Background

Randomized controlled trials (RCTs) in pediatric critical care are challenging to conduct for numerous reasons. Pilot trials can be used to evaluate the feasibility of, and inform the design and conduct of, larger RCTs.

Objectives

To systematically identify pilot RCTs in pediatric critical care and describe:
1. Key elements of their methods and reporting
2. Their impact, measured by citations and the number leading to larger trials

Methods

Searching: To identify pilot trials we searched the Evidence in Pediatric Intensive Care Database (epic.mcmaster.ca) from inception to April 16, 2013. This is a database of published pediatric critical care RCTs found by searching MEDLINE, EMBASE, LILACS and CENTRAL. To identify publications that cited these pilot trials we used Web of Science®. To identify published and ongoing trials informed by these pilot RCTs we searched the EPIECC database and the World Health Organization’s Clinical Trials Registry Platform (www.who.int/ictrp).

Inclusion criteria: Published trials that were explicitly described as pilot, feasibility, proof-of-concept, phase 2, vanguard or preliminary RCTs.

Data extraction and analysis: Pairs of reviewers screened studies for eligibility and abstracted data independently. Discrepancies were resolved by consensus. We used the Mann-Whitney U test and Fisher’s Exact test to compare resolved by consensus. We used the Mann-Whitney U test and Fisher’s Exact test to compare.

Results

Pilot trials comprised 27 (11%) of a total of 248 pediatric critical care RCTs.

The earliest pilot trial was published in 1997 and 13 (48%) since 2009.

Methods and reporting of pilot trials

Publication: Trials were published in 17 different journals. Pediatric Critical Care Medicine published the highest number, 9 (33%), of these pilot trials. 4 (15%) were registered.

Type of primary outcome: 18 trials (67%) reported the primary outcome. Of these:
• 2 (7%) used feasibility
• 9 (33%) used intermediate outcomes (e.g. laboratory or physiological measurements, severity of illness scores or measures of the process of care)
• 7 (26%) focused on clinical outcomes

1 trial reported criteria for considering the pilot trial a success.

Sample sizes: 8 trials (30%) reported how their sample size was determined.
• 4 (15%) were calculated to detect a specified difference in participant outcomes
• 3 (11%) used a fixed time period for enrollment
• 1 (4%) used 10% of the calculated size for the expected larger trial

Authors’ Conclusions: 12 (46%) publications made explicit conclusions or recommendations about the design or feasibility of future larger trials; 1 trial concluded that a larger trial was not appropriate because of safety concerns. 8 (31%) publications made clinical recommendations based on the results of the pilot trial.

Impact of pilot trials

Citations: 18 (78%) of the 23 publications indexed in Web of Science® were cited at least once. These were cited a median (IQR) number of 9.5 (2.5-27) times in total and 2.3 (0.7-4.8) times per year since publication. 3 trials were cited by at least 1 pediatric critical care RCT, none by the same researchers.

Informing future trials: We found no published trials based on these pilot RCTs. We found 5 subsequently registered trials based on these pilot trials: 4 recruiting and 1 stopped early.

Conclusions

Published pilot trials in pediatric critical care are smaller than other RCTs; they are not different with respect to other key features. There are important opportunities to improve the conduct and reporting of pilot RCTs.

These RCTs are explicitly labeled as pilot trials yet they often focus on clinical outcomes. They commonly report explicit feasibility outcomes, criteria for success or rationale for the sample size. We may have underestimated the use of pilot trials as some RCTs intended by the investigators as pilot trials may not have been explicitly labeled as such.

Pilot trials in pediatric critical care do not often lead to larger trials. Understanding and addressing the reasons for this is an important next step for the pediatric critical care research community.