Economic Plan

This document identifies the priorities for economic analysis and the proposed methods for addressing these questions as described in section 7 of the Guidelines Manual (2012).

Guideline

Full title of guideline: **Intravenous fluid therapy in children and young people in hospital** (short: Intravenous fluid therapy in children and young people in hospital)

Process for agreement

The economic plan was prepared by the guideline health economist in consultation with the rest of the National Collaborating Centre (NCC)/Internal Clinical Guidelines (ICG) technical team and Guideline Development Group (GDG). It was discussed and agreed on 30/04/2014 by the following people[a]:

For the NCC and GDG:

NCC/ICG economist:	Ed Griffin, Elisabetta Fenu
NCC representative(s)[b]:	Gill Ritchie
GDG representative(s)[c]:	Peter Crean

For NICE (completed by NICE):

CCP lead:	Sharon Summers-Ma
Commissioning manager:	Claire Ruiz
Economic lead:	Jasdeep Hayre
Costing lead:	tbc

Proposals for any changes to the agreed priorities will be circulated by email to this group. If substantive revisions are agreed, they will require to be recorded as addenda to this document (section 0) or as an updated version of the document[d].

[a] This may be done by face-to-face meeting, teleconference, or email as convenient.

[b] This may be the project manager, a systematic reviewer or research fellow and/or the centre director or manager, as appropriate for the NCC and guideline.

[c] This may be GDG chair, clinical lead and/or other members as appropriate.

[d] In case clinical questions are changed, for example, section 0 requires updating as well as other sections if modelling priorities are affected.

Topic priorities identified in the Scope

This section contains all topics, or clinical review questions as covered by the scope. These topics usually reflect selected clinical issues. Please indicate if an area is relevant for economic consideration and if modelling is deemed appropriate to address it.

Area[e]	Relevant?[f]	Appropriate for modelling?[g]

a) Assessment, monitoring and reassessment of fluid and electrolyte status:
• Clinical assessment and reassessment, including:
  ○ hypovolemia and dehydration
  ○ measuring and recording weight and surface area
• Laboratory or point-of-contact assessment of, for example:
  ○ plasma or blood (sodium, potassium, chloride, urea, creatinine, pH, bicarbonate and glucose)
  ○ urine (sodium and potassium).
• Principles and protocols including appropriate documentation for prescribing, recording and monitoring intravenous fluid therapy in children and young people.
	Yes	**Clinical assessment and reassessment**
		There are different approaches to assess and monitor fluid and electrolyte status but they are usually complementary and one intervention does not exclude the other.
		Most of the patients would undergo a clinical assessment and this question aims at identifying clinical factors associated with hypovolemia and dehydration which should be assessed, rather than comparing alternative approaches. We do not expect any important economic implications of this aspect of the clinical assessment and for this reason this area is assigned low priority for economic analysis.
		
		However, the frequency of assessment and reassessment could have economic implications. It is suggested that measurements are not documented consistently or used appropriately in current practice. If more rigorous use of fluid balance sheets and/or weight measurement was recommended, additional costs would be incurred due to increased staff time required. Should patients gain different health benefits as a result of more frequent assessments, then cost effectiveness

e This corresponds to the "Key clinical issues that will be covered " section in the scope, or if available, clinical review questions

f Please state if this area is deemed relevant for considering opportunity costs and likely disinvestments. Areas might pose a decision problem directly or implicitly inform the choice between options. Categories should include information on relevance and if of high or low priority for health economic work (see below).

g Health economic work comprises of literature reviews, qualitative consideration of expected costs and effects and/or formal decision modelling. Decision modelling is particularly useful where it can reduce uncertainty over cost effectiveness and/or where a recommendation is likely to result in considerable changes in health and/or costs. For further details please see section 7.1 of the Guidelines Manual (2012). It may not be feasible or efficient to address every relevant decision problem by de novo work. There rationale for choosing areas for cost effectiveness modelling should be discussed in detail in Sections 0 and 0.

		will vary. However data in this area may be scant. As an alternative, a cost analysis can be conducted to compare different frequencies and elements to assess (e.g. fluid balance and weight). Frequencies to be compared will be decided by the GDG. This aspect of the question has been assigned a medium priority. **Laboratory or point-of-contact assessment** The question on laboratory vs point of care assessment could have some economic implications because the point of care tests are performed quicker and give an immediate answer while the clinician could have to wait hours before receiving the results of the laboratory test and fluid therapy cannot be guided immediately; therefore potentially patients could get better sooner with point of care tests, decreasing the total hospital length of stay; however these tests are also more expensive than lab tests and may not be as accurate as laboratory tests. A cost analysis could be performed if data on length of stay and cost of tests are available. If data on clinical outcomes such as mortality and quality of life are also found in the clinical review, a cost-consequence analysis or a cost-effectiveness analysis could be conducted. This specific question is given medium priority for economic analysis. **Principles and protocols** Appropriate documentation is important especially when patients are transferred to other hospitals. The completeness and accuracy of documentation is not relevant for economic evaluation as defining the elements of the assessment and monitoring process which need to be recorded does not have important

		economic implications, although this could have economic implications for the NHS in that additional time may be required to document clinical status It is unlikely that there will be sufficient data regarding improved outcome to conduct a meaningful economic analysis. This area has therefore been assigned a low priority and recommendations are likely to be based on qualitative data or consensus.
b) Intravenous fluid therapy for fluid resuscitation: • Types, volume and rates of fluids and electrolytes to restore fluid balance (resuscitation), including: o albumin o crystalloids o synthetic colloids o balanced crystalloids.	Yes	One economic study was found comparing albumin with standard care in patients with severe sepsis and septic shock.[1] This is a non-UK cost-effectiveness analysis (cost per life year gained) conducted alongside an RCT and will be considered based on its inclusion or exclusion from the clinical review of this guideline, and on the quality assessment. There are cost differences between types of fluids, and albumin is particularly more expensive than crystalloids. There is also a cost difference between synthetic colloids, crystalloids and balanced crystalloids. If the clinical evidence shows an increase in effectiveness with the more expensive option, these health gains would need to be assessed against the higher costs. For this reason, this question was assigned high priority for economic analysis. However, if the clinical evidence did not show any conclusive results, a cost analysis would be useful to identify the least costly type of intravenous fluid.
c) Intravenous fluid therapy for routine maintenance: Types, volume and rates of fluids and electrolytes to maintain fluid balance, including: • how to calculate fluid and electrolyte maintenance requirements • the type of fluid and/or	Yes	One USA cost consequence analysis was found comparing a fluid therapy of 80 mL/kg/day with a restricted fluid therapy of 60 ml/kg/day;[2] this was based on a RCT and will be considered based on its inclusion or exclusion from the clinical review of this guideline, and on the quality assessment. The GDG experts have advised us

electrolyte to offer, including: – 0.9% sodium chloride – 0.45% sodium chloride – balanced crystalloids – other crystalloids – 0.9% sodium chloride with additional electrolytes – 0.45% sodium chloride with additional electrolytes – 0.9% sodium chloride with glucose – 0.45% sodium chloride with glucose – balanced crystalloids with glucose.		that different types, volumes and rates of fluid for maintenance are not expected to have significant cost differences. For this reason this question was assigned a low priority for economic analysis. Unit costs of fluids will be presented to the GDG to inform their recommendations, however no important variation in unit costs is expected.
d) Intravenous fluid therapy for replacement and redistribution: Types, volume and rates of intravenous fluid and electrolytes to address abnormal deficits or excesses, or to replace abnormal losses.	Yes	No economic evaluations were found on the management of IV fluid therapy for replacement and redistribution. Fluids used for replacement and redistribution are mostly crystalloids. These are not costly and there is not much variation in terms of effectiveness between them. For this reason, this question is given low priority for economic analysis. Unit costs will be presented alongside any clinical evidence available.
e) Management of hypernatraemia and hyponatraemia that develops during intravenous fluid administration.	Yes	No economic evaluations on the management of hyper/hyponatreamia were identified. Also no clinical evidence was found on these two areas. Unit costs will be presented and they show no significant difference between types of fluids. For this reason this question is given low priority for economic analysis.
f) Skills needed for adequate training and education of healthcare professionals.	Yes	Recommendations to change in the quantity and quality (content) of training and education inevitably impact costs, as an increased amount of time and human resources will be required to plan and implement new training and education. The impact from this

		recommendation will be better covered by the cost-impact analysis undertaken by NICE. A qualitative review will be conducted on this question to identify components of training that should be provided to health care staff providing intravenous fluid therapy to children. No clinical outcomes will be available. Therefore, this area was considered a low priority for economic analysis.

Planned modelling

This section will specify modelling work prioritised by the GDG. It will provide details on how cost effectiveness will be considered for relevant, prioritised clinical areas/decision problems. Proposed modelling work should be listed in chronological order. For each decision model, please state the proposed analytical methods, relevant references and any comments and justifications on, for example, possible diversions from the reference case.

Area[h] (clinical question(s)[i])	*Outline proposed analysis*
Intravenous fluid therapy for fluid resuscitation	There is variation in the type of intravenous fluid prescribed for fluid resuscitation. There are differences in cost between types of fluids, and albumin (a non-synthetic colloid) in particular is more expensive than crystalloids. There are also an inter- and intra-class cost differences between synthetic colloids and crystalloids. If the clinical review shows no difference in efficacy between types of intravenous fluid for fluid resuscitation, reducing variation in practice by recommending optimal and cheaper types of intravenous fluid for treating fluid resuscitation may significantly reduce costs without compromising health benefits to patients; in this case a formal economic analysis will not be necessary. However, if the clinical evidence shows an increase in effectiveness with the more expensive option, these health gains would need to be assessed against the higher costs and a formal economic analysis will be conducted. **Approach to Modelling** Should the clinical review identify data suitable for modelling, the analysis will incorporate the cost of the sub-class of intravenous fluid for each strategy (i.e. normal saline, balanced crystalloids, unbalanced crystalloids, the types of synthetic and non-synthetic colloids). Administration, storage and monitoring costs are similar across all intravenous fluids used for fluid and electrolyte resuscitation. Therefore manpower costs for administering and monitoring intravenous fluid therapy will not be included. If differences in length of stay or adverse events are identified in the clinical review, they will be incorporated into the analysis as cost components (e.g. cost of length of stay and the cost of adverse events will be intervention-specific and based on the clinical review data should there be any difference between interventions). If the type of adverse event is not specified in the review, or if they are heterogeneous, the cost of adverse events/complications will be based on an extended hospital length of stay. We will endeavour to conduct a cost utility analysis if mortality and quality of life outcomes are reported in the clinical review. Otherwise we will build a cost utility analysis if methods to map outcomes data, such as specific adverse events, to quality of life values, or dis-utilities associated with adverse health consequences are available. If mortality is the only available outcome from the review, we will estimate QALY gained assuming a utility similar to the general UK population for

[h] This should be the key areas relevant for considering opportunity costs and high priority for de novo modelling, as identified in section 3.

[i] Two or more questions may be addressed by a single analysis if appropriate.

	the remaining life expectancy. Where possible, we will use relevant published utility data. Otherwise, we will seek expert GDG opinion. **Comparators:** The model will compare these intravenous fluids sub-classes: • Albumin (non-synthetic colloid) • Gelatin (synthetic colloid) • Dextran (synthetic colloid) • HES starches (synthetic colloid) • Unbalanced crystalloids • Balanced crystalloids • Normal saline **Data sources:** intravenous fluid costs will be derived from the Department of Health Commercial Medicines Unit where possible. Units of bags used are constant across fluids and population; usually no more than one 500 ml bag is used and if less than a full bag is required, the bag cannot be reused anyway. Cost of intravenous fluid related major complications will be based on a focused search on the cost of the specific complications, if data from the clinical review are available to identify specific adverse events. If not, the cost of complications will be based on the NHS Reference costs for fluid and electrolyte disorder non-elective inpatient long stay. This cost will be multiplied by the additional length of stay due to complications. **Time Horizon:** the NICE reference case states that a lifetime horizon should be used if mortality is impacted. Therefore, if the interventions are found to impact mortality, a lifetime horizon will be used. Should the clinical review only identify adverse health consequences of a short-term nature, we aim to employ a short time horizon. **Threshold and discounting:** as in the NICE reference case, we will adopt a cost effectiveness threshold of £20,000, per QALY gained. Discounting of costs and outcomes will be 3.5% in line with the reference case, however it will not be applicable if a short time horizon is employed. **Sensitivity analysis:** We will aim to conduct deterministic sensitivity analysis to test the robustness of the results of the model to variations in key parameters. Dependent on the clinical data (number of independent inputs) used in the model, we may also conduct probabilistic sensitivity analysis.

a) Assessment, monitoring and reassessment of fluid and electrolyte status: • Clinical assessment and reassessment, including: o measuring and recording weight and surface area.	**Approach to modelling** Our approach to modelling will be contingent on the data identified from the clinical and economic review. A cost analysis for each intervention could be conducted if no clinical evidence is available. The population in the analysis will be children in the hospital requiring intravenous fluid therapy except those receiving intravenous fluid therapy for resuscitation (Neonates born at term, infants, children up to their sixteenth birthday). Calculation of costs will be achieved by an estimation of resource use (staff time) multiplied by the average cost (per minute) of the resource used. We will endeavour to identify resource use estimates from the clinical review and in its absence, identify resource use estimates from GDG expertise. The estimated cost of a major intravenous fluid associated complication was based on an extended hospital length of stay **Comparators:** these will be dependent on the clinical evidence and GDG expert opinion. We will be comparing the use or non-use of weight recordings conducted at different frequencies with or without fluid chart completion at relevant frequencies. Frequencies to be compared will be identified by the GDG. **Data sources:** where possible, all inputs will be taken from published sources. Costs for resource use during hospitalisations will be taken from NHS reference costs or other UK specific sources. **Time Horizon:** if no clinical consequences are incorporated in the model, then a short time horizon will be adopted (time over which the cost of the intervention is incurred). If data on clinical consequences are available, we will extend the time horizon up to the point where health benefits differ between strategies. **Threshold and discounting**: as in the reference case, we will adopt a cost effectiveness threshold of £20,000, per QALY gained. if a short time horizon is adopted, discounting will not be required. If health outcomes are available, discounting of costs and outcomes will be 3.5% in line with the reference case. **Sensitivity analysis:** a threshold analysis could be undertaken to identify the number of fluid associated complications that would need to be prevented in order for a strategy to be cost neutral compared to the strategy with the lowest cost, and the strategy which best represents current practice (if easily identifiable by the GDG).
a) Assessment, monitoring and	A cost analysis could be performed if data on length of stay and cost of tests are available. If data on clinical outcomes such as mortality and quality of life are also found in the clinical review, a cost-consequence analysis or a cost-effectiveness analysis

reassessment of fluid and electrolyte status: • Laboratory or point-of-contact assessment of, for example: ○ plasma or blood (sodium, potassium, chloride, urea, creatinine, pH, bicarbonate and glucose) ○ urine (sodium and potassium).	could be conducted. **Approach to Modelling** Should the clinical review identify data suitable for modelling, the analysis will incorporate the cost of laboratory tests and the cost of point-of-contact tests. If other cost components are deemed to be dependent on the type of tests conducted, we will incorporate those as well. If differences in length of stay or complications are identified in the clinical review, they will be incorporated into the analysis. We will endeavour to conduct a cost utility analysis if mortality and quality of life outcomes are reported in the clinical review. If mortality is the only available outcome from the review, we will estimate QALY gained assuming a utility similar to the general UK population for the remaining life expectancy. Where possible, we will use relevant published utility data. Otherwise, we will seek expert GDG opinion. **Comparators:** • Point-of-care tests • Laboratory tests **Data sources:** we will estimate the cost of tests from national sources such as the NHS Reference Costs when possible, otherwise local data from hospitals will be sought for. **Time Horizon:** should the clinical review only identify adverse health consequences of a short-term nature, we will aim to employ a short time horizon. **Threshold and discounting:** as in the reference case, we will adopt a cost effectiveness threshold of £20,000, per QALY gained. Discounting of costs and outcomes will be 3.5% in line with the reference case, however it will not be applicable if a short time horizon is employed. **Sensitivity analysis:** we will aim to conduct deterministic sensitivity analysis to test the robustness of the results of the model to variations in key parameters. Dependent on the clinical data used in the model, we may also conduct probabilistic sensitivity analysis.

Clinical Guidelines technical support unit[10]

Please indicate if any of the analyses or areas suggested in section 3 require or would benefit from the Clinical Guidelines Technical Support Unit support or validation.

No support is required.

References

1 Guidet B, Mosqueda GJ, Priol G, Aegerter P. The COASST study: cost-effectiveness of albumin in severe sepsis and septic shock. Journal of Critical Care. 2007; 22(3):197-203

2 Stroustrup A, Trasande L, Holzman IR. Randomized controlled trial of restrictive fluid management in transient tachypnea of the newborn. Journal of Pediatrics. United States 2012; 160(1):38-43

Addenda to economic plan

Please state any changes that have been made to the above agreed plan, together with date. If clinical questions have changed since the economic plan was signed off, include a new list with all clinical questions as part of the addenda, together with a comment where questions were inserted, deleted or altered and an explanation.

Scope area[11] (clinical question(s) [12])	*Proposed changes*	*Date agreed*
Intravenous fluid therapy for fluid resuscitation	Data identified in the clinical review does not allow for a network meta-analysis of mortality or adverse events in any of the four population strata specified in the clinical protocol (Age, Sepsis, Trauma, Peri-operative). As this is a requirement of a full cost-utility analysis of all comparators against one another (i.e. normal saline, balanced crystalloids, unbalanced crystalloids, the types of synthetic and non-synthetic colloids) only individual pairwise comparisons - for which evidence for a difference in treatment effect has been found and which are considered by the GDG as potentially recommendable strategies - maybe analysed for cost-utility. If clinical data on strategies which do not represent current practice are scarce, a cost-utility analysis is not feasible and not necessary as the GDG is unlikely to consider these strategies as options to be recommended. In addition we will conduct a threshold analysis of all comparators to estimate the difference in cost of individual IV fluids compared to the baseline option (cheapest strategy) and the number of additional adverse events that each fluid needs to prevent compared to the cheapest	

[10] The clinical guidelines technical support unit provides academic support to guideline developers at any point in guideline development: conduct, or support the NCC/ICG team in the development of, advanced evidence synthesis, support complex economic analyses, conduct validation of or amendments to, existing evidence syntheses used in guideline models and address concerns from stakeholder (via consultation). Please contact the senior technical adviser for further details.

[11] This should be the key areas relevant for considering opportunity costs and high priority for de novo modelling, as identified in section 3.

[12] Two or more questions may be addressed by a single analysis if appropriate.

	strategy to justify this difference. Although a threshold analysis of this nature requires the qualitative judgement of the GDG about relative treatment effects, it also provides additional context for decision making in the light of cost-utility analysis limited to selected pairwise comparisons.	
Intravenous fluid therapy for fluid resuscitation	A threshold analysis of all comparators is no longer needed as no convincing evidence of effectiveness was found to support the use of synthetic or non-synthetic colloids (the more expensive options) over isotonic crystalloids for routine use. Based on this, the GDG considered it unlikely that the more expensive IV fluids would be cost effective. Hence, there was no need to conduct a threshold analysis to assess the number of adverse events that would need to be averted to render these options cost neutral.	6/1/2015
Assessment, monitoring and reassessment of fluid and electrolyte status: • Laboratory or point-of-contact assessment of, for example: ○ plasma or blood (sodium, potassium, chloride, urea, creatinine, pH, bicarbonate and glucose) ○ urine (sodium and potassium).	Only one RCT was included in the clinical review relating to this topic. The study showed mortality benefit for using POC testing in an emergency department setting. It was originally proposed that "If mortality is the only available outcome from the review, we will estimate QALY gained assuming a utility similar to the general UK population for the remaining life expectancy." However, this RCT was conducted in adults and is applicable only to the emergency setting; for which the GDG has already made a consensus recommendation on the use of POC tests. The quality of the evidence was assessed to be very low. Additionally, there is considerable uncertainty about the cost of POC testing which varies according to the caseload of the hospital; as the initial high cost of the equipment could drive the results. Due to this uncertainty in the clinical effectiveness evidence and the cost of intervention, and the population for whom we have clinical data (adult patients in the emergency setting), it was not possible for *de-novo* economic modelling to be undertaken.	6/1/2015