Published in final edited form as:

Pediatr Crit Care Med. 2020 January ; 21(1): 92–93. doi:10.1097/PCC.0000000000002099.

THAPCA – Call me on my cell phone?

Ericka L. Fink, MD, MS¹, Karen Choong, MB, BCh, MSc, FRCPC²

¹Department of Critical Care Medicine, UPMC Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine Pittsburgh, PA, USA

²Department of Pediatrics and Critical Care, McMaster University, Hamilton, Ontario, Canada

Keywords

Outcomes; children; critical illness; methods; research trials

Conducting clinical trials in critically ill children is extremely challenging. The ethical, logistical and methodological challenges encountered may impact not only the execution of the trial, but the quality of the research(1). The Therapeutic Hypothermia after Pediatric Cardiac Arrest (THAPCA) trials evaluated the efficacy of neuroprotection using hypothermia compared to normothermia in children following in- and out-of-hospital cardiac arrest (2, 3). While the In-Hospital trial was terminated for futility, the success of THAPCA was not only in its ability to execute a time sensitive, complex intervention, but the remarkable ability of the research team to complete the long-term follow-up on almost all of the survivors. With more children surviving critical illness, the use of patient reported outcomes assessed in the post-hospital discharge are increasingly important and relevant(4). However, conducting prospective long-term outcomes research and executing patient-reported outcome measures is extremely challenging. While compliance with out-patient follow-up appointments is higher in the context of a research protocol than it is in the clinical setting (5), the long-term follow-up rates achieved in similarly sized prospective cohort studies in both adult and pediatric critical care range from 55% to 83% at best(6-8). Follow-up rates do not appear to be higher in studies in specific patient populations(9). The THAPCA team should therefore be congratulated in achieving 95% follow-up at 12 months of their 251 surviving participants from the in- and out-of-hospital cardiac arrest cohorts(10). Their follow-up rate for executing the neurobehavioral outcome measure by telephone was superior to that of their in-person neurological and neuropsychological testing follow-up. Why was the telephone follow-up high and is it appropriate to conduct follow-up by telephone as opposed to in-person? They found, as did others, that those patients in whom follow-up was difficult were in patients and families with complex needs and high burden. Travel and cost, time off work required for in-person visits can be overcome through

Corresponding Author: Ericka L. Fink, MD, MS, Associate Professor, Division of Pediatric Critical Care Medicine, Children's Hospital of Pittsburgh of UPMC, 4401 Penn Avenue, Faculty Pavilion, 2nd floor, Pittsburgh, PA 15224, (office) 412-692-5164 (fax) 412-692-6076, finkel@ccm.upmc.edu.

Copyright form disclosure: Dr. Fink's institution received funding from the National Institutes of Health (NIH), and she received support for article research from the NIH. Dr. Choong's institution received funding from AHS AFP Innovation grant, and she received funding from McMaster University.

telephone follow-up, and it has been shown to be cost effective(11). Prior researchers budgeted for home visits to overcome this challenge, but future studies can take advantage of this model, which appears to be effective in optimizing follow-up, and ultimately cost-saving.

What lessons can we learn from their methodology? In Gildea et al., the THAPCA team shares with us the various a priori and adaptive strategies that they implemented to optimize their primary outcome measure of survival and neurobehavioral outcome. They administered the Vineland Adaptive Behavioral Scale (VABS)-II through telephone interviews 3 and 12 months post-arrest. Challenges THAPCA faced included: 1) telephone communication as the sole approach, 2) an outcome measure that can take up to one hour to complete, 3) one-year outcome time point, which allows for a realistic recovery period but increases the risk of losing contact with families, 4) resources and cost of strategies employed (not fully discussed), and 5) study team trial fatigue. THAPCA's strategies to overcome these challenges thoughtfully targeted two levels, the Investigator and the Participant (patient and family caregivers). Some key Investigator strategies included: 1) mandatory monthly investigator and coordinator phone meetings to maintain engagement and trial momentum with discussion of enrollment data, lessons learned, and peer coaching, 2) annual centralized in-person training sessions, 3) celebration of successes and incentivization of follow-up completion, 4) centralized outcomes center with trained personnel, 5) a contact protocol that allowed for multiple call attempts, and 6) individual site meetings to overcome challenges. Participant strategies included: 1) multiple 'touches' between study teams and families prior to the one-year outcome mark, 2) family payments as a 'carrot' for primary outcome completion, 3) a timely call near their 1 year outcomes time point from a (familiar) local coordinator that reminded them of the appointment, confirmed contact information, and prevented the 'cold call' by an unknown person an phone number, 4) flexibility of outcomes center personnel to contact families at their convenience (day or night, 7 days per week), 5) an allowance for different caregivers to provide the pre-morbid and 1 year VABS-II responses, and 6) support for English and Spanish speaking families.

THAPCA's choice of a one-year outcome measure to evaluate a therapy that was expected to have enduring neuroprotective impact in developing children was appropriate and has been utilized successfully in neonatal trials (12-14). Further, investigators need to heed the call for consideration of patient and family centered outcomes in research trials that often stretch to the extended long term (e.g., readmissions, quality of life, school performance) (15-17). Conducting telephone interviews is a skill. Training, anticipation, sensitivity are essential tools. While the interviewer who conducted the majority of interviews was qualified with a master's in psychology, training is necessary on how to conduct interviews and communicate in a sensitive and empathetic manner with families' caregivers who now care for children with complex needs and high level of burden.

As trialists, we appreciate the THAPCA team for sharing their successful approach. We encourage more investigators to publish on their methods, beyond their result, as such papers can only improve on the success and quality of our research. An adult critical care research group has established a useful website of shared experiences, publications, and resources at <https://www.improvelto.com/>. Further, given the vast resources needed to achieve acceptable

long-term outcome rates and the evolving and personalized nature of preferences for means of contact by families, research programs need to think about more cost-effective and efficient methods to achieve similar success. Low response rates may impact validity of study results, thus setting goals or milestones, monitoring progress, and making adjustments to improve retention should be standard practices(18). As our experience with outcomes research increases, and in the context of minimizing resources and costs while maximizing retention, we should consider the appropriateness of the duration of follow-up for the specific research endpoints. For example, the THAPCA investigators found that neurobehavioral outcomes at 3 month and 12 month were strongly correlated(19).

Outcomes research is now acknowledged as essential to critical care; Core Outcomes and Measurement Sets are therefore being developed to define what outcomes are important to patients, families, and other key stakeholders (20). Hence sharing methods that can inform and improve our ability to expedite outcomes measurement is important evidence. Technological innovations that make outcomes more convenient including use of text-messaging reminders or links to online outcomes measures, social media outreach, and tracking child follow-up clinical appointments may improve retention(21). Advancements and widespread use of technology has allowed us to incorporate this not only into clinical practice but also into research. Telehealth virtual video visits have demonstrated to not only optimize patient follow-up, but enhance patient satisfaction, convenience and costs(22).

References

1. Choong K, Duffett M, Cook DJ, Randolph AG. The Impact of Clinical Trials Conducted by Research Networks in Pediatric Critical Care. *Pediatr Crit Care Med*. 2016;17(9):837–44. [PubMed: 27351267]
2. Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, et al. Therapeutic Hypothermia after In-Hospital Cardiac Arrest in Children. *N Engl J Med*. 2017;376(4):318–29. [PubMed: 28118559]
3. Moler FW, Silverstein FS, Holubkov R, Slomine BS, Christensen JR, Nadkarni VM, et al. Therapeutic hypothermia after out-of-hospital cardiac arrest in children. *N Engl J Med*. 2015;372(20):1898–908. [PubMed: 25913022]
4. Pollack MM, Holubkov R, Funai T, Clark A, Berger JT, Meert K, et al. Pediatric intensive care outcomes: development of new morbidities during pediatric critical care. *Pediatr Crit Care Med*. 2014;15(9):821–7. [PubMed: 25226501]
5. McPerson ML, Lairson DR, O'Brian Smith E, Brody BA, Jefferson LS. Noncompliance with Medical Follow-up after Pediatric Intensive Care Unit. *Pediatrics*. 2002;109(6):e94. [PubMed: 12042588]
6. Pinto NP, Rhinesmith EW, Kim TY, Ladner PH, Pollack MM. Long-Term Function After Pediatric Critical Illness: Results From the Survivor Outcomes Study. *Pediatr Crit Care Med*. 2017;18(3):e122–e30. [PubMed: 28107265]
7. Herridge MS, Chu LM, Matte A, Tomlinson G, Chan L, Thomas C, et al. The RECOVER Program: Disability Risk Groups and 1-Year Outcome after 7 or More Days of Mechanical Ventilation. *Am J Respir Crit Care Med*. 2016;194(7):831–44. [PubMed: 26974173]
8. Choong K, Fraser D, Al-Harbi S, Borham A, Cameron J, Cameron S, et al. Functional Recovery in Critically Ill Children, the “WeeCover” Multicenter Study. *Pediatr Crit Care Med*. 2018;19(2):145–54. [PubMed: 29394221]
9. Keenan HT, Runyan DK, Nocera M. Longitudinal Follow-up of Families and Young Children with Traumatic Brain Injury. *Pediatrics*. 2006;117(4):1291–7. [PubMed: 16585326]

10. Gildea MR, Moler FW, Page K, et al. Methods used to maximize follow-up: Lessons learned from the therapeutic hypothermia after pediatric cardiac arrest trials. *Pediatr Crit Care Med* 2019; IN PRESS.
11. Fischer K, Hogan V, Jager A, von Allmen D. Efficacy and utility of phone call follow-up after pediatric general surgery versus traditional clinic follow-up. *Perm J*. 2015;19(1):11–4.
12. Azzopardi D, Strohm B, Marlow N, Brocklehurst P, Deierl A, Eddama O, et al. Effects of hypothermia for perinatal asphyxia on childhood outcomes. *N Engl J Med*. 2014;371(2):140–9. [PubMed: 25006720]
13. Shankaran S, Pappas A, McDonald SA, Vohr BR, Hintz SR, Yoltan K, et al. Childhood outcomes after hypothermia for neonatal encephalopathy. *N Engl J Med*. 2012;366(22):2085–92. [PubMed: 22646631]
14. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, Donovan EF, et al. Whole-body hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Engl J Med*. 2005;353(15):1574–84. [PubMed: 16221780]
15. Manning JC, Hemingway P, Redsell SA. Survived so what? Identifying priorities for research with children and families post-paediatric intensive care unit. *Nurs Crit Care*. 2018;23(2):68–74. [PubMed: 28516470]
16. Merritt C, Menon K, Agus MSD, Choong K, McNally D, O’Hearn K, et al. Beyond Survival: Pediatric Critical Care Interventional Trial Outcome Measure Preferences of Families and Healthcare Professionals. *Pediatr Crit Care Med*. 2018;19(2):e105–e11. [PubMed: 29394234]
17. Pasek TA, Burns C, Treble-Barna A, Ortiz-Aguayo R, Kochanek PM, Houtrow AH, et al. Important Outcomes for Parents of Critically Ill Children. *Critical Care Nurse*. 2019; epub ahead of print.
18. Morton SM, Bandara DK, Robinson EM, Carr PE. In the 21st Century, what is an acceptable response rate? *Aust N Z J Public Health*. 2012;36(2):106–8. [PubMed: 22487341]
19. Silverstein FS, Slomine BS, Christensen J, Holubkov R, Page K, Dean JM, et al. Functional Outcome Trajectories After Out-of Hospital Pediatric Cardiac Arrest. *Crit Care Med*. 2016.
20. Turnbull AE, Sepulveda KA, Dinglas VD, Chessare CM, Bingham CO 3rd, Needham DM. Core Domains for Clinical Research in Acute Respiratory Failure Survivors: An International Modified Delphi Consensus Study. *Crit Care Med*. 2017;45(6):1001–10. [PubMed: 28375853]
21. Rosa C, Campbell AN, Miele GM, Brunner M, Winstanley EL. Using e-technologies in clinical trials. *Contemp Clin Trials*. 2015;45(Pt A):41–54. [PubMed: 26176884]
22. Donelan K, Barreto E, Sossong S, Michael C, Estrada JJ, Cohen AB, et al. Patient and Clinician Experiences with Telehealth for Patient Follow-up Care. *Am J Manag Care*. 2019;25(1):40–4. [PubMed: 30667610]