Rapid Centralised Randomisation in Emergency Setting Trials Using a Smartphone

Shiraz Badurdeen

Royal Women's Hospital

Kate Hodgson (✉ Kate.Hodgson@thewomens.org.au)

Royal Women's Hospital <https://orcid.org/0000-0002-2908-1049>

Georgia A Santomartino

Royal Women's Hospital

Luke Stevens

Murdoch Children's Research Institute

Susan Donath

Murdoch Children's Research Institute

Calum Roberts

Monash Health

Brett Manley

Royal Women's Hospital

Graeme R Polglase

Monash University

Stuart B Hooper

Monash University

Peter G Davis

Royal Women's Hospital

Douglas A Blank

Monash University

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Abstract

Randomised trials in emergency settings must quickly confirm eligibility and allocate participants to an intervention group without delaying treatment. We report rapid randomisation during two neonatal resuscitation trials using the non-commercial REDCap platform accessed via smartphone. This simple, reliable method has wide applicability for trials in emergency settings.

What Is Known

- Randomised trials in emergency settings need to rapidly allocate participants to an intervention group
- This process should not delay treatment

What is new

- This non-commercial, smartphone-accessible application enabled rapid, accurate randomisation at the bedside
- This has broad applicability for emergency settings trials

Introduction

Clinicians and researchers conducting randomised trials in emergency settings face the challenge of needing to quickly confirm eligibility and allocate participants to an intervention group without delaying treatment. The urgency is particularly acute in delivery room trials of neonatal resuscitation, which require participant allocation and application of the intervention within seconds of determining eligibility. As a result, trials have historically used methods that are at risk of bias such as sealed envelopes, allocation prior to eligibility confirmation, or quasi-randomisation.¹⁻³ To ensure validity, the allocation process should be methodologically rigorous, minimise treatment delay, and streamline trial procedures. We report our experience with performing rapid randomisation during neonatal resuscitation using the smartphone-accessible, non-commercial REDCap platform - a database management system.⁴ The aim of this study was to evaluate the use of the online randomisation tool for two delivery room randomised controlled trials.

Materials And Methods

We used randomisation via REDCap for two unblinded, parallel-arm neonatal resuscitation trials conducted at The Royal Women's Hospital and Monash Medical Centre in Melbourne, Australia. The Human Research Ethics Committees at each site approved both trials. In the Baby-Directed Umbilical Cord Cutting (BabyDUCC) trial (ACTRN12618000621213),⁵ eligible infants $\geq 32^{+0}$ weeks' gestation who required resuscitation within one minute of birth were randomised to receive respiratory support in the maternal space with the umbilical cord still intact (intervention) or after clamping the umbilical cord and

transferring the infant to the warming bed. In the Stabilisation with Nasal High Flow for Intubation of Neonates (SHINE) trial (ACTRN12618001498280),⁶ infants undergoing endotracheal intubation were randomised to receive nasal high flow during the intubation attempt, or to standard care (no nasal high flow). The subset of infants in the SHINE trial intubated in the delivery room during neonatal resuscitation were included in the current analysis. Infants intubated in the neonatal unit were excluded as rapid assessment of eligibility and randomisation was not required.^{5,6}

A readily accessible, rapid randomisation tool was required to allow treatment allocation at the participant's bedside without delaying essential resuscitation care. For each trial, a pre-generated randomisation schedule was uploaded to the REDCap randomisation module by an independent statistician. Site investigators accessed the 'New Randomisation' page via a password-protected mobile phone weblink that allowed advance selection of strata. The randomisation tool could be accessed by multiple investigators using their unique REDCap login profile on their smartphones, providing additional automatic stratification by site ("Data Access Group"). Enrolment and randomisation of patients could therefore occur simultaneously at the two sites. Following birth, eligibility was assessed. If the infant required resuscitation within one minute of birth (BabyDUCC trial) or endotracheal intubation (SHINE trial), the researcher or assistant would reveal the allocation via a two-step randomise-and-confirm process (Figure 1). This involved pressing the "randomise" button on the initial screen page (step 1) and again on a confirmation pop-up window (step 2). For caesarean births in the BabyDUCC trial, a midwife not involved in the study randomised the infant and revealed the allocation as the researcher was scrubbed in the operating field.

Figure 1. Screenshots of the randomisation process. A weblink to the "New Randomisation" (A) is accessed through a weblink shortcut saved on the site investigator's smartphone home screen. This page requires the user to log in. Strata are selected as shown in the red boxes. Once participant eligibility is confirmed, the investigator presses the "Randomise" button (STEP 1). A window (B) appears to confirm the strata, and the decision to randomise is confirmed by pressing the "Randomise" button again (STEP 2). The group allocation is then revealed (C) and a record simultaneously created for the participant. The allocation is permanently locked into the participant's REDCap data entry form and cannot be edited.

Both trials incorporated video and audio recordings (GoPro, USA) of resuscitation that captured the randomisation events (Supplementary Figure 1). A single researcher who was not present at the births (GS) reviewed the recordings to determine the time between the decision to randomise and the disclosure of group allocation. Decision to randomise was defined as the time when the researcher confirmed eligibility in conjunction with the clinical team. In the BabyDUCC trial, this was a call to randomise the infant following an assessment that the infant required resuscitation to establish breathing. In the SHINE trial, the decision to randomise was when the clinical team confirmed to the researcher the intention to intubate the infant. Allocation revelation was defined as the time when the study allocation was verbalised to the clinical team. Where the allocation was not immediately verbalised, for instance when the clinical team was busy with other resuscitation tasks, allocation revelation was defined as the time when the allocation appeared on the smartphone device as captured by the recording.

Results

In the BabyDUCC trial (N=123, Supplementary Figure 1), the decision to randomise occurred at a mean (SD) of 25.2 (11.9) seconds after birth. Group allocation was revealed 5.9 (2.9) seconds after the decision to randomise. Two randomisation errors occurred: in each case, an assistant had progressed through the initial “Randomise” step (step 1) followed by accidental confirmation (step 2) before birth. We subsequently enforced the planned approach of waiting until after birth to progress past step 1. Following enforcement of the two-step randomise-and-confirm process after birth and assessment of eligibility, no further errors occurred (N= 94).

In the SHINE trial (N= 68, Supplementary Figure 1), the two-step randomise-and-confirm process after confirmation of eligibility was employed throughout. Group allocation was revealed at a mean (SD) of 6.8 (4.9) seconds after the decision to randomise. One post-randomisation exclusion occurred when a randomisation was appropriately confirmed in a patient that was initially planned for endotracheal intubation but subsequently was not intubated.

All eligible infants were successfully randomised in each trial. There were no instances of technical difficulties related to internet access or REDCap server downtime. The supplementary online videos provide representative examples of the randomisation tool being used (Supplementary videos 1 & 2).

Discussion

We have described our experience with the REDCap randomisation tool accessed using a smartphone browser. The tool was reliable, easy to use and facilitated group assignment within seconds of confirming patient eligibility. We recommend adhering to the two-step randomise-and-confirm process to avoid accidental randomisation. A previously reported mobile app for randomisation⁷ is no longer available (personal communication) and we are not aware of other similar platforms. Advantages include centralised, stratified randomisation performed at the bedside using any internet or mobile data enabled smartphone. Multiple investigators can use the tool across different recruitment sites including locations worldwide. Allocation concealment is rigorous and there is automatic lock of the group allocation within the study database. The system also supports blinding of group allocation for trials where this is required. A custom module that additionally incorporates dynamic randomisation by minimisation has been developed by one of the study authors (LS). This tool has broad applicability for trials in different emergency settings.

Abbreviations

Not applicable

Declarations

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Competing interests

The authors have no relevant financial or non-financial interests to disclose

Availability of data and material

Data will be available upon reasonable request following completion and publication of each of the main trials.

Code availability

Not applicable

Author contributions

SB, KH, DB and PD contributed to the study conception and design. Data collection and analysis were performed by SB, KH, GS, LS, DB, SD, CR, BM, GP and SH. The first draft of the manuscript was written by SB and KH, and all authors revised the manuscript. All authors read and approved the final manuscript.

Ethics approval

The Human Research Ethics Committees at each site (Royal Women's Hospital and Monash Health) approved both trials.

Consent to participate

Written consent was obtained from parents/guardians for participation in each trial

Consent for publication

Not applicable

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Supplementary Videos

Supplementary Videos 1 and 2 are not available with this version

Figures

Figure 1

Screenshots of the randomisation process. A weblink to the “New Randomisation” (A) is accessed through a weblink shortcut saved on the site investigator’s smartphone home screen. This page requires the user to log in. Strata are selected as shown in the red boxes. Once participant eligibility is confirmed, the investigator presses the “Randomise” button (STEP 1). A window (B) appears to confirm the strata, and the decision to randomise is confirmed by pressing the “Randomise” button again (STEP 2). The group allocation is then revealed (C) and a record simultaneously created for the participant. The allocation is permanently locked into the participant’s REDCap data entry form and cannot be edited.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryFigure1.tif](#)