NICE National Institute for Health and Care Excellence

2020 Surveillance of intravenous fluid therapy in children and young people in hospital (NICE guideline NG29)

Surveillance report

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Contents

Surveillance decision 3

Reasons for the decision 3

Overview of 2020 surveillance methods 7

Evidence considered in surveillance 7

Ongoing research 8

Intelligence gathered during surveillance 8

Overall decision 12

Surveillance decision

We will not update the NICE guideline on intravenous (IV) fluid therapy in children and young people in hospital.

We will amend recommendation 1.4.7 on IV fluid type for routine maintenance in term neonates to specify the population that the recommendation refers to.

Reasons for the decision

New evidence was identified in the following areas:

- hypertonic (more than 0.9%) versus isotonic (0.9%) sodium chloride for resuscitation
- faster versus slower resuscitation fluid rate
- smaller versus larger resuscitation fluid volume
- standard versus restricted volumes for routine fluid maintenance
- liberal versus restricted intraoperative maintenance infusion
- balanced crystalloid versus 0.9% or 0.45% sodium chloride for maintenance infusion
- isotonic (0.9%) versus hypotonic (less than 0.9%) sodium chloride for maintenance infusion
- 3.3% versus 5% dextrose for maintenance infusion.

However, the evidence in these areas did not indicate a need to update the guideline because results were either: consistent with existing recommendations, of limited relevance to the guideline, from single trials, or based on outcomes deemed not to be critical or important by the original guideline committee. No further evidence to indicate a need to change this conclusion arose during consultation on the decision not to update the guideline.

However, during consultation, stakeholders raised concerns in the following 2 areas which, although insufficient for an update of the guideline at this time, warranted further action as detailed below.

Fluid type for routine maintenance in term neonates

During consultation, a stakeholder expressed concerns about recommendation 1.4.7 on IV fluid type for routine maintenance in term neonates. The recommendation currently 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'. The stakeholder noted that the recommended ranges of sodium and glucose could lead to hypernatraemia or hypoglycaemia, particularly in younger neonates. For example, they stated that in the first 24 hours of life, plain (usually 10%) glucose without electrolytes is standard in term neonates.

Recommendation 1.4.7 is for all term 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. When the guideline was originally developed, the full guideline (page 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 hours to 48 hours
- no evidence was identified in term neonates (0 hours to 48 hours, and 48 hours to 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 we consulted on.

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 contacted 5 topic experts and received feedback from 3 (all consultant neonatologists). All 3 agreed that in the first 24 hours to 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 to 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 feedback from the stakeholder and topic experts indicated that the current wording of recommendation 1.4.7 may not correspond with current practice and may have safety implications including hypernatraemia and hypoglycaemia, particularly in younger neonates. It was therefore agreed that the recommendation should be amended. Three experts were asked about the population for whom recommendation 1.4.7, as currently worded, was most suitable, and 2 indicated that an appropriate cut-off would be term neonates aged 8 days or over. Because this would leave a gap for management of term neonates aged up to 7 days, it was further decided to add wording to the recommendation to cover this population.

Recommendation 1.4.7 will now state:

- 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 to 154 mmol/litre with 5% to 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, that a sodium content of 131 to 154 mmol/litre may be too high (or sodium may not be needed), and a glucose content of 5% to 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.

Balanced crystalloids versus 0.9% sodium chloride

Among the new evidence identified before consultation, some studies suggested that balanced crystalloids could have some benefits over 0.9% sodium chloride for both fluid resuscitation and fluid maintenance. The guideline currently recommends crystalloids containing 131 to 154 mmol/litre of sodium (of which balanced crystalloids and 0.9% sodium chloride are examples) for resuscitation and maintenance, but does not specify a particular fluid type. However, the new evidence on balanced crystalloids was from single trials in various conditions and most outcomes were not those deemed critical by the original guideline committee. Some studies also showed no benefit of balanced

crystalloids over 0.9% sodium chloride. Overall, we did not find sufficient new evidence to support an update of the guideline in this area.

During consultation, a stakeholder disagreed with the proposal not to update the guideline regarding balanced crystalloids, noting that although the evidence is limited, there is some evidence of benefit, and no evidence of harm. We were also made aware (through an open letter to NICE) of 2 large randomised controlled trials (RCTs) that appear to demonstrate some benefits of balanced crystalloids over 0.9% sodium chloride in adults:

- SMART trial 2018 (n=15,802 critically ill adults)
- SALT-ED trial 2018 (n=13,347 noncritically ill adults).

No new evidence specifically in children was submitted during the consultation, and we therefore believe that evidence is not conclusive enough to specifically recommend balanced crystalloids over normal saline at this time, and the current recommendation allows for clinical judgement in selecting the most appropriate fluid type. However, we acknowledge that SMART and SALT-ED are large RCTs that appear to demonstrate benefits of balanced crystalloids in adults. We therefore plan to conduct an exceptional surveillance review based on these studies. Because the studies are in adults, we will initially focus on any impact of the evidence on the NICE guideline on IV fluid therapy in adults in hospital. We will consider whether any changes are needed to recommendations on fluid type in NICE guideline NG29 as part of this process.

For further details and a summary of all evidence identified in surveillance, see appendix A.

Overview of 2020 surveillance methods

NICE's surveillance team checked whether recommendations in the NICE guideline on intravenous (IV) fluid therapy in children and young people in hospital remain up to date.

The surveillance process consisted of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the proposal not to update with stakeholders.
- Considering comments received during consultation, including further engagement with topic experts, and making any necessary changes to the proposal.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Search and selection strategy

We searched for new evidence related to the whole guideline.

We found 23 studies in a search for randomised controlled trials (RCTs) and Cochrane reviews published between 22 December 2014 and 31 August 2019.

We also included:

- 1 relevant study from a total of 10 identified by topic experts, which was also identified by the searches.

From all sources, we considered 23 studies to be relevant to the guideline.

See appendix A for details of all evidence considered, and references.

Selecting relevant studies

We included RCTs of children and young people. Although the original guideline allowed evidence from adult populations, this was excluded from the surveillance review.

Ongoing research

We checked for relevant ongoing research; no relevant ongoing studies were identified.

Intelligence gathered during surveillance

Views of topic experts before consultation

We considered the views of topic experts who were recruited to the NICE Centre for Guidelines Expert Advisers Panel to represent their specialty. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to the guideline.

We sent questionnaires to 9 topic experts and received 5 responses. The topic experts who provided feedback were: a consultant nurse in paediatric emergency medicine, an advanced paediatric nurse practitioner, a specialist clinical pharmacist, a consultant paediatric nephrologist and a consultant neonatologist.

Overall, 1 topic expert thought that the guideline should be updated and 4 thought that an update was not necessary. One issue topic experts thought could be addressed in an update was whether outcomes are worse with larger versus reduced fluid resuscitation bolus volumes. The surveillance review identified evidence in this area, but it either was not applicable to the UK, or found no difference between either large and small boluses, or

treatment with or without boluses.

Experts also questioned whether there is a role for balanced crystalloids because they were being used more widely in practice. The surveillance review also identified evidence in this area, but it was not deemed sufficient to support an update of the guideline at this point in time. However, evidence on balanced crystalloids in adults was supplied to us during the consultation and we plan to examine this in more detail (see the section on views of stakeholders for details).

Implementation of the guideline

During the surveillance review, we identified variations in the information about fluids across recommendations, footnotes and the table of example fluids. Through NICE's field team, we queried with a paediatric clinical group whether this was an issue in practice. The group reassured us that they had no concerns about inconsistencies in the guideline.

Other sources of information

We considered all other correspondence received since the guideline was published.

An enquiry to NICE raised concerns about the absence of a specific maximum resuscitation bolus volume for children and young people in recommendation 1.3.1 of NICE guideline NG29 (whereas the NICE guideline on IV fluid therapy in adults in hospital gives a figure of 500 ml). This was discussed by the committee during development of the original NICE guideline NG29. 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). Additionally, recommendation 1.3.1 in NICE guideline NG29 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.

Views of stakeholders

Stakeholders are consulted on all surveillance reviews except if the whole guideline will be updated and replaced. Because this surveillance proposal was to not update the guideline, we consulted with stakeholders.

Overall, 7 stakeholders commented: 3 royal colleges, 2 professional associations, a charitable research foundation and a manufacturer. Four stakeholders agreed with the decision not to update the guideline and 3 disagreed. The following issues were raised by stakeholders.

Intravenous fluid type in term neonates

A stakeholder highlighted 2 studies in neonatal fluid resuscitation; however, they were not within scope of the surveillance review because they were not evidence types allowed by the original guideline.

The stakeholder also raised concerns about recommendation 1.4.7 relating to the sodium and glucose content of IV fluids for routine maintenance in neonates, for example, that they may deliver excess sodium or insufficient glucose. The stakeholder cited 2 guidelines in support of their comments, the first of which did not provide any references to the underlying evidence base, and the second referenced books and non-systematic reviews (which are not evidence types that can be considered by surveillance reviews).

However, to further explore these issues because of potential safety concerns, 5 topic experts were contacted, and the 3 who responded broadly agreed with the stakeholder's concerns. The stakeholder comments on IV fluids for routine maintenance in neonates, along with feedback from topic experts, led to a decision to amend recommendation 1.4.7 regarding the suitability of the recommended isotonic crystalloids for different ages of term neonates.

Balanced crystalloids

A stakeholder did not agree with the proposal not to update the guideline regarding balanced crystalloids, and noted that although the evidence is limited, there is some evidence of benefit, and no evidence of harm.

We are also aware (via an open letter to NICE) of 2 large RCTs that appear to demonstrate some benefits of balanced crystalloids over 0.9% sodium chloride in adults.

The stakeholder comments on balanced crystalloids, along with the new evidence in adults notified to us, influenced our decision to conduct an exceptional surveillance review of the NICE guideline on IV fluid therapy in adults in hospital, during which we will also consider any impact of the new studies on NICE guideline NG29.

Resuscitation fluid volume

A stakeholder noted that the Fish (fluids in shock) pilot study (2018) found no difference in clinical outcome between children receiving a 20 ml/kg bolus (in line with NICE guideline NG29, recommendation 1.3.1) and a 10 ml/kg bolus. They suggested that in the absence of evidence of superiority of either regimen, a more cautious fluid resuscitation strategy could be considered, such as a 20 ml/kg bolus with clinical review and a pause after each 10 ml/kg aliquot.

The current surveillance review identified the Fish study, noting that it was a pilot study, and concluded that no evidence has been identified to change practice, therefore no changes to the guideline can currently be proposed. However, we acknowledge the stakeholder's concerns and will log this as an issue for consideration at the next surveillance review when further evidence in this area may be available.

A stakeholder also alerted us to a paper reanalysing the FEAST trial (2019). This paper was identified as part of the intelligence gathering process for the surveillance review. It examined the reasons behind the findings of the original FEAST publication that fluid bolus was associated with increased mortality in febrile children of African family origin. The new study found that bolus resuscitation was associated with, for example, deterioration of respiratory and neurological function in some patients. But further research would be needed to examine the implications of these findings for the guideline and the evidence on its own is not of direct relevance to the guideline, particularly given that the original guideline committee felt that the FEAST trial, on which the paper is based, is not directly applicable to the UK clinical setting. The surveillance review therefore did not include this paper in the final report. However, we note its findings and may include, if relevant, any further research building on these findings in future surveillance reviews.

See appendix B for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

No equalities issues were identified during the surveillance process.

Overall decision

After considering all evidence and other intelligence and the impact on current recommendations, we decided that no update is necessary.

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