

During the 4-year surveillance review, there was new evidence on intraoperative use of plasmalyte compared with other fluids. The evidence suggests that plasmalyte might result in greater urine output and reduction of hyperchloraemia, hyperlactatemia, blood loss, and complications compared with 0.9% saline and Hartmann's solution. However, this evidence comes from 2 small RCTs with 50 and 60 participants each. NICE is developing a guideline on perioperative care and it was considered that plasmalyte and other fluids could be covered in the new guideline. Covering this area in a new guideline on perioperative care would allow plasmalyte and other fluids to be considered for their effects on wider clinical outcomes.

New evidence is unlikely to impact on the guideline.

Research recommendations

Prioritised research recommendations

At 4-year and 8-year surveillance reviews of guidelines published after 2011, we assess progress made against prioritised research recommendations. We may then propose to remove research recommendations from the NICE version of the guideline and the NICE database for research recommendations. The research recommendations will remain in the full versions of the guideline. See NICE's research recommendations process and methods guide 2015 for more information.

These research recommendations were deemed priority areas for research by the Guideline Committee; therefore, at this 4-year surveillance review time point a decision **will** be taken on whether to retain the research recommendations or stand them down.

We applied the following approach:

- New evidence relevant to the research recommendation was found and an update of the related review question is planned.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database. If needed, a new research recommendation may be made as part of the update process.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.
  - The research recommendation will be retained because there is evidence of research activity in this area.
- New evidence relevant to the research recommendation was found but an update of the related review question is not planned because evidence supports current recommendations.
  - The research recommendation will be removed from the NICE version of the guideline and the NICE research recommendations database because further research is unlikely to impact on the guideline.
- Ongoing research relevant to the research recommendation was found.
  - The research recommendation will be retained and evidence from the ongoing research will be considered when results are published.
- No new evidence relevant to the research recommendation was found and no ongoing studies were identified.
  - The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.
- The research recommendation would be answered by a study design that was not included in the search (usually systematic reviews or randomised controlled trials).
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.
- The new research recommendation was made during a recent update of the guideline.
  - The research recommendation will be retained in the NICE version of the guideline and the NICE research recommendations database.

RR – 01 What is the incidence of complications during, and as a consequence of, IV fluid therapy?

New evidence relevant to the research recommendation was found (see NQ-02) but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

The new evidence is inconsistent regarding the reduction of complications after using intraoperative intravenous fluid therapy. Therefore, it was considered that further research would be beneficial before considering for inclusion in the guideline.

Surveillance decision

The research recommendation will be retained because there is evidence of research activity in this area.

RR – 02 Are balanced solutions superior to sodium chloride 0.9% for the fluid resuscitation of patients with acute hypovolaemic shock?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

RR – 03 Are balanced crystalloids superior to a combination of a balanced crystalloid and a gelatin suspended in a balanced solution for the fluid resuscitation of patients with acute hypovolaemic shock?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

RR – 04 Does a higher sodium content IV fluid regimen for maintenance reduce the risk of developing hyponatraemia and volume depletion without increasing the risk of volume overload in hospitalised adults?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

RR – 05 Does the introduction of hospital systems that ensure:

- **all hospital healthcare professionals involved in prescribing and delivering IV fluid therapy are appropriately trained in the principles of fluid prescribing; and**
- **all IV fluid therapy-related complications are reported;**

lead to a reduction in fluid-related complications and associated healthcare costs?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

Surveillance decision

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

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