Appendix A: NICE guideline recommendations and the evidence underlying them

	Source	NG29 – Intravenous fluid therapy in children and young people in hospital & NG51- Sepsis	NG143 – Fever in under 5's	CG84 – Diarrhoea and vomiting caused by gastroenteritis in under 5's	CG102 – Meningitis and meningococcal septicaemia in under 16's	NG18 – Diabetes in children
Population		Children and young people who need fluid resuscitation	Under 5's with fever and shock	Under 5's with confirmed or suspected shock	Under 16's with meningococcal septicaemia and signs of shock	Children and young people with diabetic ketoacidosis and shock
Initial fluid bolus	*How much*	20 ml/kg bolus	20 ml/kg bolus	20 ml/kg bolus	20 ml/kg bolus	20 ml/kg bolus
	Of what	Glucose free crystalloids that contain sodium in the range of 131-154 mmol/litre	0.9% sodium chloride	0.9% sodium chloride	0.9% sodium chloride	0.9% sodium chloride
	How quickly	Over 10 minutes	Immediately	Rapid infusion	Immediately	As soon as possible
Next clinical steps			Active monitoring, further fluid boluses as necessary.	If child remains shocked: a further rapid infusion of 20 ml/kg 0.9% saline.	If signs of shock persist a second bolus of 20 ml/kg 0.9% sodium chloride or 4.5% human albumin over 5-10 minutes. If the signs of shock still persist after the first 40 ml/kg, a third bolus	When calculating the total fluid requirement, do not subtract this fluid bolus from the total fluid deficit.

					of 20 ml/kg 0.9% sodium chloride or 4.5% human albumin over 5-10 minutes is recommended.	
Other clinical considerations				Consider causes of shock other than dehydration	Further steps could include: calling for anaesthetic assistance for urgent tracheal intubation and mechanical ventilation; starting treatment with vasoactive drugs; being aware that some children and young people may require large volumes of fluid over a short period of time to restore their circulating volume; considering giving further fluid boluses at 20 ml/kg of intravenous or intraosseous sodium chloride 0.9% or human albumin 4.5% solution over 5–10 minutes based on clinical signs and	Recommendations were also made to highlight that shock is rare in children and young people with DKA, and that typical symptoms of shock can overlap with symptoms of DKA.

					appropriate laboratory investigations including urea and electrolytes.	
Evidence		NG29: Searches were conducted for systematic reviews, RCTs and cohort studies in children. The GDG did not consider that evidence in an adult population was relevant as the optimum rate of fluid administration is likely to differ for children and adults as the fluid requirements for children are higher. No relevant clinical studies comparing sodium chloride at different rates were identified. Children with shock need immediate restoration of intravascular blood volume. It is current practice to administer 20 ml/kg	One case-control study found that too little fluid therapy versus "adequate" fluid therapy was significantly associated with death. No information was given in the guideline about the volume of "adequate" therapy given. A retrospective cohort study found that fluid boluses and early use of ionotropes resulted in shock reversal and increased survival. There was no information on the volume of fluid boluses given.	There was no definitive evidence on the optimum IV fluid regimen for the management of hypovolaemic shock in the dehydrated child with gastroenteritis. However, there was widespread consensus that whatever the cause of shock, a bolus of IV fluid should immediately be given.	None identified	A combined search was conducted to identify studies which explored route of fluid administration for rehydration, type of fluids (including additives) that should be used for rehydration and the rate and volume these fluids should be administered. No studies were identified that looked at the volume of IV fluid boluses for children with both DKA and shock.

		over less than 10 minutes. No evidence was identified to change current practice. The GDG felt it important to reassess the circulation following completion of the fluid bolus and administer further fluids if indicated. NG51: In the case of children the GDG agreed that they had not found any evidence to change the recommendations made by the IV fluids in children guideline which had included children with sepsis.				
Committee discussion		NG29: The GDG acknowledged that the FEAST evidence challenges whether boluses should be used for resuscitation in resource-limited settings for children	The GDG concluded that children with fever and signs of circulatory insufficiency have reduced mortality when given intravenous fluid resuscitation. They	No discussion of the different volumes for initial boluses in fluid therapy. Discussion centred on the optimal fluid composition.	No discussion of the different volumes for initial boluses in fluid therapy. Discussion centred on the optimal fluid composition.	The committee noted that while shock is a rare occurrence in children and young people with DKA, it can occur, and such patients require more fluid boluses to improve tissue

		with shock who did not have hypotension. However, the guideline concluded that although this was an important finding, the situation was not directly applicable to the UK clinical setting. NG51: The GDG discussed the FEAST study. The FEAST study did not fit the study population defined in the protocol for this review but had been widely discussed in the paediatric sepsis community. The study was excluded from formal review because the study population consisted of children with severe febrile illness or respiratory distress rather than sepsis.	stated that current practice would be to give a bolus of 20 ml/kg.			perfusion. Furthermore, the committee highlighted that restricting initial fluid boluses can result in less fluids being administered over the 48-hour period. The committee stated that this may be problematic as recent hypothesis and data suggests that brain injury may result from cerebral hypoperfusion and the effects of reperfusion and neuro-inflammation that occurs during episodes of DKA. The committee highlighted that the 2015 recommendations could have been made with the risk of cerebral oedema in mind as the previous hypothesis stated that rapid administration of IV fluids reduces serum osmolality

		Only 16% of the study population had a working diagnosis of septicaemia.				which results in brain swelling. Based on their clinical judgment and the RCT evidence identified in the review, particularly the PECARN FLUID trial, the committee recommended that in children and young people with DKA who have signs of shock, an initial intravenous bolus of 20 ml/kg 0.9% sodium chloride should be given as soon as possible. The committee used their expertise to recommend that the aim should be to replace the fluid deficit evenly over the first 48 hours, but in critically ill children and young people, the fluid regimen should be discussed early with the senior paediatrician or paediatric intensivist (or both), because the risk of cerebral

						oedema is higher. The committee further noted that it is crucial that treatment is not delayed due to the risk of cerebral oedema.