2020 surveillance of intravenous fluid therapy in children and young people in hospital (2015) NICE guideline NG29 – summary of evidence

Overview

Studies identified in searches are summarised from the information presented in their abstracts.

No studies were found specifically in neonates.

Feedback from topic experts was considered alongside the evidence to reach a view on the need to update each section of the guideline.

Principles and protocols for intravenous fluid therapy

Surveillance proposal

No new information on <u>principles and protocols for intravenous fluid therapy</u> was identified in this surveillance review.

Assessment and monitoring

Surveillance proposal

No new information on <u>assessment and monitoring</u> was identified in this surveillance review.

Fluid resuscitation

Surveillance proposal

The section of the guideline on <u>fluid resuscitation</u> should not be updated.

Fluid type for resuscitation

2020 surveillance summary

Hypertonic (>0.9%) versus isotonic (0.9%) sodium chloride

A randomised controlled trial (RCT) (Liu et al. 2015) (n=44 children) compared 3% sodium chloride (6 ml/kg as a single bolus over 10–15 minutes, maximum 2 boluses) with 0.9% sodium chloride (guided by standard therapy) for early intravenous fluid resuscitation in septic shock in critical care. There were no significant differences between groups in oxygenation index at 1, 3, 6 and 24 hours after infusion. Plasma sodium was significantly higher with 3% than with 0.9% sodium chloride at 1 hour after infusion (though both groups were in the normal range), but not at 3, 6 and 24 hours after infusion. At 6 and 24 hours after treatment, fluid infusion volume was significantly less with 3% than with 0.9% sodium chloride.

Balanced crystalloids versus isotonic (0.9%) sodium chloride

An RCT (Allen et al. 2016) (n=100 children) across 8 emergency departments in the USA and Canada examined Plasma-Lyte A versus 0.9% sodium chloride as intravenous fluid for moderate to severe dehydration secondary to acute gastroenteritis. Both treatment groups received similar fluid volumes. Plasma-Lyte led to a significantly greater improvement in the primary outcome of 4-hour serum bicarbonate level from baseline (i.e. improvement in hyperchloraemic acidosis) than the 0.9% sodium chloride group. There was significantly less abdominal pain and better dehydration scores with Plasma-Lyte at hour 2 but not at hour 4. No patient experienced clinically relevant worsening of laboratory findings or physical examination, and hospital admission rates were similar. One patient in each group developed hyponatraemia, and 4 patients developed hyperkalaemia (1 with Plasma-Lyte and 3 with sodium chloride; between-group significance not reported in the abstract).

An RCT (Kartha et al. 2017) (n=68 children) examined Ringer's lactate versus 0.9% sodium chloride for intravenous resuscitation in acute severe diarrhoeal Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

dehydration. Patients were given 100 ml/kg of the assigned fluid according to World Health Organization Plan C to treat severe dehydration quickly (infants under 1 year: 30 ml/kg for 1 hour, then 70 ml/kg for next 5 hours; children over 1 year: 30 ml/kg for 30 minutes, then 70 ml/kg for next 2.5 hours). There was no significant difference between groups in the primary outcome (improvement in clinical status and pH ≥7.35 at the end of 6 hours) or secondary outcomes (electrolytes, renal and blood gas parameters, time to start oral feeding, and hospital stay). No patients needed a second cycle of dehydration correction. The median total cost was significantly higher with Ringer's lactate then normal saline.

Intelligence gathering

Balanced crystalloids

Topic experts queried whether balanced crystalloids were superior to 0.9% sodium chloride, and noted they were being used more widely in practice.

Impact statement

Hypertonic (>0.9%) versus isotonic (0.9%) sodium chloride

The new evidence found plasma sodium was higher with 3% than with 0.9% sodium chloride at 1 hour after infusion (though both groups were in the normal range), but not at 3, 6 and 24 hours after infusion. There were no differences between groups in oxygenation index at any timepoint after infusion (oxygenation index was not deemed an important outcome by the original guideline). Less fluid volume was needed with 3% sodium chloride, though benefits of this for patients were not apparent in the outcomes reported by the study. The evidence is unlikely to affect recommendation 1.3.1 to use glucose-free crystalloids for fluid resuscitation that contain sodium in the range 131–154 mmol/litre (of which 0.9% sodium chloride is an example).

New evidence is unlikely to change guideline recommendations.

Balanced crystalloids versus isotonic (0.9%) sodium chloride

From the new evidence, one study found Plasma-Lyte A for fluid resuscitation led to increased serum bicarbonate (i.e. less acidosis), less abdominal pain, and better dehydration scores versus 0.9% sodium chloride, but had no benefit for laboratory findings, physical examination, or hospital admission. Although there were some benefits of Plasma-Lyte A, the evidence is from a single study in a single condition (acute gastroenteritis). Evidence of benefit of balanced crystalloids from further studies in other conditions, and looking at other outcomes such as mortality and hospital stay that were deemed critical or important by the original guideline, is therefore needed before considering any changes to current recommendations. The guideline does not currently name specific fluids for resuscitation – recommendation 1.3.1 allows for any glucose-free crystalloids that contain sodium in the range 131–154 mmol/litre (of which Plasma-Lyte A and 0.9% sodium chloride are both examples). Plasma-Lyte A may not be available in the UK, however it appears to have the same formulation as Plasma-Lyte 148 which is licensed in the UK.

The finding from a second study that Ringer's lactate had no benefit over 0.9% sodium chloride but was more costly is also unlikely to affect recommendation 1.3.1 to use glucose-free crystalloids that contain sodium in the range 131–154 mmol/litre (of which Ringer's lactate and 0.9% sodium chloride are both examples). Additionally, the fluid administration protocol in the study differed considerably from recommendation 1.3.1 which limits its relevance to the guideline.

New evidence is unlikely to change guideline recommendations

Volume and rate of administration for resuscitation

2020 surveillance summary

A Cochrane review (Li at al. 2018) of 3 RCTs (n=3,402 children) compared liberal and conservative fluid therapy in initial sepsis or septic shock. The liberal and conservative therapies compared by the 3 studies were:

- 20 ml/kg of 5% albumin bolus versus 20 ml/kg 0.9% sodium chloride bolus versus 1.2 ml/kg no bolus control
- 40 ml/kg fluid over 15 minutes versus 20 ml/kg over 20 minutes
- 80% of maintenance (liberal approach) versus fluid input based on calculated fluid overload (conservative approach).

The review permitted evidence from adults and children but found only paediatric studies. Liberal fluid therapy significantly increased the risk of the 2 primary outcomes: in-hospital mortality (2 studies, n=3,288 children; moderate-quality evidence) and mortality at 4-week follow-up (1 study, n=3,141 children; high-quality evidence). However, results for in-hospital mortality in the third study were inconclusive (very low-quality evidence). The effect on adverse events was uncertain because results were imprecise and low quality.

A UK pilot RCT across 13 NHS hospitals as part of a health technology assessment (Inwald et al. 2018) (n=75 children) compared restricted fluid (10 ml/kg bolus every 15 minutes for 4 hours) with current practice (20 ml/kg bolus every 15 minutes for 4 hours) in children presenting to an emergency department with clinical suspicion of infection and septic shock after 20 ml/kg of fluid. There were no deaths. Length of hospital stay, paediatric intensive care unit (PICU) transfers, and days alive and PICU free did not differ significantly between the groups. Two adverse events were reported in each group.

An RCT (Sankar et al. 2017) (n=96 children) assessed fluid resuscitation in septic shock in paediatric emergency and critical care settings. The study examined 40–60 ml/kg of fluids as fluid boluses in aliquots of 20 ml/kg each over 15–20 minutes versus over 5–10 minutes in the first hour of resuscitation. Compared with the 5–10 minutes group, significantly fewer children in the 15–20 minutes group needed mechanical ventilation, or had an increase in oxygenation index by 5 (lower value is better) from baseline, in the first 6 hours and 24 hours after fluid resuscitation. There was no difference in secondary outcomes of death, length of stay, or resolution of shock.

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An RCT (Houston et al. 2019) in Uganda and Kenya (n=122 children) examined standard rehydration with World Health Organization Plan C for severe dehydration (100 ml/kg Ringer's lactate over 3 hours, or 6 hours if age less than 1 year, incorporating 0.9% sodium chloride boluses for shock), versus slower rehydration (100 ml/kg Ringer's lactate over 8 hours for all ages, without boluses). By 48 hours, there was no significant difference between groups in the primary outcome of number of serious adverse events (including cardiovascular, respiratory and neurological complications): 3 events with rapid versus 2 events with slower rehydration. There was also no significant difference in time to correction of dehydration or time to discharge between groups.

Intelligence gathering

Topic experts queried whether a 20 ml/kg resuscitation bolus was still appropriate, but noted that this value was still used by Advanced Paediatric Life Support – a course run by the Advanced Life Support Group.

An enquiry to NICE raised concerns about the absence from the guideline of a specific maximum resuscitation bolus volume for children and young people (whereas NICE CG174 intravenous fluid therapy in adults in hospital gives a figure of 500 ml).

Impact statement

The Cochrane review found that liberal fluid therapy for resuscitation might increase mortality. However the largest of the 3 studies in the review (FEAST trial, n=3,141 children) was included when NG29 was originally developed, but the guideline committee disregarded it when developing recommendations because it was not directly applicable to the UK clinical setting. This evidence is therefore unlikely to affect recommendation 1.3.1 for a bolus of 20 ml/kg over less than 10 minutes.

A study of direct relevance to NG29 set in NHS hospitals comparing a 20 ml/kg bolus (in line with recommendation 1.3.1) with a smaller 10 ml/kg bolus found no difference in clinical outcome between groups. Along with the Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

limitations of being a pilot study, the lack of benefit between groups is unlikely to affect the guideline, and also provides some evidence to address topic expert queries whether a 20 ml/kg resuscitation bolus is still appropriate. The authors of the study additionally noted that participants were not as unwell as expected, and that a larger trial is not feasible in its current design in the UK.

A separate trial of a bolus over less than 10 minutes (in line with recommendation 1.3.1) versus spreading the bolus over a longer period of 15–20 minutes, found that children receiving the longer bolus had less mechanical ventilation and improved oxygenation index. Although neither of these outcomes were noted as important by the original guideline, topic experts felt that they were likely to be important, though not critical. However, the lack of a difference in the study outcomes of mortality, length of stay or resolution of shock (outcomes deemed to be either critical or important by the original guideline), mean that results are unlikely to affect the guideline. Further evidence to confirm these findings, and which ideally includes outcomes deemed critical by the original guideline, is needed before impact on the guideline can be considered.

An additional trial found similar outcomes with World Health Organization Plan C for severe dehydration versus a slower rehydration approach. However, neither of these fluid administration strategies are recommended by the guideline and differ from the approach in recommendation 1.3.1, limiting the relevance of the study. This evidence is unlikely to affect the guideline.

Regarding the query to NICE about whether a maximum resuscitation bolus volume should be stated, this was discussed by the guideline committee during development of the guideline. At the time, the committee felt that including a maximum value would not be consistent with clinical practice or with other guidance (such as Advanced Paediatric Life Support – a course run by the Advanced Life Support Group). Recommendation 1.3.1 on fluid bolus is qualified by stating 'take into account pre-existing conditions as smaller fluid volumes may be needed', which allows healthcare professionals to reflect the

needs of individual patients. Topic experts involved in the current surveillance review agreed that it was correct not to state a maximum bolus volume.

New evidence is unlikely to change guideline recommendations.

Routine maintenance

Surveillance proposal

The section of the guideline on <u>routine maintenance</u> should not be updated.

Rate of administration for routine maintenance

2020 surveillance summary

A Cochrane review (Maconochie at al. 2016) of 3 RCTs (n=420 children) compared maintenance and restricted volumes of initial fluid administration (up to 72 hours after first presentation) for acute bacterial meningitis. The maintenance and restricted volumes compared by the 3 studies were:

- Intravenous maintenance fluids (100 ml/kg/day for the first 10 kg of body weight, plus 50 ml/kg/day for the next 10 kg, plus 20 ml/kg/day for subsequent weight) plus replacement fluids for any estimated deficit versus two thirds of maintenance fluids.
- Intravenous maintenance fluids (110 ml/kg/day for the first 10 kg of body weight, 50 ml/kg/day for the next 10 kg and 25 ml/kg/day for subsequent weight) versus 65% of maintenance fluids.
- Intravenous maintenance fluids (100 ml/kg/day for the first 10 kg of body weight, 50 ml/kg/day for the next 10 kg, and 20 ml/kg for subsequent weight) versus 60% of maintenance fluid equivalent as nasogastric milkbased fluids.

The review permitted evidence from adults and children but found only paediatric studies. The largest of the 3 trials was from settings with high mortality rates. There was no significant difference between maintenance and restricted fluid for the 2 primary outcomes: number of deaths (n=407 children; low-quality evidence) or acute severe neurological sequelae (n=407 children; Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

low-quality evidence). However, when neurological sequelae were defined further, there was a significant benefit of maintenance fluid for spasticity (n=357 children); and seizures at both 72 hours (n=357 children) and 14 days (n=357 children). Maintenance fluid had significant benefits over restrictive fluid for chronic severe neurological sequelae at 3 months follow-up (n=351 children; very low-quality evidence).

An RCT (Ashok et al. 2017) (n=150 children) compared restricted (10 ml/kg/h) with liberal (30 ml/kg/h) intraoperative maintenance infusion of Ringer's lactate solution in children undergoing lower abdominal and penile surgery under general anaesthesia. All patients also received a caudal block and intravenous paracetamol for analgesia. No opioids and muscle relaxants were used. Incidence of the primary outcome of nausea and vomiting during 24 hours postoperatively was significantly less in the liberal than the restricted group. The incidence of oral fluid intake during the first 6 post-operative hours was significantly higher in the restricted group, with significantly more children complaining of thirst than in the liberal group. Parent satisfaction was significantly higher in the liberal than the restricted group. No children had complications attributed to the liberal fluid therapy.

Intelligence gathering

No topic expert feedback was relevant to this section of the guideline.

Impact statement

The Cochrane review found no difference in mortality or severe neurological sequelae between maintenance and restricted fluid in acute bacterial meningitis. The maintenance rates examined by the included studies followed exactly or very closely those recommended in the guideline, therefore the lack of difference found by the review between maintenance and restricted fluids is unlikely to affect recommendation 1.4.1 to calculate routine maintenance fluid rates using the Holliday–Segar formula.

A trial found 30 ml/kg/h more effective than 10 ml/kg/h Ringer's lactate in reducing nausea and vomiting during fluid maintenance after lower abdominal Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

surgery. However, this outcome was not deemed to be critical or important by the guideline committee, and additionally the population is very specific and may not be generalisable to NG29 in which condition-specific recommendations are out of scope. The evidence is unlikely to affect the guideline which does not currently recommend either of the fluid rates examined in the study.

New evidence is unlikely to change guideline recommendations.

Fluid type for routine maintenance

2020 surveillance summary

Balanced crystalloids versus isotonic (0.9%) or hypotonic (0.45%) sodium chloride

An RCT (McNab et al. 2015) in Australia (n=690 children) examined Plasma-Lyte 148 plus 5% glucose versus 0.45% sodium chloride plus 5% glucose for patients in hospital needing intravenous maintenance hydration for 6 hours or longer. Patients received fluid for 72 hours or until their intravenous fluid rate decreased to lower than 50% of the standard maintenance rate. Significantly fewer patients experienced the primary outcome of hyponatraemia (serum sodium concentration <135 mmol/litre with a decrease of at least 3 mmol/litre from baseline) with Plasma-Lyte 148 plus 5% glucose versus 0.45% sodium chloride plus 5% glucose. No cerebral oedema occurred in either group. Two serious adverse events potentially related to intravenous fluid and 1 seizure occurred with isotonic fluid, versus none and 7 respectively with hypotonic fluid.

An RCT (Lima et al. 2019) (n=53 children) examined a balanced crystalloid (unspecified in the abstract) versus 0.9% sodium chloride for intravenous fluid administration during and for 24 hours after brain tumour resection. The absolute difference from the beginning of surgery to after surgery in both plasma chloride concentrations (the primary outcome), and base excess, significantly increased with 0.9% sodium chloride infusion compared with balanced crystalloids. Hyperchloraemic acidosis incidence was also Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

significantly greater with sodium chloride, though brain relaxation score (a measure of brain oedema) was comparable between groups.

Isotonic (0.9%) versus hypotonic (<0.9%) sodium chloride

Isotonic versus hypotonic maintenance fluids were assessed in 11 paediatric RCTs (Pemde et al. 2015, Flores Robles et al. 2016, Torres et al. 2019, Bagri et al. 2019, Kumar et al. 2019, Friedman et al. 2015, Ramanathan et al. 2016, Raksha et al. 2017, Shamim et al. 2014, Valadao et al. 2015, Omoifo et al. 2018) (table 1). Six trials compared 0.9% with 0.45% sodium chloride, 6 trials compared 0.9% with 0.18% sodium chloride, and 1 trial compared 0.9% with 0.3% sodium chloride. Almost all intervention and comparator solutions additionally contained dextrose (frequently 5%).

Results for the following outcomes were observed across the trials:

- Hyponatraemia: significantly lower with 0.9% sodium chloride than with a hypotonic solution in 8 of 12 comparisons across 9 trials (Pemde et al. 2015; Flores Robles et al. 2016; Torres et al. 2019; Bagri et al. 2019; Kumar et al. 2019; Ramanathan et al. 2016; Raksha et al. 2017; Shamim et al. 2014; Omoifo et al. 2018).
- Hypernatraemia: no difference between groups in 2 comparisons (Torres et al. 2019; Kumar et al. 2019).
- Plasma sodium level: significantly higher with 0.9% sodium chloride than
 with a hypotonic solution in 4 of 6 comparisons across 5 trials (Flores
 Robles et al. 2016; Bagri et al. 2019; Friedman et al. 2015; Ramanathan et
 al. 2016; Valadao et al. 2015). Though in the 3 comparisons quoting
 numeric values in the abstract, this did not amount to hypernatraemia.
- Other adverse events: no difference between groups in 3 comparisons across 2 trials (Flores Robles et al. 2016; Torres et al. 2019).

Table 1 Isotonic (0.9%) versus hypotonic (<0.9%) sodium chloride for routine maintenance

Reference	Study type	Sample size	Population	Intervention	Comparator	Outcome	Result
Pemde et al. (2015)	RCT	92	Hospitalised children with suspected central nervous system infections	0.9% sodium chloride in 5% dextrose	0.45% sodium chloride in 5% dextrose	Hyponatraemia after 24 hours	Improved with intervention
					0.18% sodium chloride in 5% dextrose	Hyponatraemia after 24 hours	Improved with intervention
Flores Robles et al. (2016)	RCT	151	Hospitalised children with medical or surgical disorders	0.9% sodium chloride in 5% dextrose	0.45% sodium chloride in 5% dextrose	Mean plasma sodium level at 8 hours Hyponatraemia	Higher with intervention Improved with intervention
					0.3%	Other adverse effects or length of hospital stay Mean plasma sodium level at 8 hours	No effect of intervention Higher with intervention
					sodium chloride in 3.3% dextrose	Hyponatraemia Other adverse effects or length of hospital stay	Improved with intervention No effect of intervention
Torres et al. (2019)	RCT	299	Hospitalised children	0.9% sodium chloride in 5% dextrose	0.45% sodium chloride in 5% dextrose	Hyponatraemia at 12 and 24 hours Hypernatraemia, metabolic	Improved with intervention
						acidosis or other adverse outcomes	No effect of intervention
Bagri et al. (2019)	RCT	150	Hospitalised children	0.9% sodium chloride in 5% dextrose	0.45% sodium	Hyponatraemia at 24 hours	No effect of intervention
					chloride in 5% dextrose	Mean plasma sodium at 24 hours	Higher with intervention
Kumar et al. (2019)	RCT	168	General paediatric ward (>two thirds of children had respiratory or nervous system diseases)	0.9% sodium chloride in 5% dextrose	0.45% sodium chloride in	Hyponatraemia at 12 and 24 hours	No effect of intervention
					5% dextrose	Hypernatraemia	No effect of intervention

Reference	Study type	Sample size	Population	Intervention	Comparator	Outcome	Result
Friedman et al. (2015)	RCT	110	General paediatric unit	0.9% sodium chloride in 5% dextrose	0.45% sodium chloride in 5% dextrose	Mean plasma sodium level at 48 hours	No effect of intervention
Ramanathan et al. (2016)	RCT	119	Very severe pneumonia in a general paediatric ward	0.9% sodium chloride in 5% dextrose	0.18% sodium chloride in 5% dextrose	Hyponatraemia Mean plasma sodium at 6, 12 and 24 hours	Improved with intervention Higher with intervention
Raksha et al. (2017)	RCT	240	Paediatric critical care unit	0.9% sodium chloride in 5% dextrose at standard maintenance rate	0.18% sodium chloride in 5% dextrose at two-thirds standard maintenance rate	Hyponatraemia	Improved with intervention
Shamim et al. (2014)	RCT	60	Hospitalised children	0.9% sodium chloride in 5% dextrose at 60% standard maintenance rate	0.18% sodium chloride in 5% dextrose at standard maintenance rate	Hyponatraemia at 24 and 48 hours	Improved with intervention
Valadao et al. (2015)	RCT	50	Postoperative period in children undergoing appendectomy	2,000 ml/m²/day of 0.9% sodium chloride in 5% glucose	2,000 ml/m²/day of 0.18% sodium chloride in 5% glucose	Plasma sodium levels at 24 and 48 hours after surgery Infused fluid volume Urine output	No effect of intervention No effect of intervention No effect of intervention
Omoifo et al. (2018)	RCT	65	Intraoperative fluids in children undergoing minor surgery	0.9% sodium chloride	0.18% sodium chloride in 4.3% dextrose	Hyponatraemia at end of surgery	No effect of intervention
				Ringer's lactate		Hyponatraemia at end of surgery	No effect of intervention

3.3% versus 5% dextrose

An RCT (Martinez Carapeto et al. 2018) (n=130 children) compared 0.3% sodium chloride in 3.3% dextrose with 0.9% sodium chloride in 5% dextrose as maintenance intravenous fluid in critical care after elective general surgery.

There was no significant difference between groups in the incidence of hyperglycaemia at 8, 24 or 48 hours.

Intelligence gathering

Topic experts queried whether balanced crystalloids were superior to 0.9% sodium chloride, and noted they were becoming more common practice.

During the consultation on the decision not to update this guideline, a stakeholder questioned recommendation 1.4.7, which states that if term neonates need intravenous fluids for routine maintenance, initially use isotonic crystalloids that contain sodium in the range 131–154 mmol/litre with 5–10% glucose. The stakeholder suggested that in the first 24 hours of life, plain (usually 10%) glucose without electrolytes is standard in term neonates, and that sodium in the range 131–154 mmol/litre would deliver a larger amount of sodium than is routinely given in term neonates. They also suggested that fluids containing 5% glucose are not routinely used in neonates, expressing concern that this could theoretically lead to hypoglycaemia in term babies who are relatively fluid restricted in the first days of life.

To further explore these issues because of potential safety concerns, we engaged with topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. We received feedback from 3 topic experts (all consultant neonatologists). All 3 agreed that in the first 24–48 hours, 10% glucose is standard care with 1 expert noting that sometimes 15 or 20% glucose is needed. Two experts felt there was a theoretical risk of hypoglycaemia with 5% glucose, and 2 experts agreed that isotonic crystalloids containing sodium in the range 131-154 mmol/litre would deliver excess sodium above usual requirements. One expert went on to note that newborns are managed within neonatal units, and fluid management for neonates in a neonatal intensive care unit or special care baby unit is very different to a paediatric setting.

The 3 topic experts were asked about the population for whom recommendation 1.4.7 as currently worded was most suitable, and 2 agreed that an appropriate cutoff would be term neonates aged 8 days or over.

Impact statement

Balanced crystalloids versus isotonic (0.9%) or hypotonic (0.45%) sodium chloride

A study found a lower risk of hyponatraemia during routine maintenance with Plasma-Lyte 148 plus 5% glucose than 0.45% sodium chloride plus 5% glucose without an increase in adverse effects. This evidence is unlikely to affect recommendation 1.4.3 to use isotonic crystalloids that contain sodium in the range 131–154 mmol/litre (of which Plasma-Lyte is an example). The guideline does not specify a particular isotonic fluid, however decisions on the potential superiority of Plasma-Lyte in reducing hyponatraemia would ideally be based on a comparison of Plasma-Lyte (an isotonic fluid) with another isotonic fluid, not on a comparison with a hypotonic solution as in this study.

A second trial did compare a balanced crystalloid (unspecified) with 0.9% sodium chloride for maintenance and found that it reduced both variation in plasma chloride and hyperchloraemic acidosis (an outcome deemed important by the original guideline). However, the evidence is from a single trial in a very specific population (brain tumour resection). Further evidence from other populations to support these findings, including additional outcomes deemed critical or important by the original guideline (such as mortality or hospital stay), would be useful before considering any impact on recommendation 1.4.3 which does not currently specify a particular isotonic fluid.

New evidence is unlikely to change guideline recommendations.

Isotonic (0.9%) versus hypotonic (<0.9%) sodium chloride

The new evidence found that 0.9% sodium chloride for routine maintenance is associated with less hyponatraemia, with no impact on other adverse events. This is consistent with recommendation 1.4.3 to use isotonic crystalloids that

contain sodium in the range 131–154 mmol/litre (of which 0.9% sodium chloride is an example) for routine maintenance.

New evidence is unlikely to change guideline recommendations.

5% versus 3.3% dextrose

The new evidence found no difference in hyperglycaemia with 0.3% sodium chloride in 3.3% dextrose versus 0.9% sodium chloride in 5% dextrose for post-operative fluid maintenance (though interpreting the effect of the dextrose concentration is confounded by differing sodium chloride levels in the solutions). This is consistent with recommendation 1.4.3 for fluid type for routine maintenance in children and young people which does not discuss glucose levels, nor (unlike fluid type for resuscitation) does it specify that it should be glucose-free.

New evidence is unlikely to change guideline recommendations.

Intravenous fluid type for term neonates

Recommendation 1.4.7 states 'If term neonates need IV fluids for routine maintenance, initially use isotonic crystalloids that contain sodium in the range 131–154 mmol/litre with 5–10% glucose.' When originally making these recommendations, the <u>full guideline</u> (p.107) notes some considerations from the guideline committee, including: evidence suggested a clinical benefit of isotonic fluids for hyponatraemia in term neonates from 48 hours to 28 days; there was no evidence on fluid type specifically in term neonates from 0–48 hours; and no evidence was identified in term neonates (0–48 hours and 48 hours–28 days) for the addition of glucose. The committee therefore chose to use informal consensus to develop a recommendation.

No new evidence was identified by surveillance in this area, and the absence of new evidence contributed to the decision not to update the guideline that was consulted on. During consultation, a stakeholder expressed concerns that the currently recommended ranges of 131–154 mmol/litre sodium and 5–10% glucose could possibly lead to hypernatraemia or hypoglycaemia, particularly in younger neonates. The current recommendation is for all Surveillance summary of evidence March 2020 – Intravenous fluid therapy in children and young people in hospital

neonates up to 28 days old and does not discuss the potential need for a different approach in babies in the first days of life. Topic experts agreed with the stakeholder's concerns, and noted that fluid management for the youngest neonates in a neonatal intensive care unit or special care baby unit is very different to a paediatric setting.

Because of the feedback from the stakeholder and topic experts that the current wording of recommendation 1.4.7 may not correspond with current practice and may have safety implications, particularly in younger neonates, it was agreed that it should be amended. Topic experts were therefore asked about the population for whom recommendation 1.4.7 as currently worded was most suitable, and they suggested that an appropriate cutoff would be term neonates aged 8 days or over. As this would leave a gap for management of term neonates aged up to 7 days, it was further decided that additional wording should be added to the recommendation to cover this population. The amended recommendation wording agreed upon was:

- If term neonates aged 8 days or over need IV fluids for routine maintenance, initially use isotonic crystalloids that contain sodium in the range 131–154 mmol/litre with 5–10% glucose. For term neonates aged up to 7 days, use professional judgement, taking into account:
 - the individual circumstances, and
 - for term neonates in the first days of life, a sodium content of 131–
 154 mmol/litre may be too high (or sodium may not be needed) and a glucose content of 5–10% may be too low.

This issue will be logged and we may revisit this area if we become aware of any relevant new evidence in future.

Replacement and redistribution

Surveillance proposal

No new information on <u>replacement and redistribution</u> was identified in this surveillance review.

Managing hypernatraemia that develops during intravenous fluid therapy

Surveillance proposal

No new information on <u>managing hypernatraemia that develops during</u> <u>intravenous fluid therapy</u> was identified in this surveillance review.

Managing hyponatraemia that develops during intravenous fluid therapy

Surveillance proposal

No new information on <u>managing hyponatraemia that develops during</u> intravenous fluid therapy was identified in this surveillance review.

Training and education

Surveillance proposal

No new information on <u>training and education</u> was identified in this surveillance review.

Editorial amendments

Recommendation 1.1.1 cross-refers to the principles and protocols for intravenous fluid therapy section of NICE guideline CG174 intravenous fluid therapy in adults in hospital. However, the hyperlink goes to the introduction section of CG174; it will be changed to link to the principles and protocols for intravenous fluid therapy section of CG174.

Recommendation 1.4.7 will be amended as follows to address concerns about the suitability of currently recommended isotonic crystalloids for the youngest neonates:

If term neonates aged 8 days or over need IV fluids for routine
maintenance, initially use isotonic crystalloids that contain sodium in the
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range 131–154 mmol/litre with 5–10% glucose. For term neonates aged up to 7 days, use professional judgement, taking into account:

- the individual circumstances, and
- for term neonates in the first days of life, a sodium content of 131–
 154 mmol/litre may be too high (or sodium may not be needed) and a glucose content of 5–10% may be too low.

The guideline currently has 3 footnotes related to unlicensed use in children and young people of the following intravenous fluids: glucose-free crystalloids; isotonic crystalloids with 5–10% glucose; and hypotonic solutions. These will be replaced by the following single footnote to ensure that all the many intravenous infusion solutions currently available in the UK are covered:

• At the time of review (March 2020), some intravenous fluid therapy preparations may not have a UK marketing authorisation for this indication in all ages of children and young people. Please refer to the individual summary of product characteristics for licensing information. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

The table 'Intravenous fluid types for children and young people' has a footnote which links to the British national formulary for children. However, the link goes to www.bnf.org – it will be replaced with a link to the section of the BNFc website on fluids and electrolytes.

The section of the guideline 'Intravenous fluid therapy in children and young people in hospital implementation: getting started' has the following issues:

 The first paragraph states: 'We identified these with the help of stakeholders and guideline committee members (see <u>section 9.4 of the</u> <u>manual</u>).' However, the manual has since been updated and the link now directs to the wrong section of the manual. This will be amended to link to

- <u>section 10.1 of the manual</u> (subsection 'Approaches to additional consultation').
- In 'Recording fluid and electrolyte status to ensure appropriate prescribing', there is a link to the <u>Department of Health, Social Services and Public</u> <u>Safety</u> (DHSSPS) in Northern Ireland. However, this has now been renamed Department of Health and has a new URL. This will be amended.
- In 'Raising awareness of training and education resources' there is a link to the NICE online learning tool. This link is broken and will be removed.

Research recommendations

What is the incidence of complications during, and as a consequence of, IV fluid therapy in children and young people?

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

What is the most appropriate glucose concentration in IV fluids for children and young people of different ages?

- The <u>new evidence</u> found no difference in hyperglycaemia with 0.3% sodium chloride in 3.3% dextrose versus 0.9% sodium chloride in 5% dextrose for post-operative fluid maintenance in children (aged 6 months to 14 years) and is unlikely to affect the guideline. However, <u>stakeholders questioned</u> the range of glucose concentrations of intravenous fluids for routine maintenance in term neonates in recommendation 1.4.7, which may not correspond with current practice and may have safety implications. After discussion with topic experts, this recommendation will be amended to:
 - If term neonates aged 8 days or over need IV fluids for routine maintenance, initially use isotonic crystalloids that contain sodium in the range 131–154 mmol/litre with 5–10% glucose. For term neonates aged up to 7 days, use professional judgement, taking into account:
 - ♦ the individual circumstances, and

♦ for term neonates in the first days of life, a sodium content of 131– 154 mmol/litre may be too high (or sodium may not be needed) and a glucose content of 5–10% may be too low.

For children and young people receiving IV fluids, does the use of a standardised national fluid balance chart reduce the rate of complications arising as a result of prescription and/or administration errors?

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

Does ensuring that all hospital healthcare professionals involved in prescribing and delivering IV fluids for children and young people are appropriately trained in the principles of fluid prescribing and IV fluid therapy-related complications lead to a reduction in IV fluid-related complications and associated healthcare costs?

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

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