Appendix 1: **Search Strategy for the Identification of studies:**

The following is the strategy used to search MEDLINE (Ovid):
#1 fluid therapy* in mjme
#2 infusions-intravenous* in mjme
#3 fluid management or fluid therapy of intravenous fluid* of intravenous infusion* or fluid volume* or (hypotonic* near solution*) or (isotonic* near solution*) or (glucose near solution*)
#4 (#3 in ti) or (#3 in ab)
#5 #1 or #2 or #4
#6 explode "Hyponatremia"/ all SUBHEADINGS
#7 explode "Sodium"/ all SUBHEADINGS
#8 explode "Hypernatremia"/ all SUBHEADINGS
#9 explode "Seizures"/all SUBHEADINGS
#10 explode "Brain edema"/all SUBHEADINGS
#11 hyponatremia* or hypernatremia* or sodium* or seizures* or brain edema*
#12 (#11 in ti) or (#11 in ab)
#13 # 6 or #7 or #8 or #9 or #10 or #12
#14 UK Cochrane Centre Optimally Sensitive MEDLINE Search Strategy for Identifying Randomized Controlled Trials (RCTs) - OVID Version
#15 #5 and #13 and #14
#16 limit #15 to human and child

The following is the strategy used to search EMBASE:
#1#1 exp Fluid Therapy/#2 exp Intravenous Drug Administration/
#3 (fluid adj management) or (fluid adj therapy) or (intravenous adj fluid$) or (intravenous adj infusion$) or (hypotonic adj solution$) or (isotonic adj solution$) or (glucose adj solution$)
#4 exp SODIUM/
#5 exp HYPONATREMIA/
#6 exp HYPERNATREMIA/
#7 exp SEIZURES/
#8 exp BRAIN EDEMA/
#9 (sodium$ or hyponatremia$ or hypernatremia$ or seizures or brain edema).ti,ab
#10 #1 or #2 or #3
#11 #4 or #5 or #6 or #7 or #8 or #9
#12 #10 an #11
#13 (random$ or (double adj blind$) or (single adj blind$)
#14 #12 and #13
#15 limit #14 to human and child

The following strategy was used to search the Cochrane Database:

1. hyponatremia
2. hypernatremia
3. seizures
4. cerebral edema
5. sodium
6. 1 or 2 or 3 or 4 or 5
7. intravenous fluids: me (explode mesh term)

Appendix 2:
Criteria for Quality Assessment of Studies: Controlled Trials

- Allocation concealment: i.e. investigators and participants did not know what the next allocation would be when the participant was entering the study. Did the authors take adequate measures to conceal allocation to study groups from those responsible for assessing the patients for entry into the trial (e.g. central randomization, sequentially numbered, opaque sealed envelopes, etc)
- Was the method of randomization adequate: i.e. each participant has a 50:50 chance of getting into either group (e.g. flipping unbiased coin, , computer generated random sequence, randomization tables), as opposed to quasi randomization: (days of the week), or an intentional method (investigator decides which group)
- Care Taker/patient blinded to the allocation group/intervention?
- Outcome measures clearly defined? -Were the criteria for all outcomes assessed described/defined?
- Outcomes assessment: were the investigators assessing the outcomes blind to the treatment group?
- Follow-up: was there ≥ 10% of patients lost to follow-up for assessment of outcomes?
- ITT = Intention to treat analysis stated.

Appendix 3: Newcastle-Ottawa Assessment Scale for Observational Studies

http://www.lri.ca/programs/ceu/oxford.htm

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ✵
   b) yes, eg record linkage or based on self reports
   c) no description

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases ✵
   b) potential for selection biases or not stated

3) Selection of Controls
   a) community controls ✵
   b) hospital controls
   c) no description

4) Definition of Controls
   a) no history of disease (endpoint) ✵
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview where blind to case/control status ✵
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

2) Same method of ascertainment for cases and controls
   a) yes ✵
   b) no

3) Non-Response rate
   a) same rate for both groups ✵
   b) non respondents described
   c) rate different and no designation

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ✵
   b) somewhat representative of the average _____ in the community ✵
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✵
   b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome
   a) independent blind assessment ✵
   b) record linkage ✵
   c) self report
   d) no description

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✵
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✵
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ✵
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement