# Protocol for a systematic review of the reliability and validity of capillary refill time in children

NB: this is a companion review to a systematic review of the diagnostic value of capillary refill time in children

## Change log

* Table 1 – showing examples of included secondary variables
* Clarification of definition of “premature” and proportion of subjects with cardiorespiratory disease before exclusion
* Clarification of inclusion if at least 20 non-excluded subjects (non-premature, under 18, and without cardiorespiratory disease) are separately reported
* Clarification of procedure for numerical calculations during/after data extraction
* Clarification of manual capillary refill time measurement required for inclusion – after identifying a study reporting automated capillary refill time, it was agreed that this was not directly comparable to manual CRT, nor was the technique currently applicable in clinical practice
* Updated search date (1 June 2013) added.
* Updated search date (24 June 2014) added.

## Background

Capillary refill time (CRT) is used in primary and emergency care as part of the initial assessment of unwell children. It is included in a variety of national and international guidelines such as WHO guidelines for children with severe infection or malnutrition, and UK NICE guidelines for children with feverish illness, meningococcal disease, or gastroenteritis.[1-4]

*Need for systematic review*

There appears to be considerable heterogeneity in the clinical literature (research, guideline, and textbooks) regarding the optimum method for measurement of CRT, and what threshold should be used to determine the upper bound of normality in children. In addition, there is little guidance for clinicians on the effect of potential confounding factors such as age, ambient temperature, and fever on the measured CRT in children.

*Research question(s)*

* What is the normal range of CRT in children?
* How does CRT compare to reference standard measures of circulatory physiology and perfusion?
* How reliable are CRT measurements – intra-observer, inter-observer, and repeated measures?
* What factors affect the normal value, reliability, and validity of CRT measurements? (e.g. site, method of measurement, temperature) How should CRT be measured to optimise validity and reliability?

## Search strategy

*Database search*

A search strategy was developed in conjunction with an information specialist (N Roberts). Three bibliographic databases (Medline, Embase, and Cinahl) were searched using the strategy in Table 1. This strategy was deliberately broad, due to the wide range of questions being considered as part of the review. As such a broad strategy was expected to identify a large number of results, it was decided to limit results to the English language to enable screening to be carried out in a timely manner.

|  |  |
| --- | --- |
| **Medline/Embase (via Ovid SP interface)** | **Cinahl** |
| 1. (capillary adj3 refill\*).mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, ps, rs, nm, an, ui]  2. limit 1 to english language | capillary n3 refill\*  Limiters - English Language |

Table 1: Search strategy

*Search date*

The initial search date was 28 July 2011. Updated searches were performed on 1 June 2013 and 24 June 2014.

*Additional searching*

Additional papers were identified from the reference lists of relevant papers and consultation with experts.

## Selection criteria

*Inclusion criteria*

General criteria:

* reports measurement of capillary refill time (by any manual method) on a minimum of 20 subjects under the age of 18 years
  + if a study includes a larger age range, separate reporting of results for subjects under the age of 18 years is required for inclusion
  + separate reporting of at least 20 subjects who were not born premature neonates and/or did not have pre-existing cardiorespiratory disease is also sufficient for inclusion

Additional inclusion criteria for assessments other than normal range of CRT:

* measurement and reporting of the relationship between capillary refill time and a secondary variable
* secondary variables are required to be either an objective measurement, assessed using a validated scale, or clearly defined clinical outcomes (see Table 2)

|  |  |  |
| --- | --- | --- |
| ***Reference standard measures of physiology*** | ***Reliability*** | ***Factors affecting normal values, reliability, and validity*** |
| *Arterial blood flow* | *Interobserver* | *Site* |
| *ScvO2* | *Intraobserver* | *Temperature (ambient, skin, core, including fever)* |
| *CI* | *Order effect of repeated measures* | *Duration of pressure* |
| *CVP* |  | *Birthweight* |
| *SVI* |  | *Age* |
| *SVRI* |  | *Heart rate* |
| *Core-peripheral temperature gap* |  |  |
| *Blood pressure (systolic, diastolic, mean)* |  |  |

Table 2: Outcomes included for various aspects of the systematic review

*Exclusion criteria*

General criteria:

* subjects over the age of 18
* neonates born prematurely (<35 weeks gestation)
* more than 50% of the subjects had significant pre-existing cardiorespiratory disease such as cardiac malformations

Additional exclusion criteria for assessment of normal range of CRT:

* afebrile
* free of any illnesses likely to cause changes to the capillary refill time
  + e.g. trauma, infection, respiratory, cardiac, and gastro-intestinal disease
  + subjects measured in a healthcare setting may be included only if they are well-characterised and judged likely to be free of such illnesses (e.g. those scheduled for elective surgery, or attending routine immunisation clinics).

Additional exclusion criteria for assessments other than normal range of CRT:

* results of multivariate analyses

*Selection of studies*

* Initial screening – single author screens for possible CRT content
* Secondary screening – two authors screen full papers against inclusion criteria, with disagreements resolved by consensus, any uncertain papers to be retained
* Final selection – full papers assessed against inclusion criteria by three authors (two of whom are clinicians), with adjudication by an independent clinician author

At both secondary screening and final selection stages, papers are identified as included or not within each of the four sub-areas that make up the review (normal ranges, reference standards, reliability, confounding factors). Papers may be included in one or more sub-area.

## Quality assessment

Quality assessment criteria (Table 3) have been developed based on the QUADAS-2 guidelines.[5] As no comparator is required for assessment of normal ranges of CRT in healthy children, some of the criteria (marked with an asterisk) are not applicable to some studies.

|  |  |
| --- | --- |
| Patient selection | Bias: suitable sampling method used |
| Bias: appropriate exclusion criteria |
| Applicability: appropriate inclusion criteria |
| Index test (CRT) | Bias: blinded to result of comparator \* |
| Bias: time measured OR pre-specified threshold used |
| Applicability: site and time measurement method defined |
| Comparator \* | Bias: blinded to index test result \* |
| Bias: independent of result of index test \* |
| Applicability: objective measurement \* |
| Timing and flow | Bias: contemporaneous measurement of index test and comparator \* |
| Bias: all children had index test performed |
| Bias: all children had comparator assessed \* |

Table 3: Quality assessment criteria

Assessment is carried out by two authors (the same two authors to assess all papers), with disagreements resolved by consensus. Each criterion will be marked as “yes”, “no” or “unclear”. In the case of “Applicability: site and time measurement method defined”, “yes” denotes that both are defined, with “unclear” used if only one (site or time measurement method) is defined.

## Data extraction

The data extraction procedure was designed and piloted using a small number of studies. Data is extracted onto a Microsoft Excel spreadsheet, and double-checked for accuracy by a second author. Any disagreements should be resolved by consensus.

During data extraction, no additional calculations (e.g. completing 2x2 tables) should be carried out. Missing data should be left blank.

Where additional calculations are required prior to data analysis, this should be automated if possible (e.g. using a statistical program such as R). If this is not possible, calculations should be double-checked by a second author, and sanity-checking (e.g. checking of row and column sums in 2x2 tables) should be employed where possible.

## Data analysis

Where appropriate, meta-analysis of results will be carried out using forest plots and a random-effect model.

If meta-analysis of the results is not appropriate, narrative description of the results will be employed. Tabulation of results may be used to clarify the narrative description.

## References

1 World Health Organization. Management of the child with a serious infection or severe malnutrition : guidelines for care at the first-referral level in developing countries. Geneva: Department of Child and Adolescent Health and Development UNICEF; 2000.

2 National Institute for Health and Care Excellence. Diarrhoea and vomiting caused by gastroenteritis: diagnosis, assessment and management in children younger than 5 years. CG84. London: National Institute for Health and Care Excellence; 2009.

3 National Institute for Health and Care Excellence. Bacterial meningitis and meningococcal septicaemia. CG102. London: National Institute for Health and Care Excellence; 2010.

4 National Institute for Health and Care Excellence. Feverish illness in children. CG160. London: National Institute for Health and Care Excellence; 2013.

5 Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011; 155(8): 529–36.