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Study protocol for a randomised controlled trial comparing the efficiency of two provider-endorsed manual paediatric fluid resuscitation techniques

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ABSTRACT

Introduction: Paediatric shock is a life-threatening condition with many possible causes and a global impact. Current resuscitation guidelines require rapid fluid administration as a cornerstone of paediatric shock management. However, little evidence is available to inform clinicians how to most effectively perform rapid fluid administration where this is clinically required, resulting in suboptimal knowledge translation of current resuscitation guidelines into clinical practice.

Objectives: This study aims to determine which of the two commonly used techniques for paediatric fluid resuscitation (disconnect–reconnect technique and push–pull technique) yields a higher fluid administration rate in a simulated clinical scenario. Secondary objectives include determination of catheter dislodgement rates, subjective and objective measures of provider fatiguability and descriptive information regarding any technical issues encountered with performance of each method under the study.

Methods and analysis: This study will utilise a randomised crossover trial design. Participants will include consenting healthcare providers from McMaster Children's Hospital. Each participant will administer 900 ml (60 ml/kg) of normal saline to a simulated 15 kg infant as quickly as possible on two separate occasions using the manual fluid administration techniques under the study. The primary outcome, rate of fluid administration, will be evaluated using a paired two-tailed Student t test.

Ethics and dissemination: This protocol has been approved by the Hamilton Health Sciences Research Ethics Board.

Results: These will be published in a peer-reviewed scientific journal and presented at one or more scientific conferences.

Protocol Registration: Protocol Registered on ClinicalTrials.gov NCT01774214

INTRODUCTION

Paediatric shock is a life-threatening condition with causes including sepsis, haemorrhage, dehydration and allergy.[1] Guidelines

ARTICLE SUMMARY

Article focus
- Few studies evaluate practical considerations important to the achievement of the American College of Critical Care Medicine Surviving Sepsis paediatric fluid resuscitation benchmarks.
- This article will detail the protocol for a randomised controlled trial comparing two different techniques of manual fluid resuscitation for infants in shock.

Key messages
- A randomised crossover trial design will be used to compare the efficiency of two manual fluid resuscitation techniques as performed by 16 healthcare provider subjects.
- Outcomes will be determined from data obtained by direct observation and video review by blinded independent assessors.
- Data will be used to inform paediatric fluid resuscitation practical recommendations.

Strengths and limitations of this study
- A randomised crossover trial design is the most rigorous design to address the research question.
- Findings will provide objective data upon which to base pragmatic recommendations in future resuscitation guidelines.
- Limitations include the use of a study setting involving a non-clinical model as a patient surrogate.

for the management of paediatric shock from the American Heart Association (AHA) Pediatric Advanced Life Support (PALS) and the Advanced Trauma Life Support (ATLS) recommend rapid fluid resuscitation as an essential component of treatment.[2 3] The American College of Critical Care Medicine (ACCM) Surviving Sepsis guidelines require intravascular (IV/IO) administration of up to 60 ml/kg of isotonic fluids within the first 15 min of shock recognition and state that some children may require as much as

200 ml/kg or more in the first hour of resuscitation.[4] [5] Intravascular fluid administration is a critical component of early shock management as this augments preload and improves cardiac output,[6] and has been linked with decreased morbidity and mortality.[7–10] Indeed, morbidity and mortality associated with paediatric shock has declined significantly in recent decades owing to rapid recognition and resuscitation.[11] While current guidelines stress the importance of timely fluid administration, these benchmarks are often not reached in practice.[8] [9] [12] Practical evidence-based recommendations as to how healthcare providers (HCPs) can best achieve these goals are lacking.

Manual fluid administration is commonly performed in the paediatric resuscitative setting as part of the treatment of shock.[13] Methods of manual fluid resuscitation include the 'disconnect–reconnect technique' (DRT, figure 1) and the 'push–pull technique' (PPT, figure 2). Other methods of performing rapid fluid administration include use of pressure bag support or a rapid infuser device,[12] [14–16] although the relative roles of these techniques in paediatric shock resuscitation remain unclear.[13] One previous study determined the PPT method to be equivalent to pressure bag support and superior to gravity flow in terms of fluid resuscitation speed.[17] Among commonly used manual fluid resuscitation techniques, however, it is unclear whether the DRT or PPT method is most efficient. We therefore decided to conduct a comparative trial to determine which of these manual fluid administration techniques is most efficient and should be recommended in future iterations of paediatric resuscitation guidelines.
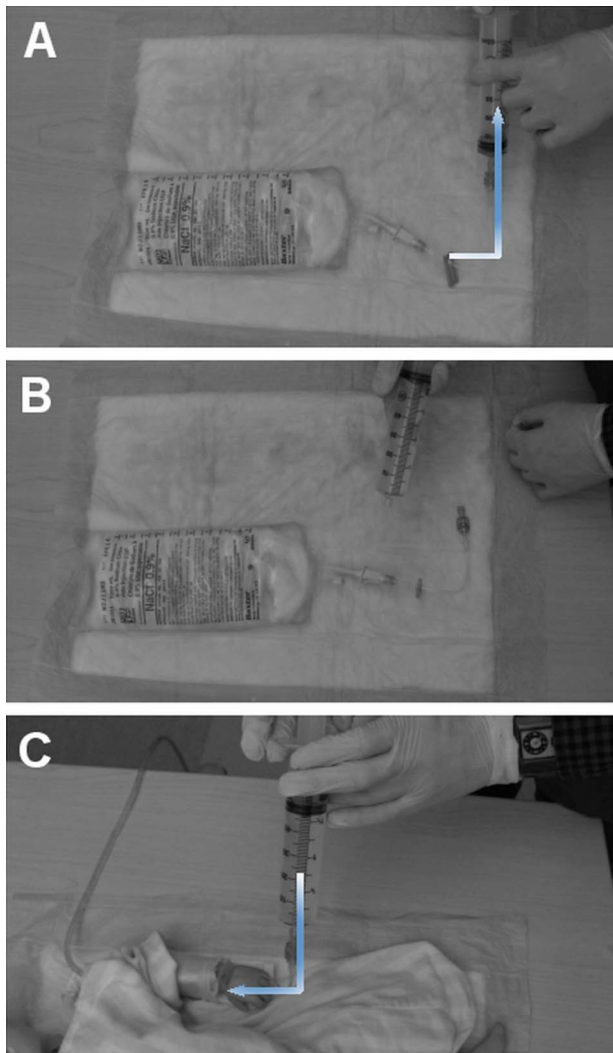

Figure 1 The 'disconnection–reconnection' technique for fluid bolus delivery involves two HCPs. (A, B) One HCP rapidly prepares fluid-filled syringes. (C) A second HCP takes and connects a fluid-filled syringe to the IV extension tubing and administers the fluid to the patient by depressing the syringe plunger. The empty syringe is then disconnected and the process repeated until the desired volume of fluid has been administered.
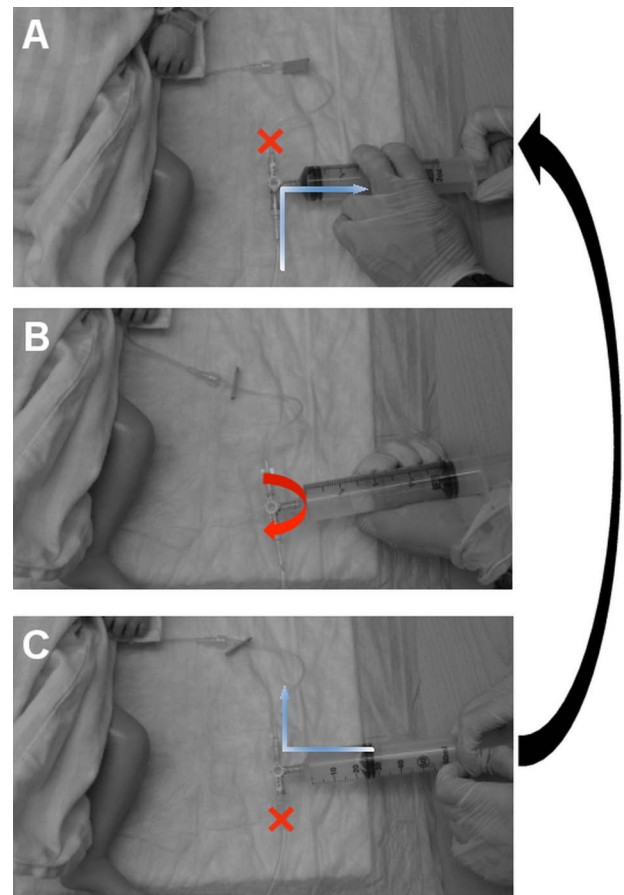

Figure 2 The 'push–pull' technique for fluid bolus delivery involves one HCP. (A) The stopcock is positioned 'off' to the patient. The HCP 'pulls' the syringe plunger to draw fluid into the syringe from the bag of saline. (B) The stopcock is then toggled 180 degrees, turning this 'on' to the patient. (C) The HCP then 'pushes' the syringe plunger to administer the fluid. The process is repeated until fluid resuscitation is complete.

AIMS AND OBJECTIVES
Aims and significance
We seek to compare the speed of fluid administration achievable with two manual fluid resuscitation techniques commonly used in infants and children. This work is significant because the relative performance of these commonly used techniques has not been previously investigated. Results will have practical application in helping to determine how HCPs can most effectively perform fluid resuscitation in children when this is emergently required. Given the high resistance and limitations in fluid flow rates related to use of small radius IV catheters in children,[18] secondary study outcomes related to provider fatigue and catheter dislodgement rates resulting from the performance of manual fluid resuscitation may also be of significance to the resuscitation community and may help to inform future guidelines.[19]

Primary objective
To determine whether a significant difference exists in the fluid administration rates of two commonly used paediatric fluid resuscitation methods: the DRT or the PPT.

Secondary objectives
1. To compare HCP participants' ability to accurately administer the requested volume (60 ml/kg or 900 ml) to the simulated patient while using the DRT versus PPT technique.
2. To compare the level of self-reported fatigue of HCPs as a result of performing the DRT versus PPT technique.
3. To compare the frequency of catheter dislodgement events that occur while fluid resuscitation is performed using the DRT versus PPT technique.
4. To compare the rates of fluid administration between the first, second and third 300 ml aliquots administered to the model for DRT and PPT, respectively.
5. To describe any technical issues that HCPs encounter while performing the DRT versus PPT technique.
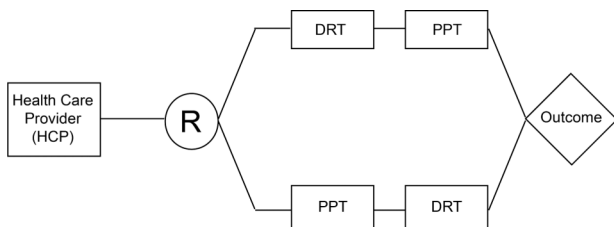

Figure 3 A randomised crossover trial design will be used. This design helps to reduce between group variability by having each participant perform each of the interventions under study. The order in which the interventions are performed is determined by randomisation, to control for any potential training or leaning effect. A washout period is included between interventions to allow for participant recovery from any resulting fatigue.

METHODS AND ANALYSIS
Design
This study will use a randomised crossover design with two study arms (see figure 3).

Setting
The study will be carried out at the McMaster Children's Hospital, an academic centre for tertiary paediatric care in Hamilton, Canada.

Recruitment and consent
Potential participants will be recruited via local study promotion by the investigators, poster advertisement and email invitation. Gift cards will be used as an incentive for participation. Written informed consent will be obtained from interested and eligible participants prior to participation (see online supplementary appendix 1).

Participant eligibility
HCPs at McMaster Children's Hospital satisfying the following inclusion and exclusion criteria will be eligible to participate in this study.

Inclusion criteria
1. HCPs working or training at McMaster Children's Hospital, which includes staff nurses, staff physicians, postgraduate medical trainees, nursing students and medical students.
2. HCPs who may be asked to perform manual fluid resuscitation as part of their clinical care activities.

Exclusion criteria
1. Inability to understand English.
2. Limited manual dexterity, specifically resulting in an inability to perform manual fluid resuscitation involving syringes.
3. Have acted in a physically strenuous capacity that may result in significant hand fatigue, in the 30 min immediately prior to performance of trial intervention (eg, resuscitative tasks such as manual fluid resuscitation or CPR). Where this is the only criteria limiting participation of a given subject, rescheduling of an alternate testing time will be permitted.

Randomisation
A third-party randomisation technique will be utilised to assign participants to one of the two study arms. This will determine the order in which the two interventions will be performed. Given the nature of the study and its small size, no stratification or blocking will be utilised.

Model and interventions
Model setup
The setup used for this study will consist of a model simulating a 15 kg child and include a peripheral IV catheter. A 22 gauge, 1.00 inch IV catheter will be affixed to the hand of the model in typical clinical fashion to simulate in vivo conditions. The distal end of the catheter will be secured in an unobstructed manner within conduit tubing leading to a graduated cylinder, in

which the accumulating fluid may be continuously visualised. The proximal end of the IV catheter will be connected to a 7-inch catheter extension set. See online supplementary appendix 2 for an illustration of the model. For the DRT setup the proximal end of the catheter extension set will be capped with a needle-less syringe lock. An excess supply of 60 ml syringes will be provided when subjects are to perform fluid administration using the DRT method, along with needle-less adaptors to facilitate the safe preparation of syringes of fluid from the provided 1-litre bag of normal saline. For the PPT setup, the proximal end of the catheter extension set will be connected to a triple stopcock, with a 60 ml syringe at the second port, and standard IV tubing leading to a 1-litre bag of normal saline at the third port. Only one syringe will be required to perform the PPT manual fluid administration method. Online supplementary appendices 3 and 4 provide schematic representations of the DRT and PPT setups, respectively, including the specific parts to be used in our trial.

Interventions

The study intervention is the method of manual fluid administration that the HCP participant will use to administer 60 ml/kg (900 ml) of normal saline to the simulated patient. As this is a randomised crossover trial, each of the two interventions will be applied to an HCP participant on two separate occasions. The interventions are

1. DRT: As DRT is a two-person technique, an assistant will be provided who will perform the role of fluid syringe preparation. It is important to note that when the DRT intervention is being performed, the HCP participant will not be permitted to switch roles with the assistant as, in our experience, this does not occur in the setting of a real resuscitation.

2. PPT: This is a single-provider technique and no assistant is required.

Trial flow

On the first day of participation, following consent, participants will undergo randomisation. HCP participants will be scheduled to attend the testing site in pairs. The reason for this is a practical one: when an HCP participant is randomised to the DRT, they will require an assistant, as this is a two-provider technique. We will engage the second study participant, who is in attendance at the same time also to be tested, to act as the assistant for the other participant in this instance. On each testing day, a coin toss will be used to determine which of the two participants in attendance is tested first.

Example:

Day 1: Participant A performs DRT (participant B assists)→30 min break→participant B performs PPT.

Day 2: Participant A performs PPT→30 min break→participant B performs DRT (participant A assists).

Standardisation procedure

Prior to undergoing formal testing, HCPs will watch a brief standardisation video that will provide an overview of the roles/techniques to be performed including a demonstration. Providers will be afforded the opportunity to practice each technique briefly prior to formal testing to account for and attempt to minimise any training or learning effect. Participants will be permitted up to 3 syringes/syringe volumes to practice the technique to be performed after which time formal testing will proceed. The practice period is limited so that this will not result in participant fatigue.

Participant testing

The research assistant will be responsible for verifying the integrity of all equipment prior to formal testing and for ensuring compliance with study procedures according to a checklist. The HCP participant will then be provided with a brief clinical vignette for the simulated clinical situation: child in decompensated shock with hypotension, fever and rash. Testing will begin on verbal prompt and cease at participants' discretion when they believe that they have administered the required 900 ml of normal saline. All testing will be video-recorded.

Washout period

A 30 min washout period is selected to mitigate for any potential fatigue which may have occurred as a result of acting as an assistant prior to undergoing formal testing as a participant. We chose 30 min based on our experience with a currently enrolling trial in which participants also perform manual fluid resuscitation using syringes. In that study, a minimum 10 min rest period is required between evaluations with an opportunity to take a longer break if desired (this has been offered to all participants and none have requested). In our upcoming study, participants will manually administer a larger volume of fluid. We therefore conservatively selected a 30 min washout period.

Data collection

Upon completion of each intervention, a research assistant will record data of interest on a data collection form (see online supplementary appendix 5). Each participant will also complete a post-trial questionnaire to collect demographic data including information regarding prior experience with paediatric fluid resuscitation (see online supplementary appendix 6). Participants will also be asked to rate how fatiguing they found the intervention to be on a seven-point Likert scale. Following testing on the second occasion, participants will be asked to complete the remaining portion of the questionnaire, related to performance of the second intervention.

All testing trials will be video-recorded as was carried out in our recently conducted study with good results. In that study, we successfully focused the video camera on the IV cannula and extension tubing site and did not capture any participant identifiers. We found actually timing participant testing with a stopwatch proved difficult in practice and that this was inaccurate. Outcome

data was therefore obtained by independent and blinded dual review of trial video recordings using a specific data extraction protocol, which showed excellent interobserver reliability (ICC=0.9997). We intend to utilise a similar procedure in the planned trial with several notable differences. In our previous trial, we carefully prepared the fluid-filled syringes for the HCP participants and colour-coded them, which allowed us to determine the fluid administration time for each 300 ml bolus by observing the administration site. In this trial, however, a different method is required as HCPs will be preparing the syringes themselves, resulting in variable volume and no colour coding of the syringes. To determine the fluid volume administered (and resulting rates), we will therefore need to film the graduated cylinder in which the fluid administered to the model will be collected.

Blinding

The investigators will be blinded to the randomisation schedule. It will not be possible to blind the investigators to the allocation of participants. The research assistants involved in extracting outcome data from the trial video recordings will not be otherwise involved in the study and will be blinded to its purpose. It will, however, be obvious from the video-recordings which technique the provider is performing. Participants will be blinded to the amount of fluid being collected in the graduated cylinder as an indicator of how much fluid has been administered to the model. We plan to shield from view of the participant the graduated cylinder in which the administered fluid is being collected.

Outcome measures
Primary outcome measure

The primary outcome is a comparison of the overall fluid infusion rates achieved by the two studied techniques. This will be calculated from total volume (determined by research assistant at completion of intervention) and time data collected by the blinded assessors from the video recordings of each trial. Two separate assessors will review each intervention video, and their results will be averaged for consistency.

Secondary outcome measures

1. The accuracy of fluid volume delivery will be determined by the research assistant based on the amount of fluid collected in the graduated cylinder, and how this differs from the requested volume of 900 ml.
2. Self-reported fatigue will be measured through use of seven-point Likert scales on the post-trial questionnaire.
3. Catheter dislodgment events will be recorded by the research assistant on the data collection form.
4. Fluid infusion rates will be determined based on a video review of the time to administer the first, second and final 300 ml 'boluses', as determined by the two independent and blinded outcome assessors.
5. Observable technical difficulties related to performance of the interventions will be noted in real time by the research assistant and during the process of video review by the blinded outcome assessors.

Statistical analysis and sample size rationale

The study is powered based on the primary outcome. Analysis and reporting of the results will follow the CONSORT guidelines for reporting randomised controlled trials[20][21] as extended to follow accepted practices for crossover trails.[22] We will adopt an intention-to-treat principle to analyse all outcomes (see table 1 below for details on study outcomes of interest and the corresponding statistical analysis plan).

Table 1	Study outcomes and analysis plan
Study outcome	**Analysis plan**
Primary outcome	
Comparison of the overall fluid infusion rates (ml/s) between the two techniques	Two-tailed paired Student t test α 0.05, β 0.20
Secondary outcomes	
Comparison of fluid volume actually administered to the model between the two techniques	Two-tailed paired Student t test
Comparison of self-reported fatigue rating of individual healthcare providers between techniques	Wilcoxon test
Comparison of the proportion of trials where a catheter dislodgement event occurs between the two techniques	McNemar's test
Comparison of infusion rate between the first, second, and third 300 ml volumes administered (separately for each technique)*	Repeated-measures ANOVA
Descriptive information regarding any technical issues that HCPs encounter while performing the DRT vs the PPT technique	Not applicable

*The final '300 ml' rate will be calculated using the total time required and volume delivered after the first 600 ml. This will be near to but not exactly 300 ml, and the rate will be accurate based on the time required to give this exact volume.
ANOVA, analysis of variance; DRT, disconnect-reconnect technique; HCP, healthcare providers; PPT, push-pull technique.

Sample size

Using the fluid infusion time and SD data from our previously conducted trial as nuisance parameters, table 2 provides a summary of the range of required sample sizes depending on what is felt to be appropriate in terms of a clinically important difference to detect between the intervention group means for a standardised volume of 900 ml administered. Note that we base our sample size calculation on total fluid intervention time although our primary outcome in this trial will be fluid infusion *rate*. Rate, of course, is calculated using the total fluid intervention time. We plan to use fluid administration rate in this trial, because the total fluid volume administered will differ between HCPs according to how accurately they are able to administer the requested fluid volume.

Given what we know about fluid resuscitation and how restoration of adequate circulatory preload can mean the difference between life and death, we believe that a mean difference of 60 s between the two different techniques would be of clinical significance to detect. This equates to a difference in fluid administration rate of approximately 0.2 ml/s and would require 12 participants with paired data to achieve 80% power. Accounting for the possibility of participant dropouts or other unanticipated issues, we conservatively plan to enrol 16 HCPs in total. If all 16 HCPs complete testing, this would yield a power level of 90% based on the calculations of our statistician co-investigators. We believe that it is reasonable to power our sample size calculation at the 90% level, knowing that if we experience any dropouts that we will retain (in all likelihood) a minimum of 80% power.

Ethics and dissemination

Ethics approval for the conduct of this study was obtained from the Hamilton Health Sciences Research Ethics Board 23 October 2012 (Project no. 12–358), and all procedures will be conducted in accordance with the Tri-council Policy Statement: Ethical conduct for research involving humans.[23] All participants will undergo a process of informed consent, and will be made aware that participation is strictly voluntary. Participants may withdraw from the study at any time. ETC and GH will function as student coprimary investigators for this trial and will work under the supervision of MP, faculty supervisor. MP will lead the steering committee, and be responsible for overall monitoring of the trial. GF and LT are statisticians and have assisted with trial planning, design and analytical considerations. GF performed the sample size calculations. All of the authors of this paper are coinvestigators on the planned study and members of the trial steering committee. Should any safety concerns arise during the conduct of the study these will be brought to the attention of the steering committee and carefully reviewed. We intend to present the results of our study at one or more major scientific conferences and we will publish our results in a peer-reviewed scientific journal.

Feasibility

Given that our investigator group successfully recruited, consented and tested 48 HCPs in a 7-week time frame in the initial Pediatric Fast Fluid Trial, we fully anticipate the successful completion of the study proposed within a 1-year time frame.

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Table 2 Study power and mean difference estimates used to determine study sample size

Mean difference in total fluid intervention rates (ml/s)	Power	Required sample size—number of HCPs (N)
0.05	0.9	203
0.05	0.8	152
0.1	0.9	53
0.1	0.8	40
0.15	0.9	25
0.15	0.8	19
0.2	0.9	16
0.2	0.8	12

HCP, healthcare providers.

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