Consent in pediatric critical care RCTs: A systematic review

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Background

Randomized controlled trials (RCTs) are difficult to conduct in critically ill children. The process of obtaining informed consent contributes to these difficulties.

The consent rate in a trial is a critical factor in determining its feasibility. The effect of trial features on consent rates has not been well characterized.

Alternative approaches to written parental consent have been used to increase the feasibility of trials, particularly in emergency settings where immediate intervention is required, or where parents are unavailable or emotionally unable to consider participation.

Reporting the characteristics of those children who do not participate is required to asses the representativeness of the children enrolled.

Objectives

To describe pediatric critical care RCTs with respect to:

1. The consent models, timing and methods used
2. Completeness of reporting of the consent process
3. Consent rates

Methods

Searching: We searched the Evidence in Pediatric Intensive Care Database[1] (epicc.mcmaster.ca) from inception to July 4, 2013. This database is part of a scoping review that searches MEDLINE, EMBASE, LILACS and CENTRAL for pediatric critical care RCTs using comprehensive search strategies.

Inclusion criteria: RCTs and quasi-randomized trials published in English that administered any intervention to children in a pediatric critical care unit.

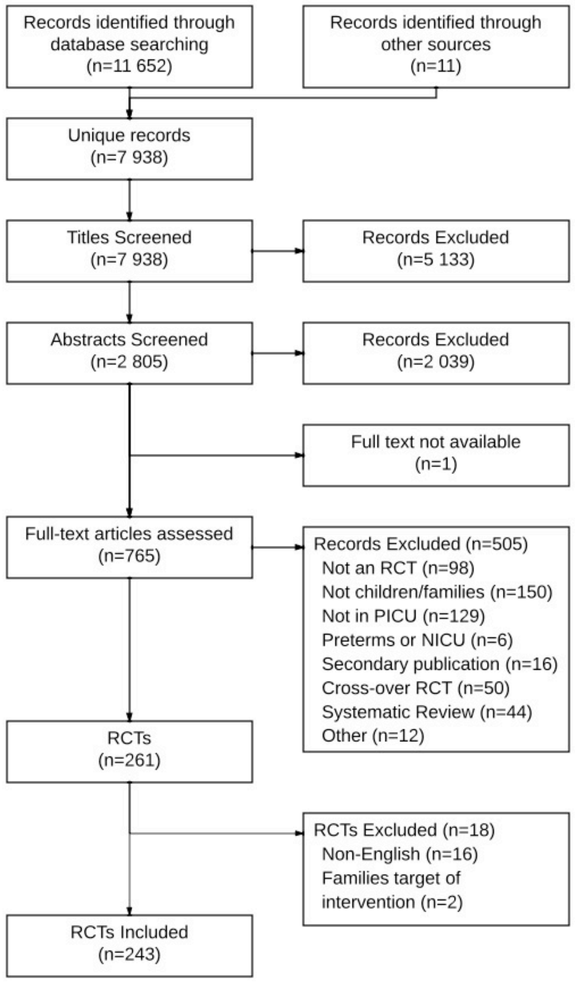
Exclusion Criteria: Trials enrolling exclusively newborns and cross-over trials .

Data extraction: Pairs of reviewers screened studies for eligibility and abstracted data independently. Discrepancies were resolved by consensus

Included trials

We included 243 RCTs. Trials were published between 1986 and 2013 and were conducted in 32 different countries. 225 (92.6%) of the RCTs reported any information on consent.

Review Flow Diagram



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Results

Mode of consent: 120 (49%) of the RCTs reported that written consent was obtained and 2 (1%) reported that consent was obtained verbally.

Assent: 13 (5%) of the RCTs reported that they sought assent from the child.

Timing of consent: 20 (8%) reported consent was obtained prior to PICU admission. The children in these trials were enrolled pre-operatively and admitted to the PICU post-operatively.

Alternative approaches to consent: 7 (3%) of trials reported the use of any approach other than written consent from the child or their parent or guardian.

Consent Models Used in 243 Pediatric Critical Care RCTs

Consent Model	Number of RCTs (%)
Parents/Guardians	210 (86%)
Deferred	2 (1%)
Waived	2 (1%)
Self	13 (6%)
Other*	1 (0.4%)
Not Reported	18 (7%)

* "relatives"

Alternative Approaches to Consent Reported in 243 Pediatric Critical Care RCTs

Author (Year)	Consent Model	Country	Intervention	Comments
Klein (1989)[2]	Deferred	USA	Protective isolation or usual care	Parents provided written consent within 24 hours of enrollment. Consent rate 99%.
Hutchison (2008)[3]	Deferred	Canada, UK and France	Hypothermia for traumatic brain injury	Deferred consent if parents not available within 8 h. Frequency of use not reported.
Beatriz (2004)[4]	Waived	Brazil	Two doses of epinephrine in cardiac arrest	Consent obtained for continued data collection and follow-up after discharge
Scoble (2001)[5]	Waived	Australia	Two methods of endotracheal suctioning	Waived because both suctioning techniques were routinely used
Yildizdas (2008)[6]	Consent in 1 group	Turkey	Terlipression in septic shock	Consent sought for children randomized to terlipression only
Schultz (2001)[7]	Verbal consent	USA	Two methods of weaning ventilation	Verbal consent obtained from parents or guardians
Chi (2013)[8]	Verbal consent	Vietnam	Milrinone for brainstem encephalitis	Written or verbal informed consent was obtained from parents or representatives

Consent Rate: 73 (30%) of the RCTs reported a consent rate.

The median (interquartile range) consent rate was 90% (71%,97%) and varied from 23% to 100%. 11 (5%) of the trials reported a consent rate of 100%.

Using linear regression none of the following were independently associated with increased consent rate: year of publication, commercial funding, prophylactic or pharmaceutical interventions, and pre-PICU consent.

Representativeness: 4 (2%) of trials reported some characteristics of those who did not consent.

References: (1) Duffett M, *et al*. Randomized controlled trials in pediatric critical care: a scoping review. Critical Care 2013;17(5):R256. (2) Klein BS, *et al*. Reduction of nosocomial infection during pediatric intensive care by protective isolation. *N Engl J Med* 1989;320:1714–21. (3) Hutchison JS, *et al*. Hypothermia therapy after traumatic brain injury in children. *N Engl J Med* 2008;358:2447–56. (4) Perondi MBM, *et al*. A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. N Engl J Med 2004;350:1722–30. (5) Scoble MK, *et al*. Effect of reusing suction catheters on the occurrence of pneumonia in children. Heart Lung 2001;30:225–33. (6) Yildizdas D, *et al*. Terlipressin as a rescue therapy for catecholamine-resistant septic shock in children. Intensive Care Med 2008;34:511-7. (7) Schultz TR, *et al*. Weaning children from mechanical ventilation: a prospective randomized trial of protocol-directed versus physician-directed weaning. Respiratory care 2001;46:772. (8) Chi C-Y, *et al*. Milrinone Therapy for Enterovirus 71-Induced Pulmonary Edema and/or Neurogenic Shock in Children: A Randomized Controlled Trial. Critical Care Medicine 2013 Jun 16.

Conclusions

The majority of the pediatric critical care RCTs reported the use of parent/guardian consent. Alternative approaches such as deferred and waived consent were used in a small proportion of studies.

There are important opportunities to improve the quality and transparency of reporting; very few trials reported the information necessary to determine the representativeness of those that consented to participate.