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ABSTRACT

Introduction Approximately 1 in 7 pregnant women in the USA report past-month alcohol use. Strong evidence connects prenatal alcohol exposure with a range of adverse perinatal outcomes, including the spectrum of conditions known as fetal alcohol spectrum disorders. Screening and Brief Intervention (SBI) has been recommended for pregnant women but has proven difficult to implement. This study will test the efficacy of single-session technology-delivered SBI (electronic SBI) for alcohol use in pregnancy, while simultaneously evaluating the possible additional benefit of tailored text messages and/or booster sessions in a 3×2 factorial trial.

Method and analysis This full factorial trial will use online advertising and clinic-based flyers to recruit pregnant women meeting criteria for unhealthy alcohol use, and randomly assign them to one of six conditions crossing three levels of brief intervention (none, single 120-minute session and single session plus two 5-minute boosters) with two levels of tailored text messaging (none vs twice weekly messages). The primary analysis will test for dose–response effects of the brief intervention on alcohol abstinence, defined as no self-report of alcohol use in the 90 days prior to 34 weeks' gestation, and negative results for ethyl glucuronide analysis of fingernail samples. Secondary analyses will examine main and interaction effects of tailored text messaging as well as intervention effects on birth outcomes.

Ethics and dissemination Ethical approval was provided by the Michigan State University Biomedical and Health Institutional Review Board (STUDY00005298). Results will be presented at conferences and community forums, in addition to being published in a peer-reviewed journal. Intervention content demonstrating sufficient efficacy and safety will be made publicly available.

Trial registration number ClinicalTrials.gov Registry (NCT04332172).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This study uses a randomised factorial design allowing simultaneous evaluation of main effects for intervention dose and tailored text messaging, as well as of their interaction.
⇒ The intervention being evaluated can be readily disseminated in the exact form tested in this trial, with no loss of fidelity when implemented in applied contexts.
⇒ Study rigour is enhanced by removing possible sources of bias (such as self-report via technology, laboratory testing for ethyl glucuronide and blinded analysis).
⇒ The factorial design allows evaluation of interaction effects, but power to detect disordinal interactions is limited.
⇒ The study sample will be recruited online, reducing generalisability to specific settings in which this intervention might be deployed, such as prenatal care settings.

INTRODUCTION

Approximately 1 in 7 pregnant women in the USA report past-month alcohol use.[1] Further, evidence suggests that current alcohol use as well as binge drinking during pregnancy increased between 2011 and 2018.[2] Strong evidence connects prenatal alcohol exposure with a spectrum of conditions known as fetal alcohol spectrum disorders (FASDs),[3] with consequences that include reductions in brain volume[4]; neurochemical and connectivity-related abnormalities[5]; deficits in executive functioning[6]; intellectual disability[7]; preterm birth[8] and fetal death.[8 9] The burden of these consequences is disproportionately borne by African-Americans.[10 11] Prevention of FASD, particularly among African-Americans, is a major public health priority.

Unfortunately, most at-risk women either fail to disclose their alcohol use[12 13] or do not feel that treatment is needed.[14] Screening and Brief Intervention (SBI) is a key intervention for pregnant women recommended by the US Preventive Services Task Force,[15] American College of Obstetricians & Gynecologists Committee on Ethics[16] and the National Task

Force on Fetal Alcohol Syndrome/Fetal Alcohol Effect.[17] SBI has clear advantages: (a) it is proactive, meaning it is not dependent on treatment seeking; (b) it can be applied broadly; and (c) it is brief and acceptable to patients, including those who are not seeking treatment. Unfortunately, the time and training needed to administer SBI impede its availability[18] and reduce its implementation and efficacy.[19] As a result, SBI for alcohol use in pregnancy is a recommended practice, but is rarely fully implemented by obstetricians.[20]

Technology-delivered SBI (e-SBI) may address these obstacles. e-SBI requires less time and training than clinician-delivered SBI, facilitates disclosure[21] and has no loss of fidelity in community implementation. Importantly, rates of smartphone ownership are rising every year and are particularly high among younger adults; for example, 96% of adults aged 18–29 years own a smartphone.[22] Further, 96% of Americans aged 18–29 years and 85% of pregnant minorities report having access to the internet.[23 24] These data are consistent with our findings from a sample of 160 low-income, African-American mothers receiving Women, Infants, and Children (WIC) nutrition assistance, in which 83% reported owning a smartphone.[25]

Pilot testing of single-session e-SBI for alcohol use among pregnant women has shown initial promise.[26 27] In an additional trial with women seeking reproductive healthcare—approximately 18% of whom were pregnant—e-SBI was not significantly different from person-delivered SBI for addressing substance use, and superior to enhanced usual care.[28] The e-SBI in this study also demonstrated greater cost-effectiveness than either enhanced usual care or person-delivered SBI.[29] However, brief intervention (BI) effects continue to be small and inconsistent,[30] and technology-based approaches are not always easily accessible, either to pregnant women or to researchers seeking to build on prior work. This study proposes two features to address these gaps.

Optimising BI efficacy

Behavioural intervention development is often static, with a single version being developed and progressively tested without any effort at optimisation or unpacking of components. This has been true of BIs for alcohol use, which have largely followed a similar approach without systematic testing of which elements might be most strongly associated with outcomes.[31] The Multiphase Optimization Strategy[32] calls for factorial trials early in the intervention development process to maximise the likelihood of success and prevent premature commitment to suboptimal interventions. In the case of BIs, some evidence suggests that two sessions may be superior to one.[33] A recent meta-analysis also suggests that text messaging interventions can reduce alcohol use,[34] with one trial demonstrating potential effects among pregnant women.[35] However, to our knowledge, no prior studies have either randomised pregnant participants to varying doses of BI for alcohol use or examined how tailored texting for alcohol use might interact with BI dose.

Addressing technological barriers

Obstacles such as cost, risk of obsolescence, cross-platform incompatibility, version management and limited modifiability can all reduce technology's potential for widespread dissemination and long-term access. The present study addresses these challenges through use of the Computerized Intervention Authoring System V.3.0 (CIAS 3.0), a non-commercial research resource and authoring tool that allows creation or editing of internet-delivered interventions without the need of a programmer. Interventions built using CIAS 3.0 feature a synthetic text-to-speech engine that reads all questions and speaks aloud to the participant; synchronous interactivity; natural language reflections; branching logic; a clean user interface; and the ability to easily incorporate specific images, graphs, figures, text, or videos. Interventions built with CIAS 3.0 are also cross-platform compatible, meaning that they deploy readily as a mobile web application on any device—including those running the Android or Apple mobile operating systems. This also means that any content developed using CIAS 3.0 is centralised and immediately available, without relying on users to download each update.

Proposed study

The proposed study will seek to confirm the efficacy of the previously pilot-tested e-SBI for alcohol use in pregnancy. We will also use intervention optimisation techniques to evaluate the extent to which intervention effects can be enhanced by adding subsequent booster sessions and/or tailored text messaging. The primary analysis will test for dose–response effects of the BI on alcohol use during pregnancy. Secondary analyses will examine main and interaction effects of tailored text messaging, as well as intervention effects on birth outcomes. Exploratory analyses will examine theory-driven mediators and moderators of intervention efficacy, as well as intervention effects on additional drinking-related outcomes (eg, days of binge use).

METHODS AND ANALYSIS

Study design

This is a randomised factorial trial crossing three levels of BI dose (no BI; one 20-minute BI; or one 20-minute BI plus two 5-minute boosters) with two text messaging conditions (tailored text messaging present or not present) for a total of six cells (table 1). This study started in March 2022 and will end in October 2024.

Patient and public involvement

The screening, BI and text messaging intervention for this study were designed with input from pregnant women and medical professionals. We elicited feedback on the BI from 18 pregnant women meeting alcohol use criteria in

Table 1 Factorial design and description of individual cells

	No BI	BI	BI+boosters
Text messaging=no	No intervention	BI only	BI+boosters
Text messaging=yes	Text messaging only	BI+text messaging	BI+boosters+text messaging

N for each cell=64 (total N=384). Allocation to all cells is random, stratified by state and binge frequency.
BI, brief intervention.

the pilot trial,[36] which revealed high ratings for acceptability, ease of use, and helpfulness, qualitative feedback in support of its helpfulness, and clear suggestions/concerns that led to changes in the intervention design. We also conducted five focus groups examining text message design with 31 women who either used alcohol in pregnancy or had a close friend or family member who used alcohol in pregnancy. These focus groups facilitated development of specific messages addressing perceived barriers, facilitators and motivators. The entire package of baseline BI, booster sessions and text messages will also be shown to pregnant women meeting alcohol risk criteria recruited online, with subsequent modifications as needed prior to beginning the trial. The entire trial was designed to involve brief interactions spread over time, using technology to obviate the need for study-related transportation or specific appointments. Study results will be disseminated to trial participants, and their involvement as well as the public's will be sought prior to further dissemination.

Setting and participants

This study will be conducted online. Participants will be 384 pregnant women aged 18–35 years who score positive on the Tolerance, Annoyed, Cut Down, Eye-opener (T-ACE),[37] a validated screen for identifying alcohol risk in pregnancy.[38] We have also added an additional requirement of either (a) drinking weekly or more in the past month, or (b) having four or more drinks at a time at least monthly in the 12 months before becoming pregnant. This definition of risk is a direct result of research showing that electronic Screening, Brief Intervention, and Referral to Treatment (e-SBIRT) effects on alcohol use in pregnancy are restricted to heavier users,[39] and research showing that pre-pregnancy drinking or other substance use is the strongest predictor of use in pregnancy.[40 41] Additional inclusion criteria are smartphone ownership, willingness to receive study-related text messages and to use their smartphone for remote follow-up assessments and boosters, being at 20 weeks' gestation or less, and planning to deliver in Connecticut, Massachusetts, or Michigan. Only those who complete the baseline assessment will be considered participants and subsequently randomised. Exclusion criteria include intention to terminate the pregnancy and inability to communicate in English. Other substance use will not be exclusionary and we will have no restrictions based on treatment seeking either before or during participation in this study.

Sample size determination

For our primary hypothesis that 90-day alcohol abstinence will be greatest with a single baseline session plus boosters, followed by a single baseline session alone, compared with no BI (BI+booster>BI alone>no intervention), we plan a test for linear trend based on the Mantel-extension test. We also considered a second dose–response pattern, that is, a plateau pattern (BI+booster=BI alone and BI with and without booster>no intervention), which would be tested with a one-sided X^2 test based on isotonic regression and the restricted likelihood ratio statistic.[42] A priori power analyses were calculated for Mantel-extension and χ^2 tests using a Monte-Carlo simulation of over 2000 iterations. We estimated that with a type 1 error rate of 0.05, 110 participants per dose level (330 participants in total) would be sufficient to achieve at least 80% power to detect small values (effect size=0.05) of the linear slope (or step values for the plateau pattern). Our proposed sample size is 128 participant per dose level (384 total) to allow for roughly 15% dropout or other unforeseen threats.

Recruitment

Participants will be recruited using flyers distributed at prenatal care clinics and ads placed on social media (Facebook and Instagram). They will contain basic information about the study and emphasise its voluntariness. Women who follow instructions on the flyer, or who click the link in the online ads, will be directed to a study website presenting an electronic information sheet. Those who agree to proceed will complete the online eligibility determination screening, which will determine whether initial inclusion criteria have been met (age, pregnancy status, state of intended delivery of infant and alcohol risk). Women who meet these inclusion criteria will be contacted by the study research assistant by telephone within 48 hours to further validate their eligibility (ability to communicate in English, owning a working smartphone, able to receive text messages and understanding study requirements) and to review the full written consent for the factorial trial (see online supplemental file 1), which will be presented electronically and reviewed by telephone. Enrolment will proceed only if participants provide written informed consent via e-signature (a signed copy of which will be emailed to each participant).

This study will follow best practices for online recruitment.[43] The following strategies will be implemented to reduce the possibility of fraudulent participation: (1)

Table 2 Schedule of enrolment, interventions and assessments

	Study period								
	Enrolment	Allocation	Post-allocation						Close-out
	$-t_1$	0	t_1	t_2	t_3	t_4	t_5	t_6	t_7
Time point	Prestudy screening	Randomisation	Baseline	4 weeks post	6 weeks post	27 weeks' gestation	30 weeks' gestation	34 weeks' gestation	4 weeks post partum
Enrolment									
Eligibility screen	X								
Informed consent	X								
Allocation		X							
Interventions									
Brief baseline intervention			X						
Booster 1 (6 weeks post-baseline)					X				
Booster 2 (30 weeks' gestation)							X		
Text messages			◆	—	—	—	—	◆	
Assessments									
Tolerance, Annoyed, Cut Down, Eye-opener (T-ACE) alcohol screening tool	X								
Timeline Follow-Back								X	
Ethyl glucuronide lab								X	
Birth outcomes									X

manual review of IP addresses to screen for duplicates; (2) manual review of survey data to detect suspicious response times (eg, completing the survey too quickly); unusual patterns in responses, respondent names, or respondent email addresses; and patterned completion timestamps indicating that one person/bot is completing the survey repeatedly until eligible; and (3) inclusion of a required open-ended narrative response to detect fraudulent completion. Only interested women who pass these screens and can be confirmed as eligible via the phone call will be enrolled.

Procedures

Eligible participants who provide written informed consent will be helped to develop a user name and password for CIAS 3.0 and will be randomised to one of the six specific cells resulting from the 3×2 factorial design (table 1). Emails will include a link to the next study element due (assessments for all participants, and intervention and/or booster sessions, if applicable), with repeated reminders as needed. Participants assigned to receive text messages will get their first messages in the week immediately following completion of the baseline assessment session. There will be four follow-up assessments, which participants will complete remotely via Qualtrics.[44] As noted in table 2, the first follow-up assessment will take place 4 weeks following the baseline session, followed by assessments at 27 and 34 weeks' gestation and a final assessment at 4 weeks post partum.

For all participants at all time points, we will send a text message and/or email with a link up to six times during a 10-day period surrounding the assessment point in order to promote completion and give participants a chance to access public WiFi (such as at their prenatal clinic) if they prefer; these messages will cease once the participant responds. In addition, before a participant is deemed to have missed any given follow-up assessment, the investigator or designee will make every reasonable additional effort to regain contact with the participant including email, text and telephone contact (depending on patient preference). If a participant does not respond to email or text, we will attempt up to three telephone calls to the participant and any available collateral contacts. Participants will only be considered as having withdrawn if they indicate that they wish to do so.

Enrolled participants will receive credits to an online gift card programme when completing study activities. Research staff will provide gift card credit remotely. Compensated sessions will include baseline ($40 credit), three brief follow-ups (see below; $20 credit each at 4 weeks post-baseline, 27 weeks' gestation and 4 weeks post partum) and a longer follow-up at 34 weeks post partum ($50 credit, with a $20 bonus if completed within 24 hours). Additionally, participants will receive a $100 credit for providing their nail clippings (using a provided sample collection kit) during the third trimester ($20 credit if provided within 1 week). Completion of booster sessions and receipt of

text messages will not be compensated in any way and will not be combined with any follow-up data collection session.

Measures

The primary outcome of alcohol use will be evaluated at the 34-week follow-up using an electronic version of the Timeline Follow-Back interview method (90-day window of recall). The Timeline Follow-Back is a reliable and valid method for assessment of alcohol use, including in electronic administration.[45–48] The primary outcome will also include evidence of alcohol use via testing of fingernail clippings during the third trimester for ethyl glucuronide (EtG), a metabolite of alcohol use. EtG is sensitive to low levels of alcohol use,[49] is not susceptible to false positives as a result of mouthwash or hand sanitiser use,[50] and provides an approximate 90-day window of detection when evaluated from fingernail clippings. Participants will be asked to send fingernail clippings via mail using pre-addressed and postage paid packages. Participants will be considered negative for alcohol use if both the Timeline Follow-Back and EtG screen are negative, and positive if either shows evidence of alcohol use. We will also obtain birth records for each participant from their state's health department (either Michigan, Massachusetts or Connecticut). See table 2 for a schedule of measures as well as intervention and assessment time points.

Randomisation

At baseline, participants will be randomised into one of the six cells (see table 1) with stratification by state of residence and baseline alcohol frequency. Allocation concealment will be facilitated by use of non-identifying codes for study condition assignment at the time of enrolment and automation of all follow-up data collection via direct participant report using online survey software. We will obtain state birth records and objective external outcome data from blinded biomarker analysis by an external laboratory. Staff at these organisations will not be informed of study conditions. In addition, the study biostatistician, the data analyst and the research assistant who enrols participants will be blinded as to study condition.

Intervention

Baseline BI

The interactive and tailored baseline MommyCheckup single-session e-SBI was built using CIAS 3.0 following principles of Motivational Interviewing[51] and Self-Determination Theory,[52] and seeks to facilitate self-change and/or treatment seeking through a 20-minute interactive session using techniques such as (a) education regarding alcohol-related pregnancy risks; (b) helping the participant evaluate the extent to which avoiding alcohol might align with deeply held values or goals; (c) personalised normed feedback regarding drinking frequency and costs; and (d) the option to choose a specific goal regarding drinking in pregnancy, with proactive problem-solving for those who set a goal. It includes videos featuring physicians providing gain-framed information about the benefits of quitting or reducing alcohol use in pregnancy, and a mother providing a testimonial regarding her decision to avoid alcohol use during

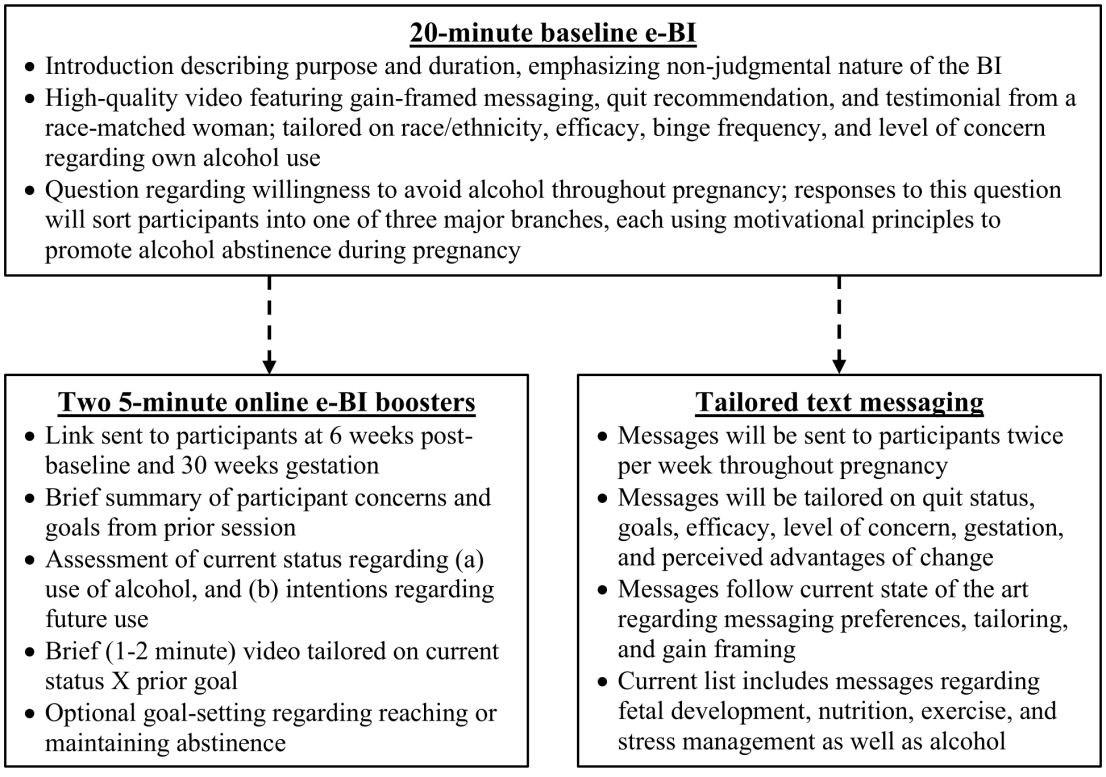

Figure 1 Baseline brief intervention (BI), booster sessions and tailored messages. e-BI, electronic BI.

Table 3 Text message examples

Text message categories	Text messages
Gestational age	At this point in your pregnancy, your baby is about the size of a tater tot, and a little over an inch long!
Perceived consequences of alcohol use	Not drinking means fewer issues with short-term memory, quicker ability to react, and more control over your mood & decisions you make.
Pregnancy-related motivations for change	Quitting isn't about one big change. It's about lots of little changes. Take 1 day at a time. Focus on your reasons for quitting drinking while you are pregnant and breast feeding. Surround yourself with support.
Self-efficacy	As you get ready for your baby, know that you are capable of doing many things, including not drinking.
Theory-based elements consistent with Self-Determination Theory	Not sure you can say 'no' if others ask you to join them for a drink? Some moms plan ahead with answers like, 'No thanks, I'm stopping for my baby.' Other women change the subject or ask a support person to help them if they feel pressured or can't avoid the situation.
Values	Not drinking means more money in your wallet. With your baby coming, some savings could go towards things you'll really need for your little one!

pregnancy (figure 1). The full baseline session will take approximately 20 min for those in the two no-BI conditions, and 40 min for those in the remaining four cells.

Booster sessions

The booster sessions are also built using CIAS 3.0 and function as tailored follow-ups to the baseline BI session. As noted in figure 1, they focus on brief assessment of current alcohol use status and intentions, followed by provision of a brief tailored video that either reinforces abstinence, promotes change or reorients participants toward a previous change goal. Booster sessions will be scheduled for 6 weeks following completion of the baseline BI session and again at 30 weeks' gestation.

Tailored text messages

The text messaging intervention is also built and deployed using CIAS 3.0 (which uses the Twilio API, https://www.twilio.com). Text messages have an average Flesch-Kincaid grade level of 4.6. They are tailored on a range of factors as well as theory-based elements consistent with Self-Determination Theory (see examples in table 3). This multifaceted tailoring approach is consistent with meta-analytical evidence regarding efficacious health communications.[53] Message design is also consistent with empirical evidence regarding participant preferences,[54] and is gain framed (focusing on advantages of change) in order to minimise guilt or other negative reactions. Text messages will be sent twice per week, following recent evidence that this frequency was not associated with greater disenrolment than that of once per week.[29] Participants in the text messaging condition will receive messages until they give birth or until they text back 'STOP' to end the messages.

Ethics and dissemination

This study has been approved by the Michigan State University (MSU) Institutional Review Board (IRB) (STUDY00005298). This study will comply with the National Institutes of Health (NIH) Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information and the Clinical Trials Registration and Results Information Submission rule. As such, this trial is registered at ClinicalTrials.gov (NCT04332172), and results from this trial will be submitted to ClinicalTrials.gov. Additionally, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) data sharing agreement requires that deidentified data be uploaded to their data archive ($NIAAA_{DA}$), where it will be stored indefinitely. The dissemination plan also includes presentation of the results at various conferences and in various community forums, and submission to a peer-reviewed journal.

All participants will provide informed consent during enrolment. The informed consent sheets will explicitly acknowledge the limited security of text messages, both because they are not encrypted, and because the participant's phone itself may be accessible to others. The text messages will also be written in a way that does not imply any details of the participant's alcohol use.

A Data Safety and Monitoring Board (DSMB) independent from the sponsor and competing interests will be responsible for developing a data safety and monitoring (DSM) plan and for monitoring this trial. All adverse events (AEs) will be reported to the NIAAA project officer annually in the form of a DSMB report. This DSMB report will include confirmation of adherence to the data and safety monitoring plan, a summary of any data or safety monitoring issues that took place since the last reporting period, a description of any changes to the research protocol or DSM plan that do or could potentially affect risk, and all new and continuing IRB approvals. Additionally, serious AEs and unanticipated events that are considered at least possibly related to the study will be reported to the MSU IRB within 48 hours.

Outcomes

Primary outcome

The primary outcome for this study is 90-day period prevalence abstinence, which is defined as no self-report of any alcohol use in the 90 days prior to the 34-week assessment, and a fingernail sample that is negative for EtG at approximately 37 weeks' gestation. Participants reporting any use of alcohol in the past 90 days or whose fingernail sample tests positive from EtG analysis will be treated as positive for alcohol use. Self-report of alcohol use for the primary outcome will be obtained using a Timeline Follow-Back measure regarding alcohol use from the month before pregnancy to the 34-week assessment.[48]

Secondary outcomes

The secondary outcome, a healthy birth outcome, is defined as a full-term live birth (>36 weeks+6 days) of normal birth weight (>2500 g), with no days in neonatal intensive care. Data regarding this and other birth outcomes and risk factors will be taken from state birth records following consent of participants and approval by the IRBs for the states of Michigan, Massachusetts and Connecticut.

Data analysis

We will follow Consolidated Standards of Reporting Trials guidelines for trial reporting (www.consort-statement.org). All analyses will be done using an intent-to-treat approach, and we will attempt to follow all participants regardless of their retention in treatment. A participant will be considered lost to follow-up if she fails to complete the 34-week assessment before the end of her postpartum hospitalisation and does not provide nail clippings for EtG testing. Missingness will be examined for quantity, type and pattern. If missing data are a significant issue, we will fill in missing values using multiple imputation methods. The possible impact of missing data on interpretation will be discussed in reports and evaluated using sensitivity analyses.

To test our primary hypothesis that there will be a dose–response relationship between 90-day alcohol abstinence and BI dose (H_0: $p_1=p_2=p_3$ against H_a: $p_1<p_2<p_3$ with at least one strict inequality), we will conduct a Mantel-extension type test if we observe a linear dose–response or a one-sided X^2 test based on isotonic regression and the restricted likelihood ratio statistic[42] if we observe a plateaued dose–response pattern. We will test if the stratification variables have a significant association with the primary outcome, and if so, we will include them in an adjusted analysis of the primary outcome in order to preserve power and estimate confounding effect.[55]

Our secondary hypotheses are that there will be a main effect for text messaging (H2), an interaction effect for e-SBI plus boosters and text messages (H3) on 90-day alcohol abstinence, and a main effect for e-SBI on healthy birth outcome as defined above (H4). These hypotheses will be tested using logistic regression. Explanatory variables in the model for H2 will include text message, e-SBI treatment group, and stratifying variables, state of residence and baseline alcohol frequency. For H3, we will also include an interaction term between text messages and e-SBI, and we will exclude participants who did not receive e-SBI (n=128) as we are only interested in testing the differences between the group e-SBI plus boosters and text messages versus e-SBI plus either supplement alone. The model for H4 will be similar to model for H2, but it will test effects on healthy birth outcome instead of abstinence and will include other substance use as an explanatory variable. Following secondary analyses, exploratory regression analyses will also consider intervention effects on alternate/continuous outcomes such as number of drinks since the baseline randomisation session, number of days of alcohol use and days of binge use. Secondary and exploratory analyses are not powered but can be used to generate hypotheses and guide design of subsequent confirmatory trials.

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Contributors SJO and KAY led the design and conceptualisation of this study and the writing of this protocol. KG-H led the writing of the power and data analyses sections. JH led the sections on internet recruitment of participants. All authors, SJO, LT, SJ, CA, KG-H, GG, AL, JH and KAY, contributed to the protocol through writing and/or editing. SJO and LT revised the draft paper.

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Competing interests JH has received research support from Pfizer. The authors declare that there are no other conflicts to report.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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