National Clinical Guideline Centre

IV fluids in children

Intravenous fluid therapy in children and young people in hospital

Appendix G

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Royal College of Physicians

The Royal College of Surgeons of England

Royal College of General Practitioners

Royal College of Nursing

NICE accredited

Disclaimer
Healthcare professionals are expected to take NICE clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

Funding
National Institute for Health and Care Excellence

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None

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None

G.1.2.2 Laboratory-based methods versus point-of-care testing

Table 1: Singer [23]

Study	Singer2014 [23]
Study type	Comparative cohort
Number of studies (number of participants)	1 (n=84)
Countries and setting	Conducted in United States; setting: tertiary academic medical care centre
Inclusion criteria	Adult patients presenting to an emergency department (ED) 12 months prior to introduction of bedside lactate testing with an initial lactate level of at least 2 mmol/litre.
Exclusion criteria	Patients presenting to the ED 12 months prior to introduction of bedside lactate testing who also had an initial lactate level of at least 2 mmol/litre, starting from 1 calendar year prior to study initiation.
Age, gender and ethnicity	Age – median (range): 71 (56-83). Gender (M:F): 1:1. Ethnicity: 90% Caucasian; other 10%.
Interventions	(n=80) Intervention 1: patients presenting to our ED 12 months prior to introduction of bedside lactate testing who

Study	Singer2014 [23]
	also had an initial lactate level of at least 2 mmol/litre, starting from 1 calendar year prior to study initiation.(n=80) Intervention 2: standard laboratory lactate measurement.
Funding	Abbott Point of care testing (Princeton, New Jersey)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: POINT-OF-CARE TEST versus LABORATORY TEST Protocol outcome 1: Mortality - Actual outcome: mortality; group 1: 5/80, group 2: 15/80; risk of bias: very high; indirectness of outcome: no indirectness Protocol outcome 2: Hospital length of stay - Actual outcome: length of stay – days; group 1: median (range) 7 (3-13). Group 2: 8 (4-13); risk of bias: very high; indirectness of outcome: no indirectness.	
Protocol outcomes not reported by the study	Neurological compromise; cardiovascular compromise; quality of life; hyperchloraemic acidosis; hypoglycaemia

G.1.2.3 Assessing dehydration and hypovolaemia

None

G.2 IV fluid therapy for fluid resuscitation

G.2.1 Fluid type for fluid resuscitation

Table 2: Akech 2006[1]

Study	Akech 2006[1]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=88)
Countries and setting	Conducted in Kenya; setting: 4 cases in each arm could not be included with baseline characteristics, as they presented to unit as emergency cases
Line of therapy	First line
Duration of study	Intervention + follow up: 1–2 hours intervention (depending on whether they had persistent shock); follow-up at 1 hour and 8 hours.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Children greater than 3 months of age presenting with either of the major clinical features of severe malaria—impaired consciousness (defined as either prostration or coma—Blantyre coma score [BCS] ≤2) or respiratory distress—were screened for inclusion in the study. Children were eligible for inclusion in the trial if they had all of the following criteria: plasmodium falciparum parasitaemia, a clinical feature of severe malaria, metabolic acidosis with a base deficit greater than 8 mmol/litre, a haemoglobin level of greater than 5 g/dl, and a clinical feature of shock.
Exclusion criteria	Children with any of the following were excluded: pulmonary oedema (defined clinically as bilateral fine crepitations in association with sustained hypoxia [oxygen saturation <95% measured by a pulse oximeter]), oedematous malnutrition, papilloedema, or refusal of consent. Ethical approval was granted to enrol children with clinical features of severe malaria who were critically ill on presentation (mainly decompensated shock), to start volume resuscitation without waiting for laboratory results.
Age, gender and ethnicity	Age – median (range): presented separately for individual groups. Gender (M:F): not reported. Ethnicity: not reported. Study conducted within urban Kenyan population.
Interventions	(n=44) Intervention 1: colloids - gelatins (Haemaccel, Gelofusine). Gelofusine (Braun, Sheffield, United Kingdom).

Study	Akech 2006[1]
	Children received an initial bolus of 20 ml/kg except for those children who presented with decompensated shock (systolic blood pressure [BP] <80 mmHg), who received 40 ml/kg over 1 hour. A further bolus of 20 ml/kg was given if features of shock persisted after 1 hour. Concurrent medication/care: patients with a base deficit of 8–15 mmol/litre received 20 ml/kg and those with a base deficit of more than 15 mmol/litre received 40 ml/kg. (n=44) Intervention 2: albumin – 3%–5% albumin. 4.5% Human Albumin Solution (Bio Products Laboratory, Elstree, UK). Children received an initial bolus of 20 ml/kg except for those children who presented with decompensated shock (systolic BP <80 mmHg), who received 40 ml/kg over 1 hour. A further bolus of 20 ml/kg was given if features of shock persisted after 1 hour. Concurrent medication/care: patients with a base deficit of 8–15 mmol/litre received 20 ml/kg and those with a base deficit of more than 15 mmol/litre received 40 ml/kg.
Funding	Academic or government funding (The Wellcome Trust)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: GELATINS (HAEMACCEL, GELOFUSINE) versus 3%–5% ALBUMIN Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: in-hospital mortality at until discharge; group 1: 7/44, group 2: 1/44; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: neurological compromise at throughout study - Actual outcome for aged 28 days to 16 years: neurological sequelae in survivors at until discharge; group 1: 1/37, group 2: 3/43; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 3: Belba 2009[4]

Study	Belba 2009[4]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=110)

Study	Belba 2009[4]
Countries and setting	Conducted in Albania; setting: intensive care unit (ICU) with approximately 200 patients
Duration of study	Intervention + follow up: 2 years
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years Trauma
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with severe burns hospitalised in ICU within 24 hours. The burn % for adults is more than 20% BSA and 15% for children.
Exclusion criteria	Admitted to unit after 24 hours and other pathologies other than burn
Age, gender and ethnicity	Age – mean (SD): 12.8 (19.35). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	Serious indirectness: the study population includes adults
Interventions	(n=55) Intervention 1: hypertonic sodium chloride – 1.8%–7.5% sodium chloride. Hypertonic lactate sodium chloride – sodium (250 mEq/l) and lactate (120 mEq/l). Duration 3 days. Concurrent medication/care: first hour of fluid-hour therapy is equal to 0.5 ml/kg/%BSA for the first 24 hours. Hourly urine levels were evaluated and volume adjusted accordingly. (n=55) Intervention 2: balanced salt solution – Ringer's lactate solution – sodium (130 mEq/l) and lactate (28 mEq/l). Duration 3 days. Concurrent medication/care: patients were resuscitated according to the Parkland formula for adults and Shriner for children.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1.8%–7.5% SODIUM CHLORIDE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days - Actual outcome: death at mean (SD) days 11 (3); group 1: 5/55, group 2: 5/55; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 4: Bowser-Wallace 1986[6]

Study	Bowser-Wallace 1986[6]
Study type	Systematic review
Number of studies (number of participants)	(n=38)
Countries and setting	Conducted in USA; setting: children's hospital ICUs
Duration of study	Intervention + follow up: 6 years
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years Traumatic injury
Subgroup analysis within study	Not applicable
Inclusion criteria	Children and young adults ranging in age from 5 months to 21 years with greater than 30% surface area burns
Exclusion criteria	Patients were excluded if they had suffered from smoke inhalation. Those who received more than one half of the calculated 24 hour fluid requirement before admission to the study were automatically randomised to the Ringer's lactate solution arm.
Age, gender and ethnicity	Age – mean (SD): 9.2 (7.2). Gender (M:F): not reported. Ethnicity: not reported.
Extra comments	Informed consent was gained from each patient/and or their legal guardian
Indirectness of population	Serious indirectness: some indirectness as some of the participants are adults
Interventions	(n=19) Intervention 1: hypertonic sodium chloride – 1.8%–7.5% sodium chloride. First 24 hours – 2 ml hypertonic lactate/kg body weight x % body surface area burn (not to exceed 50%); second 24 hours – 0.6 ml hypertonic lactate /kg body weight x body surface burn area plus replacement of insensible fluid loss. Duration 72 hours. Concurrent medication/care: not reported. (n=19) Intervention 2: balanced salt solution – Ringer's lactate solution. First 24 hours – 2ml Ringer's lactate solution/kg body weight x % body surface area burn (not to exceed 50%); second 24 hours – 0.5ml Plasmanate /kg body weight x body surface burn area plus calculated insensible fluid loss and desired urine output as 5% dextrose in water. Duration up to 72 hours. Concurrent medication/care: not reported.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1.8%–7.5% SODIUM CHLORIDE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days	

Study	Bowser-Wallace 1986[6]
- Actual outcome: death at 15 days ; group 1: 0/19, group 2: 3/19; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 5: Caldwell 1979 [7]

Study	Caldwell 1979 [7]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	(n=27)
Countries and setting	Conducted in USA; setting: children's hospital burns centre
Line of therapy	First line
Duration of study	Intervention + follow up: 3 years
Method of assessment of guideline condition	Partially adequate method of assessment/diagnosis
Stratum	Aged 28 days and under Traumatic Injury
Subgroup analysis within study	Not applicable
Inclusion criteria	Children with thermal burns covering 30% or more of the body surface area
Exclusion criteria	Not reported
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age – other: mean 8.45. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	None
Indirectness of population	Serious indirectness
Interventions	((n=17) Intervention 1: hypertonic sodium chloride – 1.8%–7.5% sodium chloride. First 24 hours–2 ml hypertonic lactate/kg body weight x % body surface area burn (not to exceed 50%) and no free water; second 24 hours – 0.6 ml hypertonic lactate /kg body weight x body surface burn area plus replacement of insensible fluid loss with Haldane's solution. Solution contained 250 mEq/litre sodium and 150 mEq/litre lactate. Duration 48 hours. Concurrent medication/care: not reported.

Study	Caldwell 1979 [7]
	(n=20) Intervention 2: balanced salt solution – Ringer's lactate solution. First 24 hours – 2 ml Ringer's lactate solution/kg body weight x % body surface area burn (not to exceed 50%); second 24 hours – 1 ml Ringer's lactate solution/kg body weight x body surface burn area plus calculated insensible fluid loss and desired urine output as 5% dextrose in water. Duration 48 hours. Concurrent medication/care: not reported.
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1.8%–7.5% SODIUM CHLORIDE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: survival at up to 15 days; group 1: 2/17, group 2: 1/20; risk of bias: very high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 6: Dung 1999[10]

Study	Dung 1999[10]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Vietnam; setting: paediatric ICU, Ho Chi Minh City
Line of therapy	First line
Duration of study	Intervention time: 2 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: history of fever; haemorrhagic phenomena, including a positive tourniquet test; clinical criteria and lab investigations to establish clinical diagnosis of grade-III dengue haemorrhagic fever. Dengue shock syndrome defined as dengue haemorrhagic fever with either low pulse pressure (<20 mmHg) or unrecordable BP, along with clinical signs of circulatory insufficiency such as cold extremities and thready pulse.
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Dengue shock syndrome; had not received IV fluid therapy during their current illness

Study	Dung 1999[10]
Exclusion criteria	Not reported
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age – mean (SD): 8.2 years (2.5 years). Gender (M:F): 33/17. Ethnicity: not reported.
Further population details	None
Indirectness of population	Serious indirectness: dengue shock syndrome rather than sepsis
Interventions	(n=12) Intervention 1: isotonic sodium chloride – 0.9% sodium chloride. Sodium 154 mmol/litre, chloride 154 mmol/litre in a plasma isotonic solution, at 20 ml/kg for first hour, 10 ml/kg for the subsequent hour. Duration 2 hours. Concurrent medication/care: none. (n=13) Intervention 2: balanced crystalloid solutions (solutions with a sodium concentration greater than 130 mmol/litre) – Ringer's lactate solution. Sodium 147 mmol/litre; potassium 4 mmol/litre; calcium 2.3 mmol/litre; chloride 156 mmol/litre. 20 ml/kg for the first hour; 10 ml/kg for the subsequent hour. Duration 2 hours. Concurrent medication/care: none. (n=12) Intervention 3: dextran – Dextran 60, Dextran 70. Dextran 70 (60 g of dextran [molecular mass, 70,000 Da] in 0.9% w/v sodium chloride,) at 20 ml/kg for the first hour; 10 ml/kg for the subsequent hour. Duration 2 hours. Concurrent medication/care: none. (n=13) Intervention 4: gelatin – succinylated gelatin – Gelofusine. Gelafundin, a polymerisate of degraded succinylated gelatin with a mean molecular mass of 35,000 Da (30 g of succinylated gelatin containing sodium [142 mmol/litre], calcium [1.4 mmol/litre], and chloride [80 mmol/litre]). 20 ml/kg for the first hour; 10 ml/kg for the subsequent hour. Duration 2 hours. Concurrent medication/care: none.
Funding	Equipment/drugs provided by industry (B. Braun)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus 0.9% SODIUM CHLORIDE

Protocol outcome 1: mortality at 28 days
- Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/13, group 2: 0/12; risk of bias: low; indirectness of outcome: serious indirectness

Protocol outcome 2: cardiovascular compromise at throughout study

Study	Dung 1999[10]
- Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 11.7 beats/minute (SD 12.21); n=13, group 2: mean 12.3 beats/minute (SD 7.83); n=12; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEXTRAN 60, DEXTRAN 70 versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/12, group 2: 0/12; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 20.4 beats/minute (SD 16.59); n=12, group 2: mean 12.3 beats/minute (SD 7.83); n=12; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEXTRAN 60, DEXTRAN 70 versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/12, group 2: 0/13; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 20.4 beats/minute (SD 16.59); n=12, group 2: mean 11.7 beats/minute (SD 12.21); n=13; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DEXTRAN 60, DEXTRAN 70 versus SUCCINYLATED GELATIN – GELOFUSINE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/12, group 2: 0/13; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 20.4 beats/minute (SD 16.59); n=12, group 2: mean 11.6 beats/minute (SD 18.46); n=13; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SUCCINYLATED GELATIN – GELOFUSINE versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/13, group 2: 0/12; risk of bias: low; indirectness of outcome: serious indirectness	

Study	Dung 1999[10]
Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 11.6 beats/minute (SD 18.46); n=13, group 2: mean 12.3 beats/minute (SD 7.83); n=12; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SUCCINYLATED GELATIN – GELOFUSINE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 2 hours; group 1: 0/13, group 2: 0/13; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: decrease in pulse rate (beats/minute) at 2 hours; group 1: mean 11.6 beats/minute (SD 18.46); n=13, group 2: mean 11.7 beats/minute (SD 12.21); n=13; risk of bias: low; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 7: Han 2009[11]

Study	Han 2009[11]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=33)
Countries and setting	Korean, hospital and medical centre
Line of therapy	First line
Duration of study	Not clear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: symptoms of severe dehydration and metabolic acidosis
Stratum	Aged 28 days and under
Subgroup analysis within study	Not applicable
Inclusion criteria	Infants who developed moderate-to-severe dehydration with metabolic acidosis due to acute watery diarrhoea within the first month of life; initial pH below 7.25 or initial base excess below -15
Exclusion criteria	Neonates without metabolic acidosis

Study	Han 2009[11]
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age – mean (SD): 9.9 (4.1) albumin group; 10.6 (2.6) 0.9% sodium chloride group. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	None
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: albumin – 4–5% albumin. 5% albumin (10 ml kg-1). Duration 3 hours. Concurrent medication/care: standard treatment protocol: sodium bicarbonate supplements (0.3xweight (kg) xBEx1/2), maintenance fluid (5% dextrose/sodium chloride 20 mEql-1 at a rate 4 ml kg-1h-1) and potassium level was <3.0 mEql-1). If there was sustained metabolic acidosis at 3 hours additional infusion of sodium bicarbonate was carried out. Further details: 1. Different administration rate: not applicable/not stated/unclear. (n=18) Intervention 2: Isotonic sodium chloride – 0.9% sodium chloride. 10 ml kg-1. Duration 3 hours. Concurrent medication/care: standard treatment protocol: sodium bicarbonate supplements (0.3xweight (kg) xBEx1/2), maintenance fluid (5% dextrose/sodium chloride 20 mEql-1 at a rate 4 ml kg-1h-1) and potassium level was <3.0 mEql-1). If there was sustained metabolic acidosis at 3 hours additional infusion of sodium bicarbonate was carried out. Further details: 1. Different administration rate: not applicable/not stated/unclear.
Funding	Academic or government funding (Korea University grant and Hin Moe Research Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 4–5% ALBUMIN versus 0.9% SODIUM CHLORIDE Protocol outcome 1: Length of hospital stay - Actual outcome for aged 28 days and under: length of hospital stay; group 1: mean 8.13 days (SD 3.23); n=15, group 2: mean 9.36 days (SD 4.16); n=18; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise at throughout study; cardiovascular compromise at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 8: Maitland 2005[16]

Study	Maitland 2005[16]

Study	Maitland 2005[16]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=159)
Countries and setting	Conducted in Kenya; setting: paediatric high-dependency unit at the Kenya Medical Research Institute
Line of therapy	First line
Duration of study	Intervention + follow up: 8 hours + 48 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: clinical diagnosis which was then confirmed by laboratory results
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Stratified then randomised: patients with moderate and severe metabolic acidosis
Inclusion criteria	Presenting with all of the following: a clinical feature of severe malaria (that is, prostration, coma, or respiratory distress), plasmodium falciparum parasitemia, metabolic acidosis with a base deficit of >8 mmol/litre, and a haemoglobin concentration of >50 g/litre
Exclusion criteria	Presenting with any of the following characteristics: pulmonary oedema, oedematous malnutrition, papilledema, parental refusal of consent
Recruitment/selection of patients	All who met inclusion criteria were randomised to treatments. If the clinical diagnosis was not subsequently confirmed the patients were withdrawn.
Age, gender and ethnicity	Age – median (interquartile range [IQR]): 2.8 years (1.8-3.5). Gender (M:F): not reported. Ethnicity: African.
Further population details	1. Different conditions: not applicable/not stated/unclear (severe acidosis and moderate acidosis)
Extra comments	Severe malaria
Indirectness of population	No indirectness
Interventions	(n=56) Intervention 1: colloid – 4–5% albumin. 20 ml/kg if the base deficit at presentation was 8–15 mmol/litre (that is, moderate acidosis) or 40 ml/kg if the base deficit was >15 mmol/litre (that is, severe acidosis). One bolus infused over the first hour. Additional boluses were prescribed after the first hour for children who fulfilled the criteria for rescue therapy. Duration 1 hour. Concurrent medication/care: none. Further details: 1. Type of crystalloid: not applicable/not stated/unclear. (n=61) Intervention 2: isotonic crystalloid solutions – 0.9% sodium chloride. 20 ml/kg if the base deficit at presentation was 8–15 mmol/litre (that is, moderate acidosis), or 40 ml/kg if the base deficit was >15 mmol/litre (that is, severe acidosis). Duration 1 hour. Concurrent medication/care: none. Further details: 1. Type of crystalloid: sodium chloride (0.9%).

Study	Maitland 2005[16]
Funding	Other (Wellcome Trust career development fellowship)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 4–5% ALBUMIN versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 8 hours; group 1: 2/56, group 2: 11/61; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: neurological compromise at throughout study - Actual outcome for aged 28 days to 16 years: neurological deterioration at 8 hours; group 1: 1/56, group 2: 9/61; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for aged 28 days to 16 years: neurological sequelae at 8 hours; group 1: 6/54, group 2: 3/50; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 3: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: pulmonary oedema at 8 hours; group 1: 0/56, group 2: 2/61; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 9: Maitland 2005[15]

Study	Maitland 2005[15]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=61)
Countries and setting	Conducted in Kenya
Line of therapy	First line
Duration of study	Intervention time: 8 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Not applicable

Study	Maitland 2005[15]
Inclusion criteria	Children >2 months of age with symptomatic SMA (severe anaemia – haemoglobin <5 g/dl) in the presence of respiratory distress (manifesting as deep breathing and/or indrawing), acidosis – base excess <-8, and asexual P. falciparum parasitaemia; informed consent from all parents or guardians.
Exclusion criteria	Any of the following: evidence of pulmonary oedema, oedematous kwashiorkor, papilloedema, severe anaemia secondary to another obvious cause (such as trauma or surgery) or refusal of consent.
Age, gender and ethnicity	Age – other: median 1.6 (SD 1.2) years. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	None
Extra comments	Patients with clinical features of SMA, who were critically ill on presentation, were enrolled in the study and treatment was commenced without waiting for laboratory results. These patients were withdrawn from the study after randomisation if the diagnosis was not subsequently confirmed.
Indirectness of population	No indirectness
Interventions	(n=23) Intervention 1: colloid – 4–5% albumin. 20 ml/kg over first hour, while awaiting blood. Duration 1 hour. Concurrent medication/care: blood transfusion given. Further details: 1. Type of crystalloid: not applicable/not stated/unclear. Comments: this was pre-transfusion management and they were measured at 8 hours which is after the transfusion was given. (n=20) Intervention 2: isotonic crystalloid solutions – 0.9% sodium chloride. 20 ml/kg over the first hour, while awaiting blood. Duration 1 hour. Concurrent medication/care: blood transfusion. Further details: 1. Type of crystalloid: sodium chloride (0.9%). Comments: blood transfusion was given before 8 hours.
Funding	Other (Wellcome Trust grant)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 4–5% ALBUMIN versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 8 hours; group 1: 4/23, group 2: 3/20; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 10: Maitland 2011[14]

Study	Maitland 2011[14]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=2126)
Countries and setting	Conducted in Kenya, multiple countries, Tanzania, Uganda; setting: general paediatric wards
Line of therapy	First line
Duration of study	Follow up (post intervention): 24 weeks
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	Stratum A: children without severe hypertension; Stratum B: children with severe hypertension (systolic BP of <50 mm Hg in children younger than 12 months of age, <60 mm Hg in children 1 to 5 years of age, and <70 mm Hg in children older than 5 years of age).
Exclusion criteria	Not reported
Recruitment/selection of patients	Consecutive patients
Age, gender and ethnicity	Age – median (IQR): albumin: 23 (14-37); sodium chloride: 23 (13-37). Gender (M:F): 53:47. Ethnicity: not reported.
Further population details	None
Extra comments	Severe febrile illness and impaired fusion
Indirectness of population	No indirectness
Interventions	(n=1063) Intervention 1: colloid – 4–5% albumin. 2.5–4 ml/kg/hour. Duration 1 hour. Concurrent medication/care: antibiotics, antimalarial, antipyretic, anticonvulsant drugs; treatment for hypoglycaemia (if the blood glucose was <2.5 mmol per litre [45 mg per decilitre]); blood transfusion (20 ml of whole blood per kg over 4 hours if haemoglobin level was less than 5 g per decilitre). Further details: 1. Type of crystalloid: not applicable/not stated/unclear. Comments: none. (n=1063) Intervention 2: isotonic crystalloid solutions – 0.9% sodium chloride. 2.5–4 ml/kg/hour. Duration 1 hour. Concurrent medication/care: antibiotics, antimalarial, antipyretic, anticonvulsant drugs; treatment for hypoglycaemia (if the blood glucose was <2.5 mmol per litre [45mg per decilitre]); blood transfusion (20 ml of whole blood per kg over 4 hours if haemoglobin level was less than 5 g per decilitre). Further details: 1. Type of crystalloid: sodium chloride (0.9%).

Study	Maitland 2011[14]
	Comments: none
Funding	Academic or government funding (Medical Research Council)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 4–5% ALBUMIN versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at 28 days; group 1: 137/1063, group 2: 135/1063; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: neurological compromise at throughout study - Actual outcome for aged 28 days to 16 years: neurological sequelae at 28 days; group 1: 22/990, group 2: 19/996; risk of bias: unclear; indirectness of outcome: no indirectness Protocol outcome 3: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: pulmonary oedema at 28 days; group 1: 14/1050, group 2: 6/1047; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 11: Ngo 2001[19]

Study	Ngo 2001[19]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=222)
Countries and setting	Conducted in Vietnam; setting: ICU of paediatric hospital
Line of therapy	First line
Duration of study	Intervention time: 1 hour
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: dengue haemorrhagic fever grade III or IV
Stratum	Sepsis
Subgroup analysis within study	Not applicable

Study	Ngo 2001[19]
Inclusion criteria	Children aged 1 to 15 years presenting at the hospital with clinically diagnosed dengue haemorrhagic fever grade III or IV
Exclusion criteria	Those who had received any IV fluid therapy
Recruitment/selection of patients	First 3 children each day at the clinic who met the inclusion criteria
Age, gender and ethnicity	Age – mean (SD): 7.7 (3.1). Gender (M:F): 94:128. Ethnicity: not reported.
Further population details	None
Indirectness of population	Serious indirectness: dengue shock syndrome rather than sepsis
Interventions	(n=55) Intervention 1: balanced crystalloid solutions (solutions with a sodium concentration greater than 130 mmol/litre) – Ringer's lactate solution. 20 ml/kg for the first hour. Duration 1 hour. Concurrent medication/care: not applicable. (n=56) Intervention 2: gelatin – succinylated gelatin – Gelofusine. Dose/quantity, brand name, extra details. Duration 1 hour. Concurrent medication/care: 20ml/kg for the first hour. (n=55) Intervention 3: dextran – Dextran 60, Dextran 70. 20 ml/kg for the first hour. Duration 1 hour. Concurrent medication/care: not applicable. (n=56) Intervention 4: isotonic sodium chloride – 0.9% sodium chloride. 20 ml/kg for the first hour. Duration 1 hour. Concurrent medication/care: not applicable.
Funding	Equipment/drugs provided by industry (B. Braun)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus SUCCINYLATED GELATIN – GELOFUSINE

Protocol outcome 1: mortality at 28 days
- Actual outcome: mortality at not reported; group 1: 0/55, group 2: 0/56; risk of bias: low; indirectness of outcome: serious indirectness

Protocol outcome 2: cardiovascular compromise at throughout study
- Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 13.2 beats/minute (SD 9.2); n=55, group 2: mean 18.5 beats/minute (SD 11.3); n=56; risk of bias: low; indirectness of outcome: serious indirectness

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus DEXTRAN 60, DEXTRAN 70

Study	Ngo 2001[19]
	Protocol outcome 1: mortality at 28 days - Actual outcome: mortality at not reported; group 1: 0/55, group 2: 0/55; risk of bias: high; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 13.2 beats/minute (SD 9.2); n=55, group 2: mean 14.9 beats/minute (SD 9.9); n=55; risk of bias: high; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus 0.9% SODIUM CHLORIDE Protocol outcome 1: mortality at 28 days - Actual outcome: mortality at not reported; group 1: 0/55, group 2: 0/56; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 13.2 beats/minute (SD 9.2); n=55, group 2: mean 13.5 beats/minute (SD 8.9); n=56; risk of bias: low; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: SUCCINYLATED GELATIN – GELOFUSINE versus DEXTRAN 60, DEXTRAN 70 Protocol outcome 1: mortality at 28 days - Actual outcome: mortality at not reported; group 1: 0/56, group 2: 0/55; risk of bias: high; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 18.5 beats/minute (SD 11.3); n=56, group 2: mean 11.5 beats/minute (SD 3.3); n=55; risk of bias: high; indirectness of outcome: serious indirectness RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SODIUM CHLORIDE versus SUCCINYLATED GELATIN – GELOFUSINE Protocol outcome 1: mortality at 28 days - Actual outcome: mortality at not reported; group 1: 0/56, group 2: 0/56; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 13.5 beats/minute (SD 8.9); n=56, group 2: mean 18.5 beats/minute (SD 11.3); n=56; risk of bias: low; indirectness of outcome: serious indirectness

Study	Ngo 2001[19]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SODIUM CHLORIDE versus DEXTRAN 60, DEXTRAN 70 Protocol outcome 1: mortality at 28 days - Actual outcome: mortality at not reported; group 1: 0/56, group 2: 0/55; risk of bias: high; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome: decrease in pulse (beats/minute) at 1 hour; group 1: mean 13.5 beats/minute (SD 8.9); n=56, group 2: mean 14.9 beats/minute (SD 9.9); n=55; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 12: Simma 1998[22]

Study	Simma 1998[22]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	(n=32)
Countries and setting	Conducted in Switzerland; setting: patients were recruited into the study at the pre-hospital stage. Children were treated at the scene by a paediatric anaesthetist and intensive care nurse.
Duration of study	Intervention + follow up: 40 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Aged 28 days to 16 years Traumatic Injury
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients were required to have a Glasgow Coma Scale (GCS) score of <8 and to be younger than 16 years of age. Intracranial pressure had to be measured before patients could be enrolled.
Exclusion criteria	GCS >8
Recruitment/selection of patients	Informed consent was provided by the parents of the patients
Age, gender and ethnicity	Age – mean (SD): 87(42) months. Gender (M:F): 1:1. Ethnicity: not reported.
Further population details	1. Different conditions: traumatic brain injury (children with severe traumatic brain injury admitted to the ICU)

Study	Simma 1998[22]
Indirectness of population	No indirectness
Interventions	(n=15) Intervention 1: hypertonic sodium chloride – 1.8%–7.5% sodium chloride. 3% hypertonic sodium chloride (sodium 268 mmol/litre, 598 mOsm/litre). Duration 72 hours. Concurrent medication/care: IV fluids were administered to patients with severe head injury prior to sedation. Sedation and analgesia were maintained with routine care including: morphine (10 to 30 ug'kg/hour), midazolam (0.2-0.3 mg/kg/hour) and phenobarbital (30, 20 and 10 mg/kg/day on days 1, 2 and 3). (n=17) Intervention 2: balanced salt solution – Ringer's lactate solution. Ringer's lactate solution (sodium 131 mmol/litre, 277 mOsm/litre). Duration 72 hours. Concurrent medication/care: IV fluids were administered to patients with severe head injury prior to sedation. Sedation and analgesia were maintained with routine care including: morphine (10 to 30 ug'kg/hour), midazolam (0.2-0.3 mg/kg/hour) and phenobarbital (30, 20 and 10 mg/kg/day on days 1, 2 and 3).
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 1.8%–7.5% SODIUM CHLORIDE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: Mortality at 28 days - Actual outcome for aged 28 days to 16 years: survival, number at 72 hours; group 1: 0/15, group 2: 2/17; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: Cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: respiratory complications (acute respiratory distress syndrome [ARDS]) at 72 hours; group 1: 4/15, group 2: 0/17; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for aged 28 days to 16 years: arrhythmias at 72 hours; group 1: 3/15, group 2: 0/17; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 3: Length of hospital stay at throughout study - Actual outcome for aged 28 days to 16 years: hospital stay duration at until discharge; group 1: mean 50 days (SD 41); n=15, group 2: mean 42 days (SD 31); n=17; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 13: Upadhyay 2005[24]

Study	Upadhyay 2005[24]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=60)
Countries and setting	Conducted in India; setting: paediatric emergency and ICU of a tertiary care referral and teaching hospital
Line of therapy	First line
Duration of study	Intervention + follow up: 12 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: defined as sepsis and hypotension (systolic BP <70 mmHg in infant; <70 +2 x age after 1 year of age) OR sepsis with 3 of the following 4 clinical signs of hypoperfusion: decreased pulse volume, capillary filling time </=3 sec, tachycardia (heart rate >190/minute in 1 month to 2 years, >140/minute in 2 to 8 years and >110/minute in >8 years) and urine output <1 m/kg/hour (<20 ml/hour in >20kg child)
Stratum	Aged 28 days to 16 years
Subgroup analysis within study	Not applicable
Inclusion criteria	1 month to 12 years of age; with septic shock
Exclusion criteria	Clinical evidence of organ failure at admission or underlying immunodeficiency
Recruitment/selection of patients	Admitted consecutively to paediatric emergency or ICU with a diagnosis of septic shock
Age, gender and ethnicity	Age – median (IQR): 36 months (9-72) in the 0.9% sodium chloride group and 30 months (11.5-96) in the gelatin group. Gender (M:F): 45/15. Ethnicity: not reported.
Further population details	None
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: isotonic sodium chloride – 0.9% sodium chloride. 20 ml/kg every 10–20 minutes. Duration every 10–20 minutes until BP normal, perfusion improved or central venous pressure >10 cm H20. Concurrent medication/care: not reported during the intervention. (n=29) Intervention 2: gelatin – polygeline – Haemaccel. 20 ml/kg every 10–20 minutes. Duration every 10–20 minutes until BP normal, perfusion improved or central venous pressure >10 cm H20. Concurrent medication/care: not reported during the intervention.
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: POLYGELINE – HAEMACCEL versus 0.9% SODIUM CHLORIDE	

Study	Upadhyay 2005[24]
Protocol outcome 1: mortality at 28 days - Actual outcome for aged 28 days to 16 years: mortality at: not reported; group 1: 9/31, group 2: 9/29; risk of bias: low; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise at throughout study - Actual outcome for aged 28 days to 16 years: haemodynamically stable at 6 hours at not reported; group 1: 22/30, group 2: 19/29; risk of bias: moderate; indirectness of outcome: no indirectness - Actual outcome for aged 28 days to 16 years: haemodynamically stable at 12 hours at not reported; group 1: 23/29, group 2: 21/26; risk of bias: moderate; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

Table 14: Wills 2005[25]

Study	Wills 2005[25]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=476), n=191 received hydroxyethyl starch (HES), therefore these results are not reported
Countries and setting	Conducted in Vietnam; setting: paediatric ICU at Hospital for Tropical Diseases in Ho Chi Minh City
Line of therapy	First line
Duration of study	Intervention + follow up: 72 hours
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: WHO guidelines used for diagnosis of dengue shock syndrome
Stratum	Sepsis
Subgroup analysis within study	Stratified then randomised: moderate severity shock (pulse pressure, >10 and </=20 mmHg) group 1 and severe shock (pulse pressure </=10 mmHg) group 2
Inclusion criteria	Aged 2 to 15 years presenting with clinical dengue shock syndrome, with parental or guardian consent
Exclusion criteria	Not specified
Recruitment/selection of patients	Children presenting at hospital
Age, gender and ethnicity	Age – median (range): 10 (4-14). Gender (M:F): 255:257. Ethnicity: not reported.
Further population details	1. Different conditions: dengue fever

Study	Wills 2005[25]
Extra comments	The children were stratified by pulse pressure at admission, and no children in the group with severe shock received a crystalloid because of concerns about the potential development of critical fluid overload without access to advanced respiratory support.
Indirectness of population	Serious indirectness: patients had dengue shock syndrome
Interventions	(n=128) Intervention 1: balanced crystalloid solutions (solutions with a sodium concentration greater than 130 mmol/litre) – Ringer's lactate solution. 15 ml per kilogram of body weight over a one hour period then 10 ml per kilogram over a second hour. Duration 2 hours. Concurrent medication/care: not applicable. (n=194) Intervention 3: dextran – Dextran 60, Dextran 70. 6% Dextran 70, 15 ml per kilogram of bodyweight over 1 hour, 10 ml per kilogram over second hour. Duration 2 hours. Concurrent medication/care: none.
Funding	Other (Wellcome Trust)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus DEXTRAN 60, DEXTRAN 70 Protocol outcome 1: mortality at 28 days - Actual outcome for sepsis: mortality at within 72 hours; group 1: 0/128, group 2: 0/194; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise at throughout study; cardiovascular compromise at throughout study; length of hospital stay at throughout study; hyperchloraemic acidosis at throughout study; quality of life at throughout study; hypoglycaemia at throughout study; hypernatraemia at throughout study; hyponatraemia at throughout study

G.2.2 Volume and rate of administration for fluid resuscitation

None

G.3 IV fluid therapy for routine maintenance

G.3.1 Fluid type for routine maintenance

Table 15: Balasubramanian 2012[2]

Study	Balasubramanian 2012[2]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=88)
Countries and setting	Conducted in India; setting: neonatal unit of a tertiary care hospital
Line of therapy	First line
Duration of study	22 months
Stratum	Age (48 hours to 28 days)
Inclusion criteria	Full-term neonates (‡37 weeks gestation), appropriate for gestational age – presenting with severe non-haemolytic hyperbilirubinemia (serum total bilirubin [STB] ‡ 20 mg/dl) – were eligible for inclusion. Gestational age assessment was based on accurate date of last menstrual period and was corroborated by New Ballard's Scoring System.
Exclusion criteria	Neonates were excluded if they had any clinical evidence of haemolysis (anaemia, organomegaly, positive Coomb's test), onset of jaundice within 24 hours, STB ‡ 25 mg/dl at presentation, clinical features of acute bilirubin encephalopathy, obvious clinical signs of dehydration, hypoxic ischaemic encephalopathy or major congenital malformations. They were also excluded if already receiving IV fluids for any reason and if they had already undergone BET. Approval was obtained from the Institute.
Recruitment/selection of patients	An informed written consent was obtained from 1 of the parents of eligible neonates before enrolment
Age, gender and ethnicity	Age 5.2 days. Gender (M:F): 1:1. Ethnicity: not reported.
Interventions	(n=44) Intervention 1: Isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. 0.9% saline in 5% dextrose. Duration 8 hours. Concurrent medication/care: the IV fluid supplementation was given for a period of 8 hours. The volume of IV fluid supplementation included a presumed deficit of 50 ml/kg (equivalent of mild dehydration), half of their daily maintenance requirement for an 8-hour period and a phototherapy allowance of 20 ml/kg/day for 8 hours. In addition, babies were allowed breast/formula feed ad libitum as they were taking before inclusion. (n=44) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.18% saline. 0.2% saline in 5% dextrose. Duration 8 hours. Concurrent medication/care: the IV fluid supplementation was given for a period of 8

Study	Balasubramanian 2012[2]
	hours. The volume of IV fluid supplementation included a presumed deficit of 50 ml/kg (equivalent of mild dehydration), half of their daily maintenance requirement for an 8-hour period and a phototherapy allowance of 20 ml/kg/day for 8 hours. In addition, babies were allowed breast/formula feed ad libitum as they were taking before inclusion.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.18% SALINE Protocol outcome 1: hyponatraemia - Actual outcome for age (48 hours to 28 days): <135 mmol/litre sodium at 24 hours; group 1: 3/42, group 2: 18/42; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome for age (48 hours to 28 days): <130 mmol/litre sodium at 8 hours; group 1: 0/42, group 2: 2/42; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome for age (48 hours to 28 days): >145 mmol/litre sodium at 24 hours; group 1: 14/42, group 2: 4/42; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of ICU stay; hyperchloraemic acidosis; hypoglycaemia

Table 16: Baron 2013[3]

Study	Baron 2013[3]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=66)
Countries and setting	Conducted in Argentina; setting: paediatric intensive care unit (PICU) of the Hospital General de Ninos "Pedro de Elizalde"
Line of therapy	First line
Duration of study	Intervention + follow up: 10 months
Stratum	Age (28 days to 16 years)

Study	Baron 2013[3]
Subgroup analysis within study	Not applicable
Inclusion criteria	Children aged 1 month to 18 years old with an expected PICU stay of more than 24 hours and a normal serum sodium level (135–145 mmol/litre) measured at the time of admission or after IV fluid resuscitation, and requiring >80% maintenance with IV fluids
Exclusion criteria	Previous kidney failure, liver failure with ascites and portal hypertension, adrenal insufficiency, nephritic syndrome, Kawasaki disease, sickle cell anaemia, diabetes insipidus, congenital metabolic disease, patients receiving cancer treatment
Age, gender and ethnicity	Age – median (range): 5 (3-9). Gender 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=32) Intervention 1: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. Isotonic fluid with a sodium concentration of 154 mmol/litre. Duration not specified. Concurrent medication/care: addition of potassium up to 20 mmol/litre was at the physician's decision. Glucose concentrations were set at 5% dextrose. (n=34) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.45% saline. Isotonic fluid with a sodium concentration of 77 mmol/litre. Duration not specified. Concurrent medication/care: addition of potassium up to 20 mmol/litre was at the physician's decision. Glucose concentrations were set at 5% dextrose.
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.45% SALINE

Protocol outcome 1: mortality at 28 days
- Actual outcome for age (28 days to 16 years): death at 28 days; group 1: 0/31, group 2: 3/32; risk of bias: low; indirectness of outcome: serious indirectness

Protocol outcome 2: length of stay
- Actual outcome for age (28 days to 16 years): length of stay in PICU at 28 days; group 1: mean 12 days (SD 11.5); n=31, group 2: mean 8.5 days (SD 5.5); n=32; risk of bias: low; indirectness of outcome: no indirectness

Protocol outcome 3: hyponatraemia
- Actual outcome for age (28 days to 16 years): incidence of hyponatraemia; group 1: 4/31, group 2: 5/32; risk of bias: low; indirectness of outcome: no indirectness
- Actual outcome for age (28 days to 16 years): severe hyponatraemia; group 1: 0/31, group 2: 1/32; risk of bias: low; indirectness of outcome: serious indirectness

Study	Baron 2013[3]
Protocol outcome 4: hypernatraemia - Actual outcome for age (28 days to 16 years): incidence of hypernatraemia; risk of bias: low; indirectness of outcome: no indirectness; group 1: 1/31, group 2: 2/32; risk of bias: low; indirectness of outcome: no serious indirectness	
Protocol outcomes not reported by the study	Neurological compromise; cardiovascular compromise; quality of life; hyperchloraemic acidosis; hypoglycaemia

Table 17: Bell 1993[5]

Study	Bell 1993[5]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=34)
Countries and setting	Conducted in USA
Line of therapy	First line
Duration of study	Intervention + follow up: 8 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Non-diabetic paediatric patients; 1 month to 5 years of age; consecutively scheduled for cardiac surgery requiring hypothermic (<28 degrees centigrade) cardiopulmonary bypass (CPB) over an 8-month study period
Exclusion criteria	Not reported
Age, gender and ethnicity	Age – mean (SD): 22.1 (20.6) 0.9% saline; 14.5 (10.9) Ringer's lactate solution and 5% dextrose. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	None
Extra comments	Children older than 1 year of age were fasted for solids and liquids for 8 hours prior to surgery, and children younger than 1 year of age were fasted for solids and liquids for 4 hours before surgery
Indirectness of population	No indirectness
Interventions	(n=16) Intervention 1: isotonic crystalloid – 0.9% saline. Patient fluid requirements determined the amount of crystalloid infused. Duration not reported. Concurrent medication/care: pump prime for all patients consisted of either 2 units of citrate-phosphate-dextrose-adenosine (CPDA) packed red blood cells (PRBC) (patients weighing less than 10 kg) or 1 unit of CPDA PRBC (patients weighing more than 10 kg), as well as 1 unit of fresh frozen plasma, 50 ml

Study	Bell 1993[5]
	of bicarbonate, 30 mg/kg of methylprednisolone, 2000 units of heparin, and sufficient D5LR to achieve a total volume of 1250 ml. A Cobe variable prime membrane oxygenator (Cobe, Arvada, CO) and a Cobe roller pump were used for bypass. (n=17) Intervention 2: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – Ringer's lactate solution. Patient fluid requirements determined the amount of crystalloid infused. Duration not reported. Concurrent medication/care: pump prime for all patients consisted of either 2 units of CPDA PRBC (patients weighing less than 10 kg) or 1 unit of CPDA PRBC (patients weighing more than 10 kg), as well as 1 unit of fresh frozen plasma, 50 ml of bicarbonate, 30 mg/kg of methylprednisolone, 2000 units of heparin, and sufficient D5LR to achieve a total volume of 1250 ml. A Cobe variable prime membrane oxygenator (Cobe, Arvada, CO) and a Cobe roller pump were used for bypass.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus RINGER'S LACTATE SOLUTION Protocol outcome 1: mortality at 28 days - Actual outcome for age (28 days to 16 years): mortality at not reported; group 1: 0/16, group 2: 1/17; risk of bias: high; indirectness of outcome: serious indirectness Protocol outcome 2: cardiovascular compromise - Actual outcome for age (28 days to 16 years): cardiorespiratory arrest (as a result of progressive ventricular failure) in the immediate post-operative period; group 1: 0/16, group 2: 2/17; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 3: length of stay - Actual outcome for age (28 days to 16 years): mean days in ICU at not applicable; group 1: mean 3.06 mean days (SD 1.95); n=16, group 2: mean 6.31 mean days (SD 6.55); n=17; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for age (28 days to 16 years): mean days to discharge from hospital at not applicable; group 1: mean 7.6 mean days (SD 2.1); n=16, group 2: mean 11.7 mean days (SD 2.93); n=17; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 4: hypoglycaemia - Actual outcome for age (28 days to 16 years): hypoglycaemia at 8 months; group 1: 0/16, group 2: 0/17; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Neurological compromise; quality of life; hyponatraemia; hypernatraemia; hyperchloraemic acidosis

Table 18: Choong 2011[8]

Study	Choong 2011[8]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=258)
Countries and setting	Conducted in Canada; setting: McMaster Children's Hospital (University Hospital)
Line of therapy	First line
Duration of study	20 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Inclusion criteria	Euvolaemic patients, 6 months to 16 years of age, within 6 hours after elective surgery were eligible if their anticipated in-patient period was >24 hours
Exclusion criteria	Patients with uncorrected plasma sodium level abnormalities before end of surgery, abnormal antidiuretic hormone (ADH) secretion, patients requiring volume resuscitation and/or vasoactive infusions, recent loop diuretic use, total parenteral nutrition required within 24 hours of surgery; and patients for whom either a hypotonic or isotonic PMS was considered necessary or contraindicated (for example because of risk of cerebral oedema, acute burns, or the risk of third space and/or sodium overload in patients with pre-existing congestive cardiac failure, renal failure, liver failure or cirrhosis)
Recruitment/selection of patients	Informed consent and assent was obtained before patient enrolment
Age, gender and ethnicity	Age – mean (SD): 9.2 (5.6). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=128) Intervention 1: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. 0.9% saline with 5% dextrose. Duration 48 hours. Concurrent medication/care: potassium chloride was added according to the treating physician's request. (n=130) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.45% saline. 0.45% saline with 5% dextrose. Duration 48 hours. Concurrent medication/care: potassium chloride was added according to the treating physician's request.
Funding	Hospital for Sick Children Grant XG 07-041

Study	Choong 2011[8]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.45% SALINE Protocol outcome 1: hyponatraemia - Actual outcome for age (28 days to 16 years): plasma sodium <135 mmol/litre at 48 hours; group 1: 29/128, group 2: 53/130; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome for age (28 days to 16 years): severe hyponatraemia plasma sodium <129 mmol/litre at 48 hours; group 1: 1/128, group 2: 8/130; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome for age (28 days to 16 years): severe hypernatraemia plasma sodium >146 mmol/litre at 48 hours; group 1: 4/128, group 2: 5/130; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of PICU stay; hyperchloraemic acidosis; hypoglycaemia

Table 19: Coulthard 2012[9]

Study	Coulthard 2012[9]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=82)
Countries and setting	Conducted in Australia; setting: the study was conducted at the Royal Children's Hospital (RCH), Brisbane, Australia between September 2006 and December 2008. RCH is a tertiary paediatric referral centre servicing a population of approximately 1.5 million. The PICU has eight beds and admits approximately 650 patients annually from all subspecialties except cardiac surgery, and including oncology, burns, trauma and liver transplantation.
Line of therapy	First line
Duration of study	Intervention + follow up: 27 months
Stratum	Age (28 days to 16 years)
Inclusion criteria	Children were eligible for enrolment if they were admitted to the PICU following spinal instrumentation for correction of scoliosis, craniotomy for excision of brain tumours and cranial vault remodelling
Exclusion criteria	Children were not recruited if they were undergoing lengthening only of spinal instrumentation rods, insertion or revision of ventriculoperitoneal shunts, intracerebral cyst fenestration, or were previously enrolled in the study

Study	Coulthard 2012[9]
Age, gender and ethnicity	Age – mean (SD): 11.42 (4.3-14.08). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=41) Intervention 1: isotonic crystalloid – Hartmann's solution. Hartmann's solution and 5% dextrose solution (AHB2074, Baxter, Sydney, Australia) at full paediatric fluid maintenance requirements. Duration 18 hours. Concurrent medication/care: children were consistently managed and cared for according to spinal and craniotomy clinical care pathways, which standardise all aspects of medical care (see supplemental web file). A checklist outlined parameters to guide post-operative fluid bolus administration including capillary refill time, heart rate, BP, hourly urine output and wound or drain losses. (n=41) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.45% saline. 0.45% saline and 5% dextrose solution (AHK6028, Baxter, Sydney, Australia) at two-thirds of paediatric fluid maintenance requirements. Duration 18 hours. Concurrent medication/care: children were consistently managed and cared for according to spinal and craniotomy clinical care pathways, which standardise all aspects of medical care (see supplemental web file). A checklist outlined parameters to guide post-operative fluid bolus administration including capillary refill time, heart rate, BP, hourly urine output and wound or drain losses.
Funding	Other (The Henry Blackwood Trust)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: HARTMANN'S SOLUTION versus 0.45% SALINE Protocol outcome 1: hyponatraemia - Actual outcome for age (28 days to 16 years): <135 mmol/litre sodium at 16-18 hours; group 1: 0/39, group 2: 7/40; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome for age (28 days to 16 years): <130 mmol/litre sodium at 16-18 hours; group 1: 0/39, group 2: 1/40; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome for age (28 days to 16 years): >145 mmol/litre sodium at 16-18 hours; group 1: 0/39, group 2: 0/40; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of PICU stay; hyperchloraemic acidosis; hypoglycaemia

Table 20: Kannan 2010[12]

Study	Kannan 2010[12]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=167)
Countries and setting	Conducted in India; setting: 60 bed paediatric service within a university hospital in northern India
Line of therapy	First line
Duration of study	Intervention + follow up: 18 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Inclusion criteria	Patients who were judged by the treating physician to require IV fluid maintenance fluid administration for at least the following 24 hours of their hospital stay
Exclusion criteria	Children with hyponatraemia (plasma sodium >150 mEq/L) or hypoglycaemia (blood glucose >180 mg/dl), dehydration, shock, severe malnutrition, cirrhosis of liver, congestive heart failure, acute or chronic renal failure and nephrotic syndrome. Children who were receiving drugs that alter plasma sodium levels, such as frusemide, hydrochlorthiazide, vasopressin or desmopressin and mannitol, were also excluded.
Recruitment/selection of patients	Written informed consent was obtained from the parent or guardian of all patients before enrolment
Age, gender and ethnicity	Age – mean (range): 40 (10-84). Gender (M:F): 2:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=58) Intervention 1: isotonic crystalloid solution + glucose (up to 2.5%, 2.6%–5%, 5.1%–10%) + potassium chloride (20 mmol/litre or 40 mmol/litre) – 0.9% saline. 0.9% saline in 5% dextrose at standard maintenance rate. Duration not specified. Concurrent medication/care: maintenance potassium was added to the fluid as 20 mEq/litre. (n=56) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.6%–5%, 5.1%–10%) + potassium chloride (20 mmol/litre or 40 mmol/litre) – 0.18% saline. 0.18% saline in 5% dextrose at standard maintenance rate. Duration not specified. Concurrent medication/care: maintenance potassium was added to the fluid as 20 mEq/litre.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.18% SALINE Protocol outcome 1: mortality at 28 days	

Study	Kannan 2010[12]
- Actual outcome for age (28 days to 16 years): death at 72 hours; group 1: 1/58, group 2: 0/56; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: hyponatraemia - Actual outcome for age (28 days to 16 years): plasma sodium level <130 mEq/litre at 72 hours; group 1: 1/58, group 2: 8/56; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 3: hypernatraemia - Actual outcome for age (28 days to 16 years): plasma sodium level >150 mEq/litre at 72 hours; group 1: 2/58, group 2: 2/56; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Neurological compromise; cardiovascular compromise; quality of life; length of stay; hyperchloraemic acidosis; hypoglycaemia

Table 21: Montanana 2008[17]

Study	Montanana 2008[17]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=122)
Countries and setting	Conducted in Spain; setting: PICU at Hospital Infantil La Fe in Valencia
Line of therapy	First line
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Specialist ward
Subgroup analysis within study	Not applicable
Inclusion criteria	Children requiring hospitalization when their physician prescribed IV maintenance fluid therapy
Exclusion criteria	Patients with chronic or acute kidney failure, at risk of cerebral oedema (diabetic ketoacidosis or craneopencephalic trauma), with plasma sodium levels at admission <130 mEq/litre or >150 mEq/litre and/or dehydration >5% of the patient's body weight were excluded from the study
Age, gender and ethnicity	Age – mean (range): 3.0 (1.0-9.0). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness

Study	Montanana 2008[17]
Interventions	(n=59) Intervention 1: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. Sodium concentration 140 mEq/litre and potassium concentration 15 mEq/litre (tonicity =155 mOsm/litre) delivered using Holliday-Segar formula. Duration 24 hours. Concurrent medication/care: made up in 5% dextrose. (n=63) Intervention 2: hypotonic saline – 0.45% saline. Sodium concentration 20–100 mEq/litre delivered using Holliday-Segar formula. Duration 24 hours. Concurrent medication/care: made up in 5% dextrose.
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.45% SALINE Protocol outcome 1: hyponatraemia - Actual outcome: sodium concentration 130–135 mEq/litre at 24 hours; group 1: 3/59, group 2: 13/63; risk of bias: low; indirectness of outcome: no indirectness - Actual outcome: sodium concentration <130 mEq/litre at 24 hours; group 1: 0/59, group 2: 3/63; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome: sodium concentration >145 mEq/litre at 24 hours; group 1: 1/59, group 2: 1/63; risk of bias: low; indirectness of outcome: no indirectness Protocol outcome 3: hypoglycaemia - Actual outcome: hypoglycaemia at 24 hours; group 1: 1/59, group 2: 0/63; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of stay; hyperchloraemic acidosis

Table 22: Neville 2010[18]

Study	Neville 2010[18]
Study type	RCT (randomised; parallel)
Number of studies (number of participants)	1 (n=62)
Countries and setting	Conducted in Australia; setting: Sydney Children's Hospital
Line of therapy	First line
Duration of study	Intervention + follow up: 28 months

Study	Neville 2010[18]
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Inclusion criteria	Children undergoing elective or emergency surgery aged between 6 months and 15 years were expected to be taking nothing by mouth for at least 8 hours after surgery and weighed more than 8 kg
Exclusion criteria	Significant blood loss was expected during surgery or the type of surgery was known to be associated with excess ADH secretion (cranial and thoracic) or if they had a known abnormality of ADH secretion, diabetes insipidus, pituitary or hypothalamic disease, kidney disease, acute or chronic lung disease, or were receiving drugs known to stimulate ADH secretion
Recruitment/selection of patients	Informed consent was obtained from a parent/guardian of all children
Age, gender and ethnicity	Age – mean (range): 8.75 (0.6-14.9). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. 0.9% saline in 2.5% dextrose. Duration 24 hours. Concurrent medication/care: full maintenance rates for a 24-hour period were calculated as follows: 8–10 kg body weight 100 ml/kg/24 hours; 10.1–20 kg 1000 ml + 50 x [wt (kg) -10]ml/kg/24 hours; >20 kg 1500 ml + 20 x [wt (kg) -20]ml/24 hours. (n=31) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.45% saline. 0.45% saline in 5% dextrose. Duration 24 hours. Concurrent medication/care: full maintenance rates for a 24-hour period were calculated as follows: 8–10 kg body weight 100 ml/kg/24 hours; 10.1-20 kg 1000 ml + 50 x [wt (kg) -10]ml/kg/24 hours; >20 kg 1500 ml + 20 x [wt (kg) -20]ml/24 hours.
Funding	Academic or government funding (Sydney Children's Hospital Foundation)

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.45% SALINE

Protocol outcome 1: hyponatraemia
- Actual outcome: <135 mmol/litre sodium at 24 hours; group 1: 1/31, group 2: 9/31; risk of bias: high; indirectness of outcome: no indirectness
- Actual outcome: <130 mmol/litre sodium at 24 hours; group 1: 0/31, group 2: 0/31; risk of bias: high; indirectness of outcome: no indirectness

Protocol outcome 2: hypernatraemia
- Actual outcome: >145 mmol/litre sodium at 24 hours; group 1: 1/31, group 2: 0/31; risk of bias: high; indirectness of outcome: no indirectness

Study	Neville 2010[18]
Protocol outcome 3: hypoglycaemia - Actual outcome: blood glucose <3 mmol/litre at 24 hours; group 1: 2/31, group 2: 3/31; risk of bias: low; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of stay; hyperchloraemic acidosis

Table 23: Nicolson 1992[20]

Study	Nicolson 1992[20]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=36)
Countries and setting	Conducted in USA; setting: children's hospital, Philadelphia, USA
Line of therapy	First line
Duration of study	Intervention + follow up: 3 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: not applicable
Stratum	Age (28 days to 16 years): all under 1 year of age
Subgroup analysis within study	Not applicable: no subgroups
Inclusion criteria	Non-diabetic, fasted infants under 1 year of age; scheduled for elective surgical procedures in which hypothermic CPB with circulatory arrest was planned
Exclusion criteria	Not reported
Recruitment/selection of patients	Consecutive patients; no further details
Age, gender and ethnicity	Age – mean (SD): Ringer's lactate solution group: 6.1 (4.9) months; Ringer's lactate solution with dextrose group: 5.8 (2.4) months. Gender (M:F): not reported. Ethnicity: not reported.
Further population details	None
Indirectness of population	No indirectness
Interventions	(n=19) Intervention 1: isotonic crystalloid – Ringer's lactate solution. Infused at a rate to meet the deficit fluid requirements. Duration not reported. Concurrent medication/care: not allowed milk or solid foods from 8pm the night before surgery, but were allowed glucose-containing clear liquids up to 4 hours (<6 months of age) or 6 hours (6 to 12 months of age) before induction of anaesthesia.

Study	Nicolson 1992[20]
	(n=17) Intervention 2: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – Ringer's lactate solution. Given by calibrated infusion pump calculated to deliver 7 mg/kg/minute of dextrose. Duration not reported. Concurrent medication/care: not allowed milk or solid foods from 8pm the night before surgery, but were allowed glucose-containing clear liquids up to 4 hours (<6 months of age) or 6 hours (6 to 12 months of age) before induction of anaesthesia.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus RINGER'S LACTATE SOLUTION + 5% DEXTROSE Protocol outcome 1: neurological compromise - Actual outcome for age (28 days to 16 years): neurological sequelae (gross motor seizures [tonic-clonic motor activity]); group 1: 1/19, group 2: 3/17; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; cardiovascular compromise; quality of life; length of stay; hyponatraemia; hypernatraemia; hyperchloraemic acidosis; hypoglycaemia

Table 24: Saba 2011[21]

Study	Saba 2011[21]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=37)
Countries and setting	Conducted in Canada; setting: Montreal Children's Hospital, a tertiary care paediatric hospital
Line of therapy	First line
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Inclusion criteria	Two populations of children between 3 months and 18 years of age were recruited: children with medical illnesses admitted via the emergency department (medical), and children admitted following elective surgery (surgical). Only those requiring at least 8 hours of IV fluids were eligible.
Exclusion criteria	Exclusion criteria included a baseline serum (sodium) of less than 133 or greater than 145 mmol/litre, renal disease, cardiac dysfunction, pre-existing hypertension, diuretic use, oedema, known adrenal dysfunction, and acute or severe chronic neurological illness. Children with neurological illnesses were excluded for safety reasons (high risk of non-

Study	Saba 2011[21]
	physiologic ADH secretion, and difficulty in assessing changes in neurological status).
Age, gender and ethnicity	Age – mean (range): 8.55 (1.7-16.5). Gender (M:F): 1:1. Ethnicity: not reported.
Interventions	(n=16) Intervention 1: isotonic crystalloid + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.9% saline. 0.9% saline in 5% dextrose. Duration 12 hours. Concurrent medication/care: treating physicians were informed that the study fluid was either 0.9% or 0.45% saline in 5% dextrose, and advised to prescribe it as they would normally prescribe maintenance fluids. (n=21) Intervention 2: hypotonic saline + glucose (up to 2.5%, 2.5–5%, 5–10%) – 0.45% saline. 0.45% saline in 5% dextrose. Duration 12 hours. Concurrent medication/care: treating physicians were informed that the study fluid was either 0.9% or 0.45% saline in 5% dextrose, and advised to prescribe it as they would normally prescribe maintenance fluids.
Funding	Academic or government funding (Montreal Children's Hospital Research Institute)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: 0.9% SALINE versus 0.45% SALINE Protocol outcome 1: hyponatraemia - Actual outcome for age (28 days to 16 years): <136 mmol/litre sodium at 18 hours; group 1: 1/16, group 2: 1/21; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome for age (28 days to 16 years): >145 mmol/litre sodium at 18 hours; group 1: 1/16, group 2: 0/21; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of stay; hyperchloraemic acidosis; hypoglycaemia

G.3.2 Rate of administration for routine maintenance

Table 25: Neville 2010[18]

Study	Neville 2010[18]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=124)
Countries and setting	Conducted in Australia; setting: Sydney Children's Hospital
Line of therapy	First line
Duration of study	Intervention + follow up: 28 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Subgroup analysis within study	Not applicable
Inclusion criteria	Children undergoing elective or emergency surgery aged between 6 months and 15 years were expected to be taking nothing by mouth for at least 8 hours after surgery and weighed more than 8 kg
Exclusion criteria	Significant blood loss was expected during surgery or the type of surgery was known to be associated with excess ADH secretion (cranial and thoracic) or if they had a known abnormality of ADH secretion, nephrogenic diabetes insipidus, pituitary or hypothalamic disease, kidney disease, acute or chronic lung disease, or were receiving drugs known to stimulate ADH secretion
Recruitment/selection of patients	Informed consent was obtained from a parent/guardian of all children
Age, gender and ethnicity	Age – median (range): 8.75 (0.6-14.9). Gender (M:F): 1:1. Ethnicity: not reported.
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: any rate calculation at maintenance or reduced maintenance rate – any sodium-containing IV in the range of 130–154 mmol/litre sodium. 0.9% saline in 2.5% dextrose administered at full maintenance rate during and after surgery. Duration 24 hours. Concurrent medication/care: full maintenance fluid rates for a 24-hour period were calculated as follows: 8 to 10 kg body weight 100 ml/kg/24 hours; 10.1 to 20 kg 1000 ml + 50 x[wt(kg) − 10]ml/24 hours; > 20 kg 1500 ml + 20 x[wt(kg) − 20]ml/24 hours. (n=31) Intervention 2: any other rate calculation at maintenance or reduced maintenance rate – any sodium-containing IV in the range of 130–154 mmol/litre sodium. 0.9% saline in 2.5% dextrose administered at half full maintenance rate during and after surgery. Duration 24 hours. Concurrent medication/care: full maintenance fluid rates for a 24-hour period were calculated as follows: 8 to 10 kg body weight 100 ml/kg/24 hours; 10.1 to 20 kg 1000

Study	Neville 2010[18]
	ml + 50 x[wt(kg) − 10]ml/24 hours; > 20 kg 1500 ml + 20 x[wt(kg) − 20]ml/24 hours.
Funding	Academic or government funding (Sydney Children's Hospital Foundation)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ANY SODIUM-CONTAINING IV IN THE RANGE OF 130–154 MMOL/LITRE NA versus ANY OTHER SODIUM CONTAINING IV IN THE RANGE OF 130–154 MMOL/LITRE NA Protocol outcome 1: hyponatraemia - Actual outcome: sodium <135 mmol/litre at 8 hours; group 1: 1/31, group 2: 5/31; risk of bias: high; indirectness of outcome: no indirectness - Actual outcome: sodium <135 mmol/litre at 24 hours; group 1: 4/19, group 2: 1/12; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 2: hypernatraemia - Actual outcome: sodium >145 mmol/litre at 8 hours; group 1: 0/31, group 2: 3/31; risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 3: hypoglycaemia - Actual outcome: blood glucose <3 mmol/litre at 24 hours; group 1: 2/31, group 2: 0/31; risk of bias: high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of stay; hyperchloraemic acidosis

Table 26: Yung 2009[26]

Study	Yung 2009[26]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=50)
Countries and setting	Conducted in Australia, unknown; setting: the PICU of Women's and Children's Hospital is the tertiary paediatric referral centre in South Australia
Line of therapy	First line
Duration of study	Intervention + follow up: 10 months
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Age (28 days to 16 years)
Subgroup analysis within study	Not applicable

Study	Yung 2009[26]
Inclusion criteria	Children admitted to the PICU who would normally receive IV fluid as DS at traditional maintenance rates for at least 12 hours, with normal (sodium) (135–145 mmol/litre) and no hypoglycaemia
Exclusion criteria	Neonates, and those with diabetes, renal failure or shock
Age, gender and ethnicity	Age – mean (SD): not reported. Gender (M:F): not reported. Ethnicity: not reported.
Indirectness of population	Serious indirectness: age not reported (PICU) unit only
Interventions	(n=11) Intervention 1: any rate calculation at maintenance or reduced maintenance rate – any sodium-containing IV in the range of 130–154 mmol/litre sodium. Isotonic saline administered at normal maintenance rate. Duration 12–24 hours. Concurrent medication/care: rate calculated from Holliday equation. (n=13) Intervention 2: any other rate calculation at maintenance or reduced maintenance rate – any sodium-containing IV in the range of 130–154 mmol/litre sodium. Isotonic saline administered at restricted maintenance rate. Duration 12–24 hours. Concurrent medication/care: rate calculated from Holliday equation.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: ANY SODIUM-CONTAINING IV IN THE RANGE OF 130–154 MMOL/LITRE SODIUM versus ANY OTHER SODIUM CONTAINING IV IN THE RANGE OF 130–154 MMOL/LITRE SODIUM Protocol outcome 1: hypoglycaemia - Actual outcome for age (28 days to 16 years): hypoglycaemia at 12–24 hours; group 1: 1/11, group 2: 0/13; risk of bias: very high; indirectness of outcome: no indirectness	
Protocol outcomes not reported by the study	Mortality at 28 days; neurological compromise; cardiovascular compromise; quality of life; length of stay; hyponatraemia; hypernatraemia; hyperchloraemic acidosis

G.4 IV fluid therapy for replacement and redistribution

Table 27: Majahan 2012[13]

Study	Mahajan 2012[13]

Study	Mahajan 2012[13]
Study type	RCT (patient randomised; parallel)
Number of studies (number of participants)	1 (n=22)
Countries and setting	Conducted in India; setting: paediatric emergency facilities at a tertiary care referral hospital
Line of therapy	First line
Duration of study	Not clear
Method of assessment of guideline condition	Adequate method of assessment/diagnosis: see inclusion criteria
Stratum	Overall: no strata
Subgroup analysis within study	Not applicable: no subgroup analysis
Inclusion criteria	Children aged 1 month to 18 years, with acute diarrhoea and severe dehydration; acute diarrhoea was defined as >/=3 liquid stools in previous 24 hours. Severe dehydration was defined as presence of hypotension or any of the 2 out of 4 signs: lethargic or unconscious, sunken eyeballs, drinks poorly or not able to drink, skin pinch goes back very slowly (>2 seconds) (WHO criteria); informed consent.
Exclusion criteria	Persistent diarrhoea (>14 days); clinical signs of severe malnutrition (WHO criteria), known systemic disease (cardiac, endocrine, neurologic, chronic renal failure), lethal malformations, and hypoglycaemia (dextrostix value <40 mg/dl)
Recruitment/selection of patients	Not reported
Age, gender and ethnicity	Age – mean (SD): 73 (28) months in RL group, 58 (24) in NS group. Gender (M:F): 13/9. Ethnicity: not reported.
Further population details	1. Volaemic status on presentation: not stated
Indirectness of population	Possible indirectness 55% of population had cholera
Interventions	(n=11) Intervention 1: balanced crystalloid solutions – Ringer's lactate solution. For rapid IV rehydration: doses of 100 ml/kg over 3 or 6 hours. Children <1 year received fluid correction over 6 hours, and >1 year olds over 3 hours. Children were monitored every 15–30 minutes for vital signs and reassessed at end of 100 ml/kg infusion for clinical signs of dehydration. If any child was found in severe dehydration at the end of first correction, rapid IV rehydration (100 ml/kg) was repeated. If there were no features of severe dehydration the child was treated according to standard WHO guidelines. Duration 3–6 hours. Concurrent medication/care: all children received replacement fluids for ongoing losses (watery stools or vomit) and maintenance fluids. Either reduced-osmolarity WHO oral rehydration solution or an IV solution of 0.45% sodium chloride in 5% dextrose and 2 mEq/litre potassium chloride – as replacement fluids depending upon the child's ability to drink. The volume of replacement fluids was calculated by 10 ml/kg of body weight per stool or vomit. The replacement fluids were chartered every 2 hours after assessment of ongoing losses. Children also received age-appropriate maintenance fluids throughout the study period. All children received oral zinc supplements (10–20mg/day).

Study	Mahajan 2012[13]
	(n=11) Intervention 2: Isotonic sodium chloride – 0.9% sodium chloride. For rapid IV rehydration: doses of 100 ml/kg over 3 or 6 hours. Children <1 year received fluid correction over 6 hours, and >1 year olds over 3 hours. Children were monitored every 15–30 minutes for vital signs and reassessed at end of 100 ml/kg infusion for clinical signs of dehydration. If any child was found in severe dehydration at the end of the first correction, rapid IV rehydration (100 ml/kg) was repeated. If there were no features of severe dehydration the child was treated according to standard WHO guidelines. Duration 3 to 6 hours. Concurrent medication/care: all children received replacement fluids for ongoing losses (watery stools or vomit) and maintenance fluids. Either reduced-osmolarity WHO oral rehydration solution or an IV solution of 0.45% sodium chloride in 5% dextrose and 2 mEq/litre potassium chloride – as replacement fluids depending upon the child's ability to drink. The volume of replacement fluids was calculated by 10 ml/kg of body weight per stool or vomit. The replacement fluids were chartered every 2 hours after assessment of ongoing losses. Children also received age-appropriate maintenance fluids throughout the study period. All children received oral zinc supplements (10–20 mg/day).
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: RINGER'S LACTATE SOLUTION versus 0.9% SODIUM CHLORIDE Protocol outcome 1: length of stay - Actual outcome: length of stay at study period; other: median (IQR): 38 hours (27,50) in RL group; 51 hours (36,71) in NS group (p value 0.03); risk of bias: high; indirectness of outcome: no indirectness Protocol outcome 2: mortality at 28 days - Actual outcome: mortality at study period; group 1: 0/10, group 2: 1/11; risk of bias: high; indirectness of outcome: serious indirectness	
Protocol outcomes not reported by the study	Quality of life; neurological compromise; cardiovascular compromise; other organ dysfunction; hyperchloraemic acidosis; hypoglycaemia; hypernatraemia; hyponatraemia; hospitalisation

G.5 Managing hypernatraemia and hyponatraemia developing during IV fluid administration

G.5.1 Management of hypernatraemia

None

G.5.2 Management of hyponatraemia

None

G.6 Training and education of healthcare professionals for management of IV fluid therapy

None

G.7 References

1 Akech S, Gwer S, Idro R, Fegan G, Eziefula AC, Newton CRJC et al. Volume expansion with albumin compared to gelofusine in children with severe malaria: results of a controlled trial. PLoS Clinical Trials. 2006; 1(5):e21

2 Balasubramanian K, Kumar P, Saini SS, Attri SV, Dutta S. Isotonic versus hypotonic fluid supplementation in term neonates with severe hyperbilirubinemia - a double-blind, randomized, controlled trial. Acta Paediatrica. 2012; 101(3):236-241

3 Baron FAJ, Meregalli CN, Rombola VA, Bolasell C, Pigliapoco VE, Bartoletti SE et al. Hypotonic versus isotonic intravenous maintenance fluids in critically ill pediatric patients: A randomized clinical trial. Archivos Argentinos De Pediatria. 2013; 111(4):281-287

4 Belba MK, Petrela EY, Belba GP. Comparison of hypertonic vs isotonic fluids during resuscitation of severely burned patients. American Journal of Emergency Medicine. 2009; 27(9):1091-1096

5 Bell C, Hughes CW, Oh TH, Donielson DW, O'Connor T. The effect of intravenous dextrose infusion on postbypass hyperglycemia in pediatric patients undergoing cardiac operations. Journal of Clinical Anesthesia. 1993; 5(5):381-385

6 Bowser-Wallace BH, Caldwell FTJ. A prospective analysis of hypertonic lactated saline v. Ringer's lactate-colloid for the resuscitation of severely burned children. Burns, Including Thermal Injury. 1986; 12(6):402-409

7 Caldwell FT, Bowser BH. Critical evaluation of hypertonic and hypotonic solutions to resuscitate severely burned children: a prospective study. Annals of Surgery. 1979; 189(5):546-552

8 Choong K, Arora S, Cheng J, Farrokhyar F, Reddy D, Thabane L et al. Hypotonic versus isotonic maintenance fluids after surgery for children: a randomized controlled trial. Pediatrics. 2011; 128(5):857-866

9 Coulthard MG, Long DA, Ullman AJ, Ware RS. A randomised controlled trial of Hartmann's solution versus half normal saline in postoperative paediatric spinal instrumentation and craniotomy patients. Archives of Disease in Childhood. 2012; 97(6):491-496

10 Dung NM, Day NP, Tam DT, Loan HT, Chau HT, Minh LN et al. Fluid replacement in dengue shock syndrome: a randomized, double-blind comparison of four intravenous-fluid regimens. Clinical Infectious Diseases. 1999; 29(4):787-794

11 Han JJ, Yim HE, Lee JH, Kim YK, Jang GY, Choi BM et al. Albumin versus normal saline for dehydrated term infants with metabolic acidosis due to acute diarrhea. Journal of Perinatology. 2009; 29(6):444-447

12 Kannan L, Lodha R, Vivekanandhan S, Bagga A, Kabra SK, Kabra M. Intravenous fluid regimen and hyponatraemia among children: a randomized controlled trial. Pediatric Nephrology. 2010; 25(11):2303-2309

13 Mahajan V, Sajan SS, Sharma A, Kaur J. Ringers lactate vs normal saline for children with acute diarrhea and severe dehydration- a double blind randomized controlled trial. Indian Pediatrics. 2012; 49(12):963-968

14 Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO et al. Mortality after fluid bolus in African children with severe infection. New England Journal of Medicine. 2011; 364(26):2483-2495

15 Maitland K, Pamba A, English M, Peshu N, Levin M, Marsh K et al. Pre-transfusion management of children with severe malarial anaemia: a randomised controlled trial of intravascular volume expansion. British Journal of Haematology. 2005; 128(3):393-400

16 Maitland K, Pamba A, English M, Peshu N, Marsh K, Newton C et al. Randomized trial of volume expansion with albumin or saline in children with severe malaria: preliminary evidence of albumin benefit. Clinical Infectious Diseases. 2005; 40(4):538-545

17 Montanana PA, Alapont V, Ocon AP, Lopez PO, Lopez Prats JL, Toledo Parreno JD. The use of isotonic fluid as maintenance therapy prevents iatrogenic hyponatremia in pediatrics: a randomized, controlled open study. Pediatric Critical Care Medicine. 2008; 9(6):589-597

18 Neville KA, Sandeman DJ, Rubinstein A, Henry GM, McGlynn M, Walker JL. Prevention of hyponatremia during maintenance intravenous fluid administration: a prospective randomized study of fluid type versus fluid rate. Journal of Pediatrics. 2010; 156(2):313-2

19 Ngo NT, Cao XT, Kneen R, Wills B, Nguyen VM, Nguyen TQ et al. Acute management of dengue shock syndrome: a randomized double-blind comparison of 4 intravenous fluid regimens in the first hour. Clinical Infectious Diseases. 2001; 32(2):204-213

20 Nicolson SC, Jobes DR, Zucker HA, Steven JM, Schreiner MS, Betts EK. The effect of administering or withholding dextrose in pre-bypass intravenous fluids on intraoperative blood glucose concentrations in infants undergoing hypothermic circulatory arrest. Journal of Cardiothoracic and Vascular Anesthesia. 1992; 6(3):316-318

21 Saba TG, Fairbairn J, Houghton F, Laforte D, Foster BJ. A randomized controlled trial of isotonic versus hypotonic maintenance intravenous fluids in hospitalized children. BMC Pediatrics. 2011; 11:82

22 Simma B, Burger R, Falk M, Sacher P, Fanconi S. A prospective, randomized, and controlled study of fluid management in children with severe head injury: lactated Ringer's solution versus hypertonic saline. Critical Care Medicine. 1998; 26(7):1265-1270

23 Singer AJ, Taylor M, LeBlanc D, Williams J, Thode HCJ. ED bedside point-of-care lactate in patients with suspected sepsis is associated with reduced time to iv fluids and mortality. American Journal of Emergency Medicine. 2014; 32(9):1120-1124

24 Upadhyay M, Singhi S, Murlidharan J, Kaur N, Majumdar S. Randomized evaluation of fluid resuscitation with crystalloid (saline) and colloid (polymer from degraded gelatin in saline) in pediatric septic shock. Indian Pediatrics. 2005; 42(3):223-231

25 Wills BA, Nguyen MD, Ha TL, Dong THT, Tran TNT, Le TTM et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. New England Journal of Medicine. 2005; 353(9):877-889

26 Yung M, Keeley S. Randomised controlled trial of intravenous maintenance fluids. Journal of Paediatrics and Child Health. 2009; 45(1-2):9-14