NICE National Institute for Health and Care Excellence

Appendix B: Stakeholder consultation comments table

2020 surveillance of Intravenous fluid therapy in children and young people in hospital (2015)

Consultation dates: 9am, Monday 7 October to 5pm, Friday 18 October 2019

1. Do you agree with the proposal to not update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Association of Paediatric Emergency Medicine	No	Our comments primarily relate to fluid resuscitation volume. We agree that evidence is currently limited, and indeed the FiSh (Fluids in Shock) pilot study of 2018 showed us that as so few children in our population were sick enough to require fluid resuscitation, further evidence may not be forthcoming. In the absence of evidence to suggest that volumes of 10 ml/kg are no worse or better than 20 ml/kg, we feel that it would not be inappropriate to move to a more cautious strategy with fluid resuscitation, recommending planning a 20 ml/kg bolus, but with clinical review and a pause after each 10 ml/kg aliquot.	Thank you for your comment. The surveillance review identified the Fluids in Shock pilot study that you refer to. We noted it found no difference in clinical outcome between children receiving a 20 ml/kg bolus (in line with recommendation 1.3.1) and a 10 ml/kg bolus, and along with the limitations of being a pilot study, we therefore concluded that this evidence is unlikely to affect the guideline. As you note, there is an absence of evidence to indicate the superiority of a 10 or 20 ml/kg bolus, and we are not aware of any evidence examining your proposed strategy of clinical review and a pause after each 10 ml/kg aliquot. The full version of the guideline (p.87-88) notes the following considerations when the guideline was originally being developed: 'Children with shock need immediate restoration of intravascular

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			blood volume. It is current practice to administer 20 ml/kg over less than 10 minutes. No evidence was identified to change current practice.' It remains the case that no evidence has been identified to change practice, and the surveillance review is therefore currently unable to propose any changes to the guideline. We acknowledge your concerns and will log this as an issue for consideration at the next surveillance review when further evidence in this area may be available.
Baxter Healthcare Ltd	Yes	There is no new data that will significantly change the current guidelines	Thank you for your comment. We are glad that you agree with our decision not to update the guideline.
British Association of Paediatric Nephrology	Yes	This was sent to clinical leads for paediatric nephrology in the UK through the BAPN network and I did not receive any comments to suggest there was disagreement with the proposal not to update the guideline.	Thank you for your comment. We are glad that you agree with our decision not to update the guideline.
Royal College of Nursing	Yes	Also note that editorial review and the checking process has already identified the need to correct web links and make amendments to clarify footnotes.	Thank you for your comment. We are glad that you agree with our decision to make some editorial amendments.
Royal College of Paediatrics and Child Health	No	The overview section states 'no studies were found specifically for neonates'. There are relevant published clinical studies in neonates as well as animal studies which are important to be considered and evaluated for guideline purposes. Below are examples of two such studies: Finn D1, Roehr CC, Ryan CA, Dempsey EM. Optimising Intravenous Volume Resuscitation of the Newborn in the	Thank you for your comment. The 2 studies that you have highlighted are not within scope of the surveillance review because they are not evidence types allowed by the original guideline: Finn et al. (2017) is a non-systematic review and is not within the scope of evidence types included in the relevant review questions in

		Delivery Room: Practical Considerations and Gaps in Knowledge. Neonatology. 2017;112(2):163-171. doi: 10.1159/000475456. Epub 2017 Jun 2. Mendler MR, Schwarz S, Hechenrieder L, Kurth S, Weber B, Höfler S, Kalbitz M, Mayer B, Hummler HD. Successful Resuscitation in a Model of Asphyxia and Hemorrhage to Test Different Volume Resuscitation Strategies. A Study in Newborn Piglets After Transition. Front Pediatr. 2018 Jul 10;6:192. doi: 10.3389/fped.2018.00192. eCollection 2018. The reviewer does not agree with the proposal not to make a recommendation regarding balanced crystalloid. Although the evidence is limited, there is some evidence of benefit, and no evidence of harm. The following comments relate to the guidance on IV fluids for term neonates. 1.4.7. It is not routine neonatal practice to initially use isotonic crystalloids in term neonates as the current guideline suggests. In the first 24 hours of life it is standard to use plain (usually 10%) dextrose in all term neonates (not just those described in 1.4.8). (The reviewer referenced the NW newborn clinical guideline[1] – Although a New Zealand guideline, it provides a good summary of the current practice in the two UK tertiary neonatal units where the reviewer has been working over the past 3 years). 1.4.7. Isotonic crystalloids with Na concentration 131/154mmol/L would deliver a larger amount of Na than is routinely given in term neonates. Usual Na requirement around 3mmol/kg/d (adjusted according to blood electrolytes). (See NW newborn clinical guideline[1]) 1.4.7. Fluids containing 5% dextrose are not routinely used	the original guideline (systematic reviews of RCTs, RCTs, abstracts of RCTs, non-randomised prospective or retrospective cohort studies of 50 children or more). Mendler et al. (2018) is an animal study. The original guideline excluded laboratory studies (including human, animal or in vitro) as these settings were considered to be artificial and not comparable to the guideline population. Regarding balanced crystalloids, the current surveillance review found some evidence of benefit of balanced crystalloids in children, such as reduced hyperchloraemic acidosis and hyponatraemia. But also showed no differences in other outcomes such as clinical status or hospital stay. Additionally, most studies did not report any outcomes deemed critical by the original guideline committee (mortality or neurological or cardiovascular compromise), and the evidence was from single small trials. We therefore concluded there was currently no impact of the evidence on recommendations 1.3.1 and 1.4.3 to use crystalloids for resuscitation and maintenance that contain sodium in the range 131–154 mmol/litre. The recommendation wording allows for the use of balanced crystalloids, and the table of example IV fluid types in the guideline also gives an example of a balanced crystalloid – Hartmann's solution. We believe that evidence in children 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 are aware of the SMART and SALT-ED studies in adults, which are large randomised trials that appear to demonstrate some benefits of balanced crystalloids in adults for renal outcomes. We therefore plan to conduct an exceptional surveillance review based on these studies, which will focus on any impact of the evidence on NICE

		in neonates in the reviewer's experience. The reviewer is concerned that following this recommendation in clinical practice could theoretically lead to low blood sugars in term babies who are relatively fluid restricted in the first days of life. Adequate glucose intake is usually 4-6mg/kg/min for a normal, term neonate (Neonatal transfer Service [NTS] guideline[2]). This lower limit is only just achieved by 60ml/kg/d of 10% dextrose. 5% dextrose would fall short. However, in practice, term neonates are often given only 40ml/kg/d of 10% dextrose on Day 0 and blood sugars are not, in the reviewers experience, usually low on this regime so the actual clinical impact of giving 5% is not clear. [1]http://www.adhb.govt.nz/newborn/Guidelines/Nutrition/Electrolytes.htm [2]https://london-nts.nhs.uk/wp-content/uploads/2015/01/Hypoglycaemia-NTS-Guideline.pdf	guideline CG174 Intravenous 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. Regarding IV fluids for term neonates. The full wording of the recommendations you refer to are: • 1.4.7 '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.' • 1.4.8 'For term neonates in critical postnatal adaptation phase (for example, term neonates with respiratory distress syndrome, meconium aspiration, hypoxic ischaemic encephalopathy), give no or minimal sodium until postnatal diuresis with weight loss occurs.' When originally making these recommendations, the full guideline (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. We note the 2 guidelines you have cited in support of your comments. The first of these does not provide any references and the second references books and non-systematic reviews. We are therefore unable to formally include evidence from these guidelines in the surveillance review. However, we acknowledge your concerns

			in this area, particularly given the very limited evidence base used to originally develop the recommendations. To further explore the issues you have raised 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% dextrose is standard care with 1 expert noting that sometimes 15 or 20% dextrose is needed. Two experts felt there was a theoretical risk of hypoglycaemia with 5% dextrose, and 2 experts agreed that isotonic crystalloids containing sodium in the range 131-154 mmol/litre would deliver excess sodium than 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. Recommendation 1.4.7 as currently worded may not correspond with current practice and may have safety implications, particularly in younger neonates. It was therefore agreed that the recommendation should be amended. Topic experts were 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 to add wording to the recommendation to cover this population.
Royal College of Physicians (RCP)	Yes	Not answered	Thank you for your answer.

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Meningitis Research Foundation	No	because I'm concerned that the decision was taken without considering some recent relevant evidence, see below. This may still be insufficient to warrant updating of the guideline, but needs to be considered by the topic experts. The current surveillance review seems to have missed a relevant paper published in June/July, reanalysing the FEAST trial: *Levin M, Cunnington AJ, Wilson C, Nadel S, Lang HJ, Ninis N, McCulloch M, Argent A, Buys H, Moxon CA, Best A, Nijman RG, Hoggart CJ. Effects of saline or albumin fluid bolus in resuscitation: evidence from re-analysis of the FEAST trial. Lancet Respir Med. 2019 Jul;7(7):581-593. doi: 10.1016/S2213-2600(19)30114-6. Epub 2019 Jun 10.* This paper suggests that normal saline or 5% albumin for fluid resuscitation may be harmful, as well as needing greater care in patients with raised intracranial pressure. This may not on its own constitute sufficient evidence for changing the guideline, but does suggest further research to investigate it (although it may not be possible to run such a trial when units are already adopting balanced fluids in preference to saline or albumin).	Thank you for your comments. The full version of the guideline (p.89) states that 'The guideline committee noted the FEAST study findings [...] the study did demonstrate more deaths for both albumin and 0.9% sodium chloride fluid boluses when compared to no fluid bolus. The deaths were caused by underlying conditions, but there remains a question as to why the fluid boluses increased the likelihood of death. [...] The guideline committee felt that although this is an important finding, the situation is not directly applicable to the UK clinical setting.' The paper you have highlighted by Levin et al. (2019) used data from the FEAST trial to examine why fluid bolus was associated with increased mortality. It helps to answer the question posed by the guideline committee of why the fluid boluses increased the likelihood of death. The authors of the paper found that bolus resuscitation was associated with, for example, deterioration of respiratory function and neurological function in some patients, and therefore postulated that caution in use of fluids might be needed in patients with respiratory or central nervous system compromise. This paper was identified as part of the intelligence gathering process for the surveillance review. However, as you note, this may not on its own constitute sufficient evidence for changing the guideline, and further research would be needed to examine the implications of these findings for the guideline. 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 upon 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.

2. Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
Association of Paediatric Emergency Medicine	No	Not answered	Thank you for your answer.
Baxter Healthcare Ltd	No	Not answered	Thank you for your answer.
British Association of Paediatric Nephrology	No	Not answered	Thank you for your answer.
Royal College of Nursing	No	Not answered	Thank you for your answer.
Royal College of Paediatrics and Child Health	Yes	The reviewer agrees that it is entirely appropriate not to include preterm neonates in this guideline. Each mention of 'neonate' is preceded by 'term' – very clear.	Thank you for your comment. We acknowledge your support of not including preterm neonates in this guideline.
Royal College of Physicians (RCP)	Not answered	Not answered	Thank you.
Meningitis Research Foundation	Not answered	Not answered	Thank you.

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3. Do you have any comments on equalities issues?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Association of Paediatric Emergency Medicine	No	Not answered	Thank you for your answer.
Baxter Healthcare Ltd	No	Not answered	Thank you for your answer.
British Association of Paediatric Nephrology	No	Not answered	Thank you for your answer.
Royal College of Nursing	No	Not answered	Thank you for your answer.
Royal College of Paediatrics and Child Health	No	Not answered	Thank you for your answer.
Royal College of Physicians (RCP)	Not answered	Not answered	Thank you.
Meningitis Research Foundation	Not answered	Not answered	Thank you.

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