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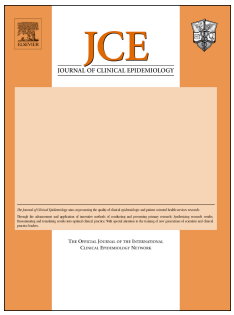

Phone reminders did not increase screening uptake more than SMS reminders: a recruitment study-within-a-trial (SWAT)

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Article title: **Phone reminders did not increase screening uptake more than SMS reminders: a recruitment study-within-a-trial (SWAT)**

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ABSTRACT

Objective

To compare the response rates and costs of phone call versus short message service (SMS) screening reminders to prospective randomised controlled trial (RCT) participants.

Study design and setting

A randomised evaluation within a large Australian diabetes prevention RCT. Participants were men aged 50–74 years, overweight or obese, without a previous Type 2 diabetes diagnosis. Those eligible on a pre-screening questionnaire who did not attend a further screening assessment within four weeks were randomised to receive an SMS or phone call reminder (N=709). The primary outcome was attendance for further screening assessment within eight weeks of pre-screening.

Results

Attendance was 18% (62/354) in the SMS reminder group and 23% (80/355) in the phone reminder group, with no statistically significant difference in response according to reminder type (RR=1.29, 95% CI 0.96–1.73, p=0.09). The lower confidence limits for response to SMS (95% CI 14% – 22%) and phone reminders (95% CI 18% – 27%) did not include the eight-week attendance rate prior to this evaluation, 12%. Phone reminders cost substantially more than SMS reminders (AU$6.21 versus AU$0.53 per reminder).

Conclusion

SMS reminders were as adequate a method as phone reminders to boost RCT screening uptake, and were considerably more affordable.

Key words: Participant recruitment; recruitment strategies; randomized controlled trials; telephone reminders; text message reminders; study within a trial

Running title: Phone and SMS participant screening reminders

What is new?

Key findings:

- There was no statistically significant difference in screening uptake based on whether an SMS or phone call reminder was performed, however either reminder was more effective than no reminder.
- SMS reminders were substantially cheaper to perform than phone call reminders.
- Phone call reminders may be more effective than SMS reminders in men aged 65 years and older.

What this adds to what is known:

- Compared to phone call reminders, short message service (SMS) reminders are an adequate and affordable method of boosting randomised controlled trial (RCT) screening uptake.

What is the implication, what should change now:

- RCTs with high participant attrition during the screening process may benefit from implementing SMS screening reminders to improve recruitment, particularly if phone call reminders are not feasible due to the large numbers of reminders to be made or the limited trial budget available for reminder activities.

INTRODUCTION

Recruitment of participants to randomised controlled trials (RCTs) is challenging and an estimated 50% of trials fail to reach their recruitment targets [1, 2]. Disease prevention RCTs face additional recruitment challenges compared to those for disease treatment, reporting higher attrition of volunteers at each stage of recruitment [3]. Several explanations for this observation have been proposed. Firstly, disease prevention RCTs commonly seek to enrol healthy individuals who may perceive their risk of disease to be low, reducing their motivation to participate in clinical research [4, 5]. Secondly, participants in disease prevention RCTs must usually be identified directly from the general public rather than through clinician referral [6, 7]. Lack of involvement in recruitment by a potential volunteer's personal clinician may leave an individual unsure about the suitability of the trial for them [8] or misunderstanding the trial processes [4], reducing interest in participation.

In RCTs where attrition during early recruitment and initial screening phases is important, interventions to address participant uncertainty and low motivation may boost recruitment, saving time and money. In studies evaluating the use of participant reminders [9-11], phone calls increased RCT enrolment among individuals who failed to respond to an initial mailed invitation compared to no reminder [10], and to a mailed reminder [11]. Also, a series of four short message service (SMS) reminders increased enrolment (compared to no reminder) among participants who did not respond after initial screening [12]. Elsewhere, health services research shows strong evidence that SMS reminders are as effective as phone reminders for improving attendance at clinic appointments [13-15]. However, to our knowledge, no randomised evaluation has been published comparing SMS and phone reminders to improve recruitment to RCTs[16]. Unlike an SMS, a phone reminder provides the opportunity to build rapport and to clarify specific uncertainties, arguably more important for participants interested in joining an disease prevention RCT than for patients due to attend a pre-booked clinic appointment for disease management. By contrast, SMS reminders have the advantage of being cheaper [13], less intrusive, and providing written information that participants can refer to later.

Men are under-represented in disease prevention and health promotion RCTs [7, 17] despite experiencing higher rates of avoidable mortality than women [18]. In the past, men have been mischaracterized as disinterested in health promotion and disease prevention but there is growing recognition that men care about their health and engage with health services if they are tailored to their needs [19, 20]. Men may prefer to monitor their own health needs and to gather information independently before making the decision to engage with professional health services [21]. We hypothesized that SMS reminders may address this preference for independent decision-making in our male participants.

This study aimed to compare, in randomised fashion, the efficacy and cost effectiveness of phone call and SMS reminders in improving attendance for screening assessments for a large multicentre diabetes prevention RCT.

METHODS

Setting

This reminder study was conducted in the context of the Testosterone for Diabetes Mellitus (T4DM) trial. The design of the T4DM study is published elsewhere [22], but briefly, T4DM is a Phase III, multicentre, double-blind, placebo-controlled trial of testosterone for the prevention of diabetes, or reversal of newly diagnosed diabetes (trial registration ACTRN12612000287831). The trial is run through six Australian hospital-based centres and is coordinated by a central university-based coordinating centre. Eligible T4DM participants were men aged 50 to 74 years, obese or overweight, with pre-diabetes or newly diagnosed Type 2 diabetes, and a serum testosterone ≤14mmol/L. The trial used a three-step semi-automated approach to participant screening (Figure 1). Men from the general population were invited to complete a pre-screening questionnaire (Step 1), either online or over the phone. Those who were eligible were then invited by email or mail to attend one of 1300 contracted pathology collection centres for lab screening tests (Step 2), and if eligible, for final screening and study enrolment at the nearest study centre (Step 3).

Figure 1: T4DM study screening process and reminder study design

[Figure 1 here]

Rationale for the reminder study

Of participants who were eligible on the pre-screening questionnaire prior to the commencement of this reminder study, approximately 50% attended lab screening within four weeks of pre-screening. Non-attenders received up to ten screening reminders per year, including: an automated email reminder at four weeks after pre-screening, quarterly email and SMS reminders, and approximately annual phone and postal reminders. Despite these reminders, only 12% of non-responders at four weeks proceeded to attend by eight weeks and a further 8% proceeded to attend after eight weeks. In total, 40% of all potentially eligible participants did not proceed past pre-screening, representing a substantial missed recruitment opportunity. This reminder study was conceived to evaluate the impact on lab screening rates of phone or SMS reminders at four weeks after pre-screening.

Design of the reminder study

The reminder study was a parallel-group, RCT. Individual participants were randomised in a 1:1 ratio to receive either an SMS or phone reminder four weeks after completing the T4DM pre-screening questionnaire if they had not attended lab screening within four weeks of pre-screening. Participants were excluded if they had declined lab screening. All participants had previously consented to receive reminders as part of the standard pre-screening consent process and so further consent to randomisation was deemed unnecessary.

Interventions

SMS screening reminder

SMS reminders were sent by the central coordinating centre within one to two days of randomisation using an online bulk SMS service. The SMS reminder message (see text below) was designed to provide key enrolment information as well as including a peripheral cue based on the

concept of social proof [23] (looking to the actions of others for reassurance in situations of uncertainty) to encourage action by the study participants.

SMS reminder text:

> It's not too late to join the T4DM study. [Number] men around Australia are already taking part. Why not book your blood tests today?
> Text *FORMS* if you need another copy of your blood test forms. Text *DECLINE* to opt out.
> More info: askt4dm@ctc.usyd.edu.au or 1300 865 436.

Phone screening reminder

Phone reminders were conducted by two staff at the central coordinating centre. Calls were made within four days of randomisation with one further attempt made if the first call was not answered. If the participant could not be reached on the second attempt a voicemail message was left, if possible. Staff members were provided with a reminder call script which included the following discussion points:

- Reminding the participant that they had registered for the T4DM study
- Asking if they were still interested in joining the study
- Explaining that the next step was to attend for their lab screening tests and explaining what this involved
- Asking if they needed to have another copy of their lab screening forms sent to them
- Asking if they had any other questions about lab screening or joining the T4DM study in general
- Giving the participant the opportunity to decline further study screening and enrolment

Ethics

The use of phone and SMS screening reminders was approved by each ethics committee overseeing the main T4DM study: Sydney Local Health District HREC — CRGH, the Human Research Ethics

Committee (TQEH/LMH/MH), the South Metropolitan Health Service Human Research Ethics Committee, and Bellberry Human Research Ethics Committee.

Outcomes

The primary study endpoint was attendance for lab screening within eight weeks of pre-screening completion (i.e. within four weeks of receiving the phone or SMS reminder). Attendance at the collection centre was determined using assay results uploaded electronically, in real time, by the contracted pathology company and imported into the main study's clinical data management database using a validated process.

The secondary endpoint was the cost of performing the reminders. Total cost was made up of direct and indirect (staffing) costs. The direct cost of SMS reminders was measured by referring to invoices and billing information from the bulk SMS service. The direct cost of phone reminders was estimated based on the flag fall and per minute costs of calling a mobile number from the coordinating centre. This information was combined with the average call duration to calculate an average phone call cost. The time taken to conduct SMS and phone reminder calls was estimated by maintaining a log of the time spent on reminders over two one-week periods, one at the beginning of the reminder study and one at the end. Time tracking included not only the time to make or send the reminder but also the time to reply to participant questions either by phone or SMS. This information was combined with the hourly staffing cost to calculate the indirect (staffing) cost. All costs are quoted in Australian dollars.

Sample size

Based on prior experience, a response rate of 17% in the SMS reminder arm was assumed. To achieve 80% power, with a two-sided significance level of 5%, 540 participants would be required to detect a 10% higher response rate in the phone reminder as compared to the SMS arm (27%). If the response rate in the SMS arm was only 14%, 540 patients would have more than 95% power to

detect an increase in response to 27% in the phone arm. 10% was chosen as the likely minimum effect that would be considered operationally meaningful.

Randomisation

Confirmation of eligibility and randomisation were performed weekly by a central, automated computer system. After confirmation of eligibility, men were randomised by minimisation, and stratified by centre, age group (50–59, 60–64, 65–69, 70–74) and participant's screening questionnaire completion method (online or phone).

Statistical methods

All analyses were performed according to the intention to treat principle. Baseline characteristics were summarised using counts and percentages for categorical variables, and mean and standard deviation for continuous variables. Intervention groups were compared using a chi squared test. Relative risks and 95% CI were used to summarise this effect. P values for interaction terms were obtained from logistic regression. Subgroup analyses for age (50–64 years and 65–74 years), how men heard about the study (mail, radio, other) and pre-screening questionnaire completion mode (online vs. phone) were pre-specified in the protocol. However, as 98% of men completed their screening questionnaire online and only 2% by phone, this subgroup analysis was not undertaken. Cost effectiveness was estimated by calculating incremental cost effectiveness ratios. No adjustments were made for multiple comparisons. Analyses were performed using SAS v 9.4 (Cary, USA).

RESULTS

The T4DM study was open to recruitment from January 2013 to February 2017. In that time 19,022 participants were screened and 1007 were randomised. The reminder study opened to recruitment in June 2016 and closed in October 2016, the week that the calculated sample size was attained. During that period, 2315 participants were screened to the main study and 709 of them were eligible for the reminder study (having neither attended nor declined lab screening within four weeks of

completing the screening questionnaire). All 709 eligible participants were randomised, with 354 men allocated to SMS reminders and 355 men to phone reminders (Figure 2). Of the 709 men who participated in the reminder study, 142 (20%) attended for lab screening within eight weeks and 28 (4%) went on to be enrolled in the main T4DM study. Enrolment was ceased the week that the calculated sample size was reached. Characteristics of the men participating in the screening reminder study are shown in Table 1, with the two intervention arms well-balanced.

Figure 2: Reminder study CONSORT diagram

[Figure 2 here]

Table 1: Characteristics of all reminder study participants (N=709)

	SMS reminder at 4 weeks (n=354)	Phone reminder at 4 weeks (n=355)
Age, mean ± SD years	58.5 ± 6.0 years	58.1 ± 6.0 years
Centre		
Centre 1	89 (25%)	90 (25%)
Centre 2	74 (21%)	76 (21%)
Centre 3	69 (19%)	66 (19%)
Centre 4	57 (16%)	54 (15%)
Centre 5	38 (11%)	42 (12%)
Centre 6	27 (8%)	27 (8%)
Pre-screening completion method		
Online	350 (99%)	348 (98%)
Information line (phone)	4 (1%)	7 (2%)
How they heard about the study		
Mail-out	197 (56%)	195 (55%)
Radio	123 (35%)	121 (34%)
Other/Not specified	34 (10%)	39 (11%)

Reminder delivery

Of participants randomised to receive an SMS reminder, 312/354 (88%) were sent the reminder, with the remaining 25 participants not sent a reminder due to having attended lab screening before the reminder could be sent, having provided an invalid mobile phone number or having only provided a landline number (Figure 2). By comparison, of the participants randomised to receive a phone reminder, staff spoke to 237/355 (67%) and left a voicemail for an additional 38 (11%). The

remaining 99 participants did not receive a phone reminder due to having attended lab screening before the reminder phone call could be made, having provided an invalid phone number, or having not picked up the phone reminder calls and having no facility to leave a voicemail message. All participants were followed for response and included in the analysis, regardless of whether the allocated intervention was delivered or not.

Response to the reminder

There was no statistically significant difference in response to phone versus SMS reminders (23% vs 18%, respectively, RR = 1.29, 95% CI 0.96–1.73, p=0.09) (Table 2). The difference in response was not affected by how men heard about the study (p=0.13) (data not shown). However, in older men (65–74 years), as compared to younger men (50–64 years), there was a trend for greater uptake in the phone compared to the SMS arm (39% vs 15%, RR=2.26, 95% CI: 1.12–4.56; p for age interaction=0.07). This difference could not be explained by higher success rates in reaching men by phone in the older group. In fact, a higher proportion of younger men were contactable by phone, with staff successfully speaking to 68% of men aged 50–64 years and 59% of men aged 65–74 years.

Table 2: Response to reminder delivered 4 weeks after completing pre-screening[a]

	SMS reminder (n=354)	Phone reminder (n=355)	R.R. (95% C.I.)	p value	Interaction p value
Attended lab	62 (18%)	80 (23%)	1.29 (0.96 – 1.73)	0.09	
Attended lab by age					0.07
50–64 years	53/292 (18%)	60/294 (20%)	1.12 (0.81-1.57)		
65–74 years	9/62 (15%)	20/61 (33%)	2.26 (1.12-4.56)		
Randomised to T4DM trial[b]	6 (3%)	9 (2%)			

[a] Response defined as attendance for lab screening tests by 8 weeks after completing pre-screening

[b] Participants who attended laboratory screening within 8 weeks after completing pre-screening and went on to be randomised to the main T4DM trial at any time following laboratory screening. The study was not powered for this outcome and so statistical testing is not presented.

Cost of reminders

The cost of phone reminders ($6.21 per reminder) was more than ten times that of SMS reminders ($0.53 per reminder), with most of the additional cost due to the additional staff time required to

make the phone calls (Table 3). Staff spent approximately four minutes on each phone call reminder made. By comparison, the staff time per SMS reminder was negligible. It took a total of three minutes to send an entire batch of SMS reminders, irrespective of the number of reminders included.

Table 3: Cost of performing SMS and phone reminders[a]

	SMS	Phone
Direct cost per reminder	$0.18	$0.54
Cost of staff time per reminder	$0.35	$5.67
Total cost per reminder	$0.53	$6.21

[a] All costs are quoted in Australian dollars

The incremental cost effectiveness ratio (ICER) of phone reminders compared to SMS was AU$112.05, meaning that if reminders were made by phone, an additional AU$112.05 would be spent for each additional participant that attended lab screening. However, in men aged 65–74 years, the ICER of phone calls compared to SMS was AU$31.45.

DISCUSSION

Summary of findings

In this randomised evaluation of screening reminders, there was no statistically significant difference in response to phone call and SMS reminders (RR = 1.29, 95% CI 0.96–1.73, p=0.09). However, the overall attendance rate in those who received a phone or SMS reminder was 20% at eight weeks, compared to the previously observed attendance rate of 12% in the main study. As in similar studies [13, 14], we found that phone reminders were substantially more expensive to perform than SMS reminders (AU$6.21 versus AU$0.53 per reminder). We hypothesise that the personal nature of phone reminders may have been more important to participants aged 65 years and older, as in that subgroup, we observed a higher response rate to phone reminders (33% compared to 15% to SMS reminders) and the ICER for phone calls compared to SMS reminders was consequently lower (AU$31.45 compared to the overall ICER of AU$112.05).

Implications for future practice

SMS messages are an effective communication tool in various healthcare settings including reminders for: clinic appointments [13, 24], repeat testing after mass screening [25, 26] and adherence to treatment regimens [27, 28]. Still, published accounts of using SMS reminders to boost recruitment to RCTs remain scarce. Our results provide evidence that SMS reminders may be an appropriate lower cost, but similarly effective, alternative to phone reminders in the RCT recruitment setting. SMS reminders may be particularly worthwhile when phone reminders are not feasible due to the large numbers of reminders to be made or the limited trial budget available for reminder activities.

Limitations and areas for future research

The overall response rate to reminders in our study (20% by eight weeks) was higher than has been reported in previous reminder studies (13%[11], 12%[10], 8% [9] and 3.5% [12]). A possible explanation for the higher rate may be that the recipients of reminders in our study had already completed a pre-screening questionnaire, selecting for willingness to participate in the trial. Additionally, the responses to phone and SMS reminders were evaluated in the context of our existing screening processes, including email and SMS communications with participants after pre-screening (see Figure 1), and these communications may have increased the observed response rate. These factors may impact the generalisability of our results. For example, it remains possible that phone reminders remain superior to SMS reminders in situations where participants are yet to respond to the initial invitation to participate in the trial and where no prior communications have been sent to participants. Furthermore, the T4DM study recruited only men aged 50–74 years. Our findings suggest that older participants may prefer phone reminders, and this has implications for RCTs recruiting participants who are older or younger than those included in our study. We hypothesize that SMS reminders may have been particularly appealing to our all-male participant cohort since they supported men to make an independent decision about trial participation. Reminder preferences in women may therefore differ, and would merit investigation.

In a non-randomised comparison, we found that attendance following either SMS reminder (18%, 95% CI 14% – 22%) or phone reminder (23%, 95% CI 18% – 27%) was higher than the previously observed attendance rate at eight weeks of 12%. We elected not to include a "standard care" arm (neither phone call nor SMS reminder) in this randomised evaluation due to concerns that it might hamper the main study, particularly given the existing evidence on the effectiveness of screening reminders [9-11]. Future studies, if conducted earlier in their host trial's recruitment phase, could include a "standard care" or no reminder arm. This would allow calculation of a reminder cost per randomised participant to guide decisions about whether reminders (either phone or SMS) are more or less cost effective than other strategies designed to boost recruitment, for example mass mail outs or advertising to invite more people to participate in the study.

In addition to the analyses reported here, we conducted an exploratory evaluation of subsequent reminders conducted more than 8 weeks after pre-screening. These data are not shown here but suggested that a subsequent phone reminder to men who did not respond to an initial SMS reminder was almost three times more effective than a further SMS reminder (13% and 5% respectively). Thus, further investigation of the impact of subsequent reminders may be of merit.

We reported higher reminder delivery in the SMS group (88% delivered) compared to the phone group (67% delivered, 78% if voicemail messages are also included). However, this apparent difference in intervention delivery fidelity is likely to be an artefact of how delivery was measured in each group. For phone reminders, we recorded whether the participant was spoken to on the phone, or if a voicemail message was left. For SMS reminders, we could record only whether the SMS message was sent without bouncing back. We could not determine whether the participant received and read the SMS reminder. Thus, the actual delivery rates in each arm may be more similar than our estimates suggest. Furthermore, any difference in reminder delivery fidelity between the arms would likely also occur if these reminders were incorporated into practice.

The SMS reminder message in this evaluation included key information about trial participation, and informed the participant that large numbers of men had already joined the trial, a peripheral cue to action based on the concept of social proof. This approach is underpinned by the Elaboration Likelihood Model of persuasion [23], which states that persuasion to action can occur through either a central (cognition-based) or peripheral (cue-based) route, with the peripheral route requiring less motivation and effort to process. Elsewhere, messages of scarcity (communicating that limited number of places are available) [9] and quotes from participants [12] were effective in boosting RCT recruitment using SMS reminders. Future research could extend these findings by evaluating manipulations in the content of SMS reminders using a theory-based approach [29, 30]. It is possible that by optimising the content of SMS reminder messages, response rates can be further improved.

CONCLUSION

Compared to SMS reminders, phone reminders were more costly and did not significantly increase the screening uptake rate of non-responders in this large multicentre RCT. There was some suggestion that phone reminders were more effective than SMS reminders in men aged 65 years and over. SMS reminders were substantially cheaper and quicker to perform than phone reminders, making them a promising approach for boosting recruitment in RCTs with limited budgets.

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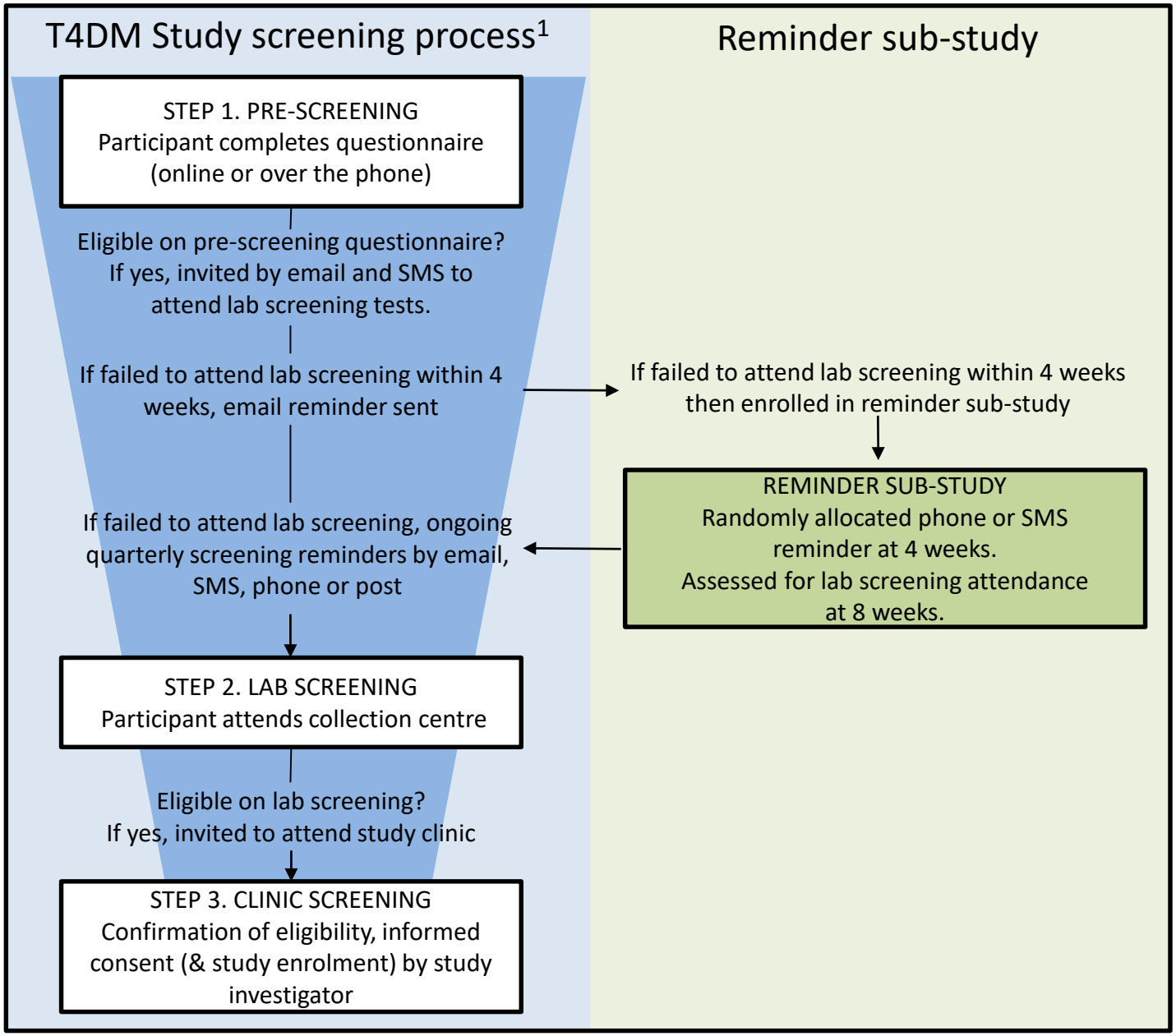
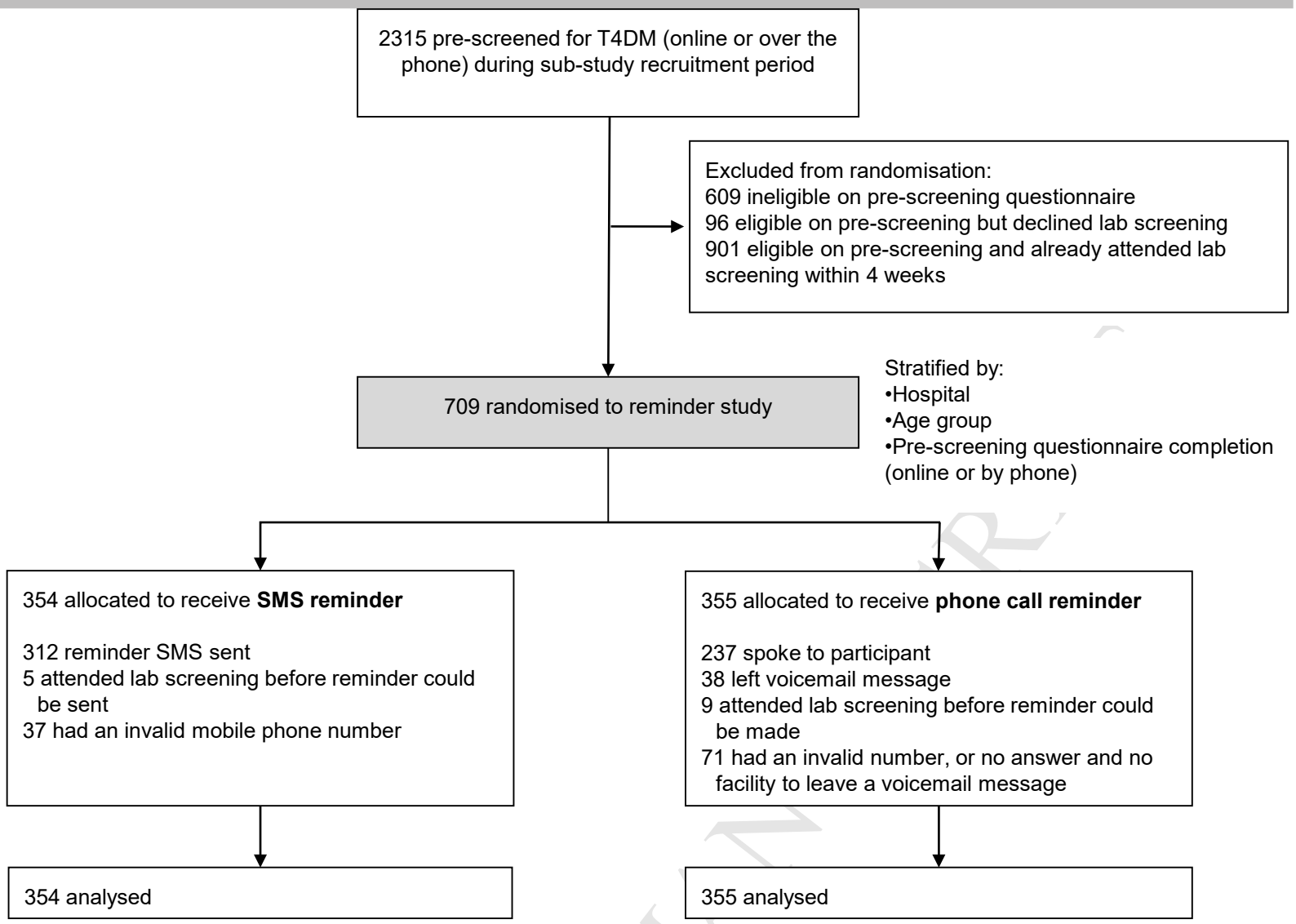


[1] Participants could decline further screening at any time by phoning, emailing, mailing or text messaging the coordinating centre or the study site



GW, CA, AC, MD, VG, MG, WH, DJH, WI, AJ, AKe, RM, BS and BYY conceived the T4DM study. KB, GW, WH, AKe and AKi designed the evaluation presented in this paper. KB and KPR carried out the evaluation and collected the data. KB, KPR and AKi performed the statistical analyses. KB wrote the first draft of the manuscript. KB, AKe, WH, AKi, KPR, CA, AC, MD, VG, MG, DJH, WI, AJ, RM, BS, BBY and GW revised and approved the manuscript.

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KB, AC, MD, WH, VG, WI, AJ, RM, KR, BS and A Kirby declare no relevant conflicts of interest.