NHS
Health Research Authority

FULL/LONG TITLE OF THE STUDY
Using text messages to boost COVID-19 vaccination appointment booking and vaccination rates: A randomised controlled field trial.

SHORT STUDY TITLE / ACRONYM

Using text messages to boost COVID-19 vaccine booking rate (v1.0).

PROTOCOL VERSION NUMBER AND DATE

- Version number: 1.2
- Date: May 27th, 2021

RESEARCH REFERENCE NUMBERS

IRAS Number:	298649
SPONSORS Number:	Not applicable
FUNDERS Number:	Not applicable

This protocol has regard for the HRA guidance and order of content

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Michellekane

Date: 16/April/2021

Name: (please print):

Michelle Kane

Chief Investigator		

Signature: Michellekane

Date: 16/April/2021

Name: (please print):

Michelle Kane

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Committees	Not applicable

STUDY SUMMARY

Study Title	Using text messages to boost COVID-19 vaccination appointment booking and vaccination rates: A randomised controlled field trial.
Internal ref. no. (or short title)	BIT's ref No. 2021035 Short title: Using text messages to boost COVID-19 vaccination appointment booking and vaccination rates
Study Design	An 8-arm field RCT with randomisation at individual level **EXTENSION** A 7-arm field RCT with randomisation at individual level
Study Participants	Inclusion criteria: - Aged between 40-49 (most likely 40-44) who are eligible for COVID-19 vaccination; - Registered in the NHSEI system with a mobile phone number; - Haven't received an NHS COVID-19 SMS invitation via the national immunisation management service system. **EXTENSION** - Aged between 18-29 (most likely 29-26) who are eligible for COVID-19 vaccination; - Registered in the NHSEI system with a mobile phone number; - Haven't received an NHS COVID-19 SMS invitation via the national immunisation management service system.
Planned Size of Sample (if applicable)	1.63 million **EXTENSION** 2.88 million
Follow up duration (if applicable)	Not applicable
Planned Study Period	April 23rd - May 30th, 2021 The trial will be launched on Apr 23rd. Given that it takes at least 2 weeks to collect secondary outcome measures and potential time lag in data processing, each participant is expected to be in the study for up to 5 weeks. **EXTENSION** June 7th - July 1st The trial will be launched on June 7th. Given that it takes at least 2 weeks to collect secondary outcome measures and potential time lag in data processing, each participant is expected to be in the study for up to 5 weeks.

Research Question/Aim(s)	Which BI-informed text messages can increase the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination, compared to a control text message?

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this study)	**FINANCIAL AND NON FINANCIAL SUPPORT GIVEN**
NHS England and NHS Improvement Skipton House 80 London Road, SE1 6LH, London	Non-financial support: project leadership and project management support **EXTENSION** Financial support: funding BIT's researchers' time spent on the project
Department of Health and Social Care, 39 Victoria Street; London; SW1H 0EU	Financial support: funding BIT's researchers' time spent on the project

ROLE OF STUDY SPONSOR AND FUNDER

The study may be subject to inspection and audit by NHSEI under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the NHS Research Governance Framework for Health and Social Care. The Sponsor holds responsibility for initiation and management of the study. They are responsible for the implementation of the interventions in this research and control the final decision regarding dissemination of the results of the study. The sponsor contributed to the study design and will contribute to data analysis.

The study design, as well as data analysis and interpretation are led by the Behavioural Insights Team.

The Department of Health and Social Care as one of the funders is informed of progress with this study.

EXTENSION

The Department of Health and Social Care is no longer a funder, but is still informed of progress with this study.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITTEES/GROUPS & INDIVIDUALS

This research has a study steering group that meets twice a week to coordinate the design and delivery of this trial. The members of this steering group are from NHS England and NHS Improvement (NHSEI), the Behavioural Insights Team (BIT), the Department of Health and Social

Care (DHSC), and Public Health England (PHE). They have been listed as protocol contributors. The organisational roles within this committee as as follows:

- NHSEI: sponsor, project management and implementation leadership
- BIT: research design leadership and technical advice
- PHE: independent technical advice
- DHSC: funder and observer

We have involved members in developing the interventions to be tested in this study. This has included pre-testing the content of the coronavirus vaccine SMS invitation messages with an online panel. NHSEI has also shared insights from relevant focus groups with members of the general public that have been conducted.

EXTENSION

NHSEI is taking over as project funder from DHSC.

PROTOCOL CONTRIBUTORS

The roles of protocol contributors from different institutions are as follows:

- NHSEI: Sponsor, project management and implementation leadership
- BIT: research design leadership and technical advice
- PHE: independent technical advice

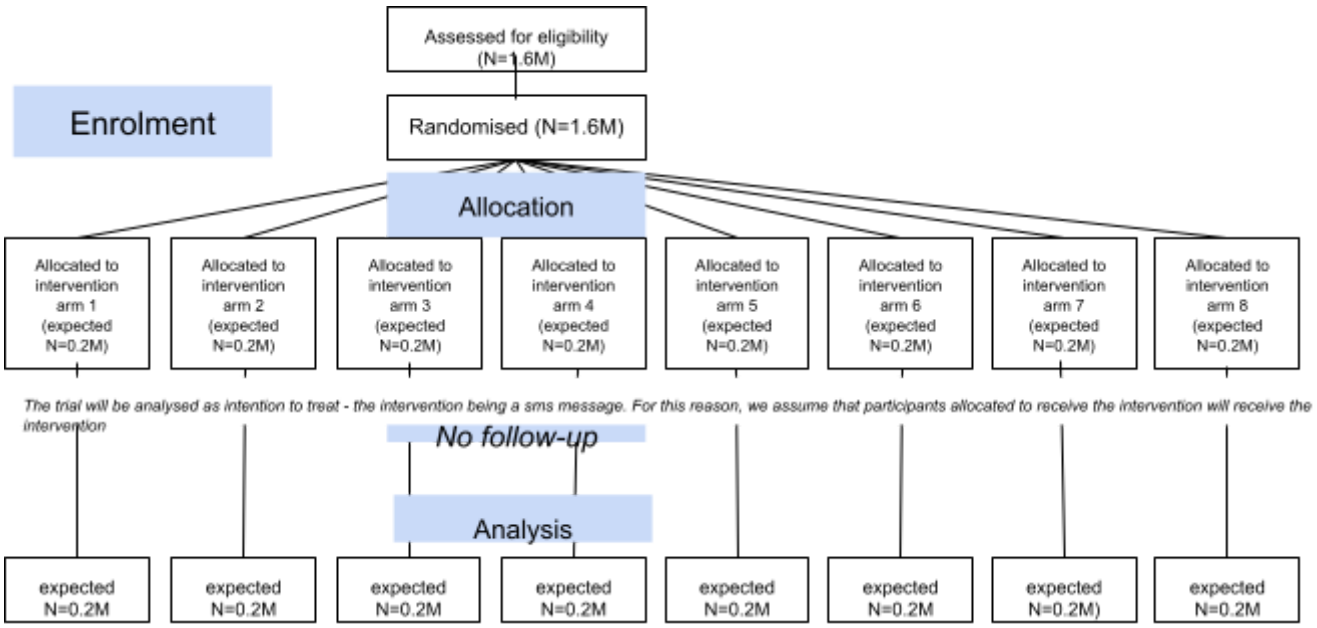
The Sponsor holds responsibility for initiation and management of the study. They are responsible for the implementation of the interventions in this research and control the final decision regarding dissemination of the results of the study.

KEY WORDS:	Field RCT, COVID-19 vaccine, text intervention, vaccine booking, vaccination, behavioural insights

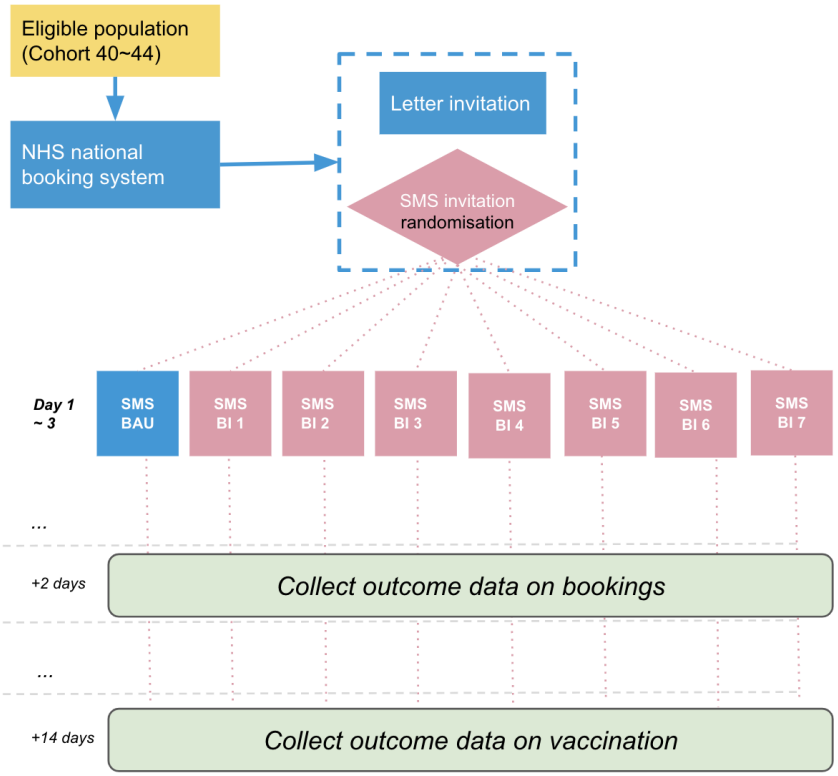
STUDY FLOW CHART

The following two charts outline the study design in CONSORT format and in BIT's internal format (which provides additional information on timelines of the two outcome measures collected):

Consort format



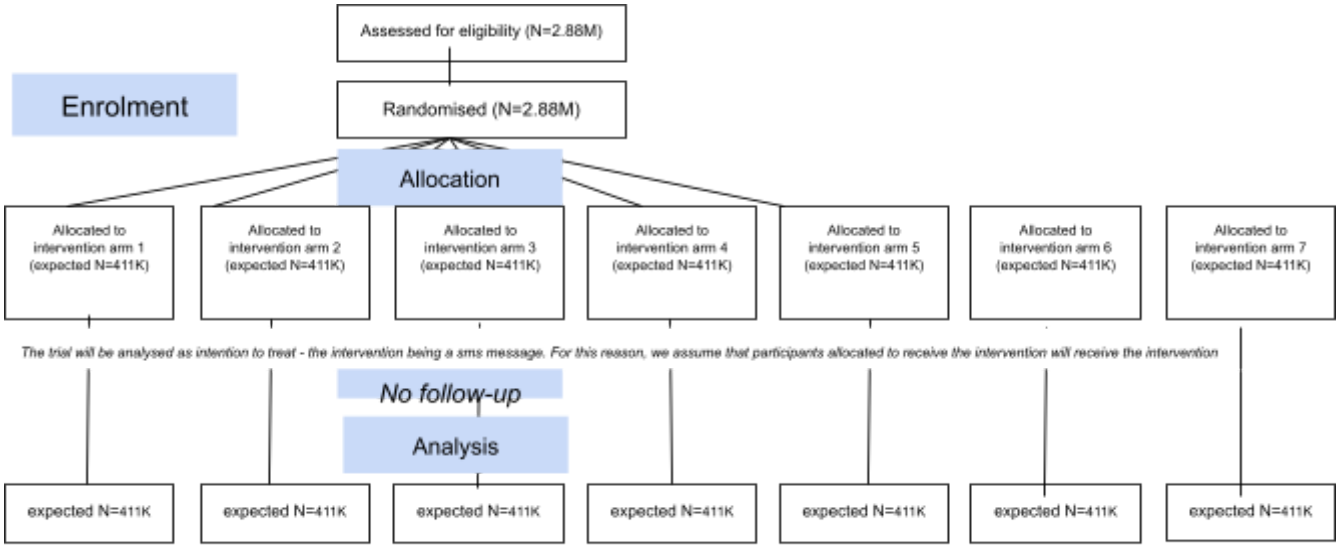
Flow chart in BIT format



EXTENSION STUDY FLOW CHART

The following chart outlines the study design of the extension in CONSORT format:

Consort format



Intervention messages

Trial arm	Theme	Content of text messages
1	Control (BAU)	You are now eligible for your free NHS Covid-19 vaccine. Please book yours now at [LINK] or by calling 119.
2	Simple	You can now book your free NHS Covid-19 vaccine. Please book yours now at [LINK] or by calling 119.
3	Reserved	Your free NHS Covid-19 vaccine is waiting for you. Please book yours now at [LINK] or by calling 119.
4	Top of queue	You've reached the top of the queue and are a priority for getting a free NHS Covid-19 vaccine. Please book yours now at [LINK] or by calling 119.
5	Social norm	You are now eligible for your free NHS Covid-19 vaccine. Join the millions who have already had theirs. Please book yours now at [LINK] or by calling 119.
6	Convenience	You are now eligible for your free NHS Covid-19 vaccine. Choose a time and place that suits you. Please book yours now at [LINK] or by calling 119.
7	Protection against virus	You are now eligible for your free NHS Covid-19 vaccine. Getting vaccinated is the best protection against coronavirus. Please book yours now at [LINK] or by calling 119.
8	Protect you and those close to you	You are now eligible for your free NHS Covid-19 vaccine. Getting the vaccine is the best way to protect yourself and those close to you against coronavirus. Please book yours now at [LINK] or by calling 119.

Note. These messages have all been approved by Simon Enright, Director of Communications at NHS England and NHS Improvement.

EXTENSION

Intervention messages

Theme	Message
1. Control	*You are now eligible for your free NHS COVID-19 vaccine. Please book yours now at [LINK] or by calling 119.*
2. Top of queue	*You have reached the top of the queue and are a priority for getting a free NHS COVID-19 vaccine. Please book yours now at [LINK] or by calling 119.*
3. Convenience	*You are now eligible for your free NHS COVID-19 vaccine. Choose a time and place that suits you. Please book yours now at [LINK] or by calling 119.*
4. Reserved	*Your free NHS COVID-19 vaccine is waiting for you. Please book yours now at [LINK] or by calling 119.*
5. Top of queue + convenience	*You have reached the top of the queue and are a priority for getting a free NHS COVID-19 vaccine. Please book yours now - choose a time and a place that suits you at [LINK] or by calling 119.*
6. Reserved + convenience	*Your free NHS COVID-19 vaccine is waiting for you. Please book yours now - choose a time and a place that suits you at [LINK] or by calling 119.*
7. Front of queue	*You have reached the front of the queue and are a priority for getting a free NHS COVID-19 vaccine. Please book yours now at [LINK] or by calling 119.*

Note: The control message (message 1) is the same as the control message sent to the cohort aged 40 - 44. Three of the treatment messages (2, 3 and 4) are the three highest-performing messages from the experiment among the 40 - 44 cohort.

The remaining three messages (5, 6, 7) have been newly developed for the 18 - 29 cohort. These two messages test slightly revised wording or combine elements of the three most successful messages from the initial experiment.

Due to time-constraints imposed by the ongoing vaccine rollout it is not possible to pre-test the proposed messages with an online panel. For this reason we have taken a conservative approach to selecting the messages, either implementing or building on the messages that were most successful among the 40 - 44 cohort.

These messages have all been approved by James Lyons, Director of Communications at NHS England and NHS Improvement. (having succeeded Simon Enright in this role since the start of this study)

STUDY PROTOCOL

Using text messages to boost COVID-19 vaccination appointment booking and vaccination rates: A randomised controlled field trial.

1 BACKGROUND

The aim of this study is to test whether behaviourally-informed (BI) text messages can increase the likelihood of booking and receiving a COVID-19 vaccination among the cohort aged 40 to 49 (particularly those aged 40~44) in England. The study is a collaboration between NHS England and NHS Improvement (NHSEI), the Behavioural Insights Team (BIT), the Department of Health and Social Care (DHSC), and Public Health England (PHE).

Evidence suggests that whilst willingness to get vaccinated against COVID-19 is generally high in the UK, it may be lower among certain age and ethnicity groups. Additionally, high willingness to get vaccinated may not translate into high uptake, particularly as the vaccine rollout extends to younger cohorts. Currently, adults in England receive a text message when they are eligible for a COVID-19 vaccination with instructions on how to book an appointment. This study aims to increase the effectiveness of text messages to improve vaccination uptake.

Anonymised vaccination booking and uptake records will be analysed to determine whether people who received BI-informed text messages are more likely (compared to those receiving a non-BI-informed control text message) to book for a COVID-19 vaccine within 72 hours of receiving the text message and subsequently receive a COVID-19 vaccination within 14 days.

EXTENSION

Based on findings of this trial from cohort aged 40-44, the best performing message (top of queue) has been rolled out to all groups being newly invited to receive their first COVID-19 vaccine in England.

2 RATIONALE

Although the UK's Phase I coronavirus vaccine rollout has been a huge success (more than 58% adults have received the first dose as of Mar 30th), the uptake might decline during the Phase II rollout when the vaccination invitation is extended to younger, less vulnerable cohorts. A recent ONS survey reveals that young and Black minorities were twice as likely to report vaccine hesitancy.

As the younger cohort in the UK will soon be receiving invitations from the NHS to book their coronavirus vaccine appointment, it's important to test which behaviourally informed **vaccine invitation text messages** could increase their likelihood of **booking** and **receiving** a coronavirus vaccination. This trial will also help DHSC, NHSEI and PHE establish a protocol to iterate the design of messages for younger cohorts.

EXTENSION

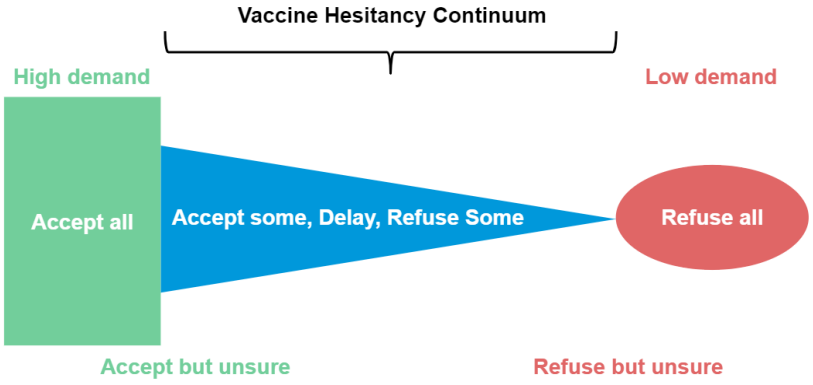
The extension to the research will determine which messages increase COVID-19 vaccine booking and vaccination rates in the cohort aged between 18 and 29 years old. The trial also analyses whether certain messages are more effective in different ethnicity groups. The research aims to inform ongoing COVID-19 vaccination messaging to boost uptake in the populations with lower uptake to date. It will also help us understand whether different age groups respond differently to behaviourally-informed text messages designed to increase booking and receiving of a coronavirus vaccination.

3 THEORETICAL FRAMEWORK

In 2014, the SAGE working group proposed the '3Cs' model of vaccine hesitancy determinants, advancing that complacency, convenience and vaccine confidence explain many of the factors that contribute to vaccine hesitancy. This has been one of the main models of vaccination used in the behavioural literature.

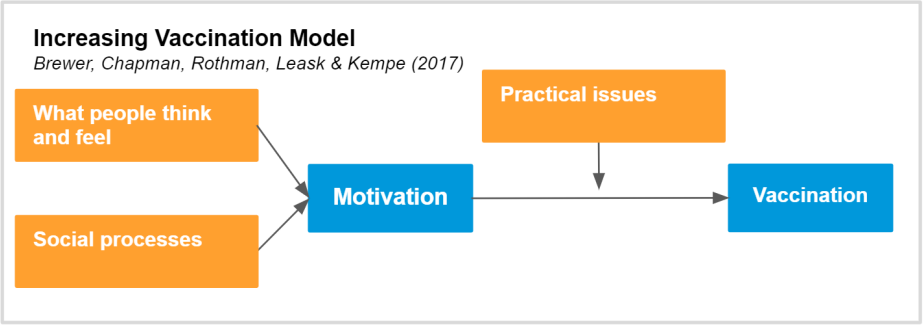
Vaccine **confidence** refers to people not having trust in vaccines and/ or the health system that delivers them. **Complacency** describes situations where people do not consider vaccines to be important. This is likely driven by the fact that the diseases they prevent are not prevalent in many places so people are naive to their potentially devastating effects. Lastly, vaccines might theoretically be available but are not necessarily **convenient** to access. In a separate paper Betsch et al. proposed an additional fourth 'C': **calculation**, to describe individuals who do not receive vaccination because they consider the costs to outweigh the benefits.

The SAGE report also describes vaccine hesitancy as a continuum, with some people accepting some vaccines and refusing others.



More recently, a paper by Brewer et al. proposed the 'Increasing Vaccination Model' to help structure thinking about the behavioural barriers to vaccination (see Figure below). The model suggests that people's attitudes (what they think and feel) and wider social processes jointly influence people's motivations and intentions towards vaccination. Practical barriers then mediate the relationship between favourable intentions to vaccinate and ultimate vaccination behaviour.

Our trial draws on these models in the following ways:



1. It aims to change behaviour amongst people who sit along the middle section of the vaccine hesitancy continuum - those who might be encouraged to get vaccinated
2. The intervention messages relate to different elements of the 'Increasing Vaccination Model' proposed by Brewer et al.. Sending SMS invitations in itself addresses practical issues relating to vaccination (e.g. by making it easier to book an appointment, as recipients can simply click a link within the SMS). The content of the SMS has also been designed specifically to make booking as easy as possible. In addition, different arms in the RCT specifically draw on the three determinants of vaccination behaviour in the model:
    - **Practical barriers:** one of the intervention arms is specifically emphasizing convenience of vaccine appointments available, as this has been identified as a specific practical barrier in the literature;
    - **What people think and feel:** different messages we aim to test draw on different individual motivations that people might have for vaccination;
    - **Social processes:** in one of the intervention arms we are planning to test a message that highlights positive social norms relating to Covid-19 vaccination.

Recent field trials have shown that reminder text messages about vaccination appointments can improve vaccine uptake by up to 8-11% (1.9-4.6pp in absolute terms), and that some messages may be more effective for specific groups. However, it's not clear to what extent the exact wording of these messages would be effective in the UK context given the cultural and linguistic differences between the US and the UK.

The proposed RCT will allow us to determine whether such behaviourally informed **vaccination invitation text messages** could increase UK patients' likelihood of **booking** and **receiving** a coronavirus vaccination.

4 RESEARCH QUESTION/AIM(S)

1. Primary research question: Which BI-informed text messages can increase the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination, compared to the control text message?

2. Secondary research question: Which BI-informed text messages can increase the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination ***among the following specific subgroups,*** compared to the control text message?

- Missing (99)
- Mixed White and any Black (D, E, M, N, P)
- "Other" ethnic group (R, S)
- White any other (C)
- Asian Indian and Mixed White and Asian or other (F, G, H)
- Pakistani, Bangladeshi and other (J, K, L)

Note. The coding and categorisation scheme of the ethnicity groups is adopted from the NIMS system. The number and categorisation of specific subgroups was decided by preliminary power calculation based on expected sample size. A more granular ethnicity breakdown than the one described here would require a larger sample size.

EXTENSION
1. Primary research question: Which BI-informed text messages can increase the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination, compared to the

control text message?

2. Secondary research question: Can we rule out that BI-informed text messages backfire (decrease by more than 2 percentage points the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination) ***among the following specific subgroups,*** compared to the control text message?

- Missing (99)
- Mixed White and any Black (D, E, M, N, P)
- "Other" ethnic group (R, S)
- White any other (C)
- Asian Indian and Mixed White and Asian or other (F, G, H)
- Pakistani, Bangladeshi and other (J, K, L)

Note. *See section 8.1 for a more detailed definition of backfire.*

4.1 Objectives

Primary Objective:
The primary objective of this study is to identify which BI-informed text messages are effective in increasing the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination among the younger cohort in England (aged 40~44).

Secondary Objective:
The secondary objective of this study is to examine the primary objective by ethnicity groups.

EXTENSION

Primary Objective:
The primary objective of this study is to identify which BI-informed text messages are effective in increasing the likelihood of booking a COVID-19 vaccination appointment and receiving first-dose vaccination among the individuals in England aged 18~29.

Secondary Objective:
The secondary objective of this study is to rule out a backfire effect of BI-informed messages (compared to control) among ethnic minority groups.

4.2 Outcome

Primary outcome: whether participants book a COVID-19 vaccination appointment (either online or by calling 119) within 72 hours of receiving the SMS invitation. This is a binary outcome, i.e. the booking status will be coded as 1 if the participant makes the booking within the time frame, and coded as 0 if they don't.

Secondary outcome: whether participants receive their first-dose vaccination within 14 days of receiving the SMS invitation. This is also a binary outcome, i.e. the vaccination status will be coded as 1 if participants receive a COVID-19 vaccination within the time frame, and coded as 0 if they don't.

EXTENSION

Primary outcome: whether participants book a COVID-19 vaccination appointment (either online or by calling 119) within 72 hours of being sent the SMS invitation. This is a binary outcome, i.e. the booking status will be coded as 1 if the participant makes the booking within the time frame, and coded as 0 if they don't.

Secondary outcomes:

- whether participants receive their first-dose vaccination within 14 days of being sent the SMS invitation. This is also a binary outcome, i.e. the vaccination status will be coded as 1 if participants receive a COVID-19 vaccination within the time frame, and coded as 0 if they don't.
- whether participants book a COVID-19 vaccination appointment (either online or by calling 119) within 14 days of being sent the SMS invitation. This is a binary outcome, i.e. the booking status will be coded as 1 if the participant makes the booking within the time frame, and coded as 0 if they don't.

5 STUDY DESIGN AND METHODS of DATA COLLECTION AND DATA ANALYSIS

5.1 Study design

This is an 8-arm field RCT with randomisation at individual level.

- **Control group** will receive the business-as-usual SMS invitation.
- **Treatment groups** will receive a behaviourally-informed (BI) SMS vaccination invitation, and the content of the messages will cover several evidence-based BI concepts. (All groups - Treatment and Control - will also receive the BAU letter invitation).
- **Spillover effects.** In individual randomisation trials, we typically consider spillover risks to be low. However, given that the trial will target the universe of eligible NHS patients, the chance of two people in the same household receiving different messages is not negligible. Our stance is that i) even if spillover happens, it will shrink the between-arm difference, thus we will only under-estimate rather than over-estimate the treatment effects; ii) implementation risks in running this trial as a clustered RCT (household level) exceed the risks of running this trial with individual randomisation. The NHSEI communications team have also drafted copy to address potential issues if people were to question the authenticity of the NHS SMS invitations on social media.

EXTENSION

This is a 7-arm field RCT with randomisation at individual level.

- **Control group** will receive the control SMS invitation (same message as in the main trial).
- **Treatment groups** will receive a behaviourally-informed (BI) SMS vaccination invitation, and the content of the messages will cover several evidence-based BI concepts. (All groups - Treatment and Control - will also receive the BAU letter invitation).

5.2 Data collection

We will collect three types of data: 1) a pseudonymised identifier, i.e. a unique identifier linked to a patient's NHS number as well as information on which version of the SMS invitation received; 2) demographic profile, including age, gender, and ethnicity; 3) outcome-related data, including vaccine booking rate within 72 hours of receiving the text message invitation and vaccination status within 14 days of receiving the text message. We will **NOT** receive data such as participants' names, addresses, GP practice, location, phone numbers or any information on medical conditions. The table below illustrates what a dummy final data set looks like.

Pseudonymised randomly generated number to merge data extracts

Note. This data set will be received for analysis by BIT and NHSEI researchers

Randomisation *Variables to construct primary outcomes* *Personal characteristics*

Pseudony-mised identifier	Message	Timestamp first message sent	Timestamp appointment booked	First appointment date	Received first-dose vaccine	Age	Gender	Ethnicity
1234XXX	A	23/03/21 10.00	23/03/21	30/03/21	Y	49	M	African
4678XXX	B	23/03/21 10.00	23/03/21	31/03/21	Y	48	M	White and Black Caribbean
9101XXX	C	23/03/21 10.00	24/03/21	30/03/21	N	48	F	Pakistani or British Pakistani
1213XXX	D	23/03/21 10.00	NA (not booked)	NA	NA	49	M	British, Mixed British
11617XXX	E	23/03/21 10.00	24/03/21	1/04/21	N	47	M	Any other White background
1617XXX	A	23/03/21 10.00	NA (not booked)	NA	Y	48	F	Bangladeshi or British Bangladeshi
1367XXX	B	23/03/21 11.00	NA (not booked)	NA	N	47	F	Caribbean

5.3 Data analysis

Primary analysis

The trial will be analysed as intention-to-treat (message sent rather than message read).
In order to estimate the impact of different SMS invites on vaccine booking and vaccination rate, we will use the following logistic model:

$$Outcome_i \sim bernoulli(p_i);$$
$$logit(p_i) = \alpha + \beta_1 BImessage1 + \beta_2 BImessage2_i + ... + \beta_7 BImessage7_i + \gamma X'$$

where:

- Outcome_i refers to*:*
    - Any booking made within 72 hours of sending the message (*primary outcome, ITT*). The booking status outcome will be coded as 1 if participants make the booking within the time frame, and coded as 0 if they don't.
    - Any first-dose vaccination received within 14 days of receiving the SMS (*secondary outcome*). The vaccination status will be coded as 1 if participants receive their vaccination within the time frame, and coded as 0 if they don't.

- BImessage_1...BImessage_7 is a set of dummies, each representing one of the 7 behaviorally inform messages drafted. The reference group is the group receiving the control message - this is why there are 7 dummies instead of 8

- X' is a vector of characteristics such as age, gender and ethnicity subgroups (the reference group will be White – British and Irish (A, B), and the other subgroups are specified in the research question section slide). It also includes timestamps e.g. date and time of receiving the text.

$\hat{\beta}_1 ... \hat{\beta}_7$ constitute the estimated parameter of interest. They represent the impact of BImessageX on the outcome, compared to the control sms.

P-values will be adjusted for multiple comparisons using Benjamini-Hochberg correction, treating each ethnicity as a separate family of hypothesis tests in which each arm is compared to the control with a maximum false discovery rate of 5%.

Secondary analysis

In order to estimate the impact of different SMS invites on vaccine booking and vaccination rate **among each ethnic group**, we will use the following logistic model:

$$Outcome_i \sim bernoulli(p_i);$$
$$logit(p_i) = \alpha + \beta_1 BImessage1 + \beta_2 BImessage2_i + ... + \beta_7 BImessage7_i + \gamma X' \ if \ ethnic \ group \ = k$$

where:

- Outcome_i refers to*:*
    - Any booking made within 72 hours of sending the message (*primary outcome, ITT*). The booking status outcome will be coded as 1 if participants make the booking within the time frame, and coded as 0 if they don't.
    - Any first-dose vaccination received within 14 days of receiving the SMS (*secondary outcome*). The vaccination status will be coded as 1 if participants receive their

vaccination within the time frame, and coded as 0 if they don't.

- X' is a vector of characteristics such as age, gender. It also includes timestamps e.g. date and time of receiving the text.
- k=1...7 are the different ethnicity subgroups. The **reference group** will be White – British and Irish (A, B), and **the other subgroups** 1...6 are specified in the research question section slide).

$\hat{\beta}_1 \ldots \hat{\beta}_7$ constitute the estimated parameter of interest. In each regression, they represent the impact of BImessageX on the outcome, compared to the control SMS, for the ethnic group k considered.

P-values will be adjusted by multiple comparisons using Benjamini-Hochberg correction, treating each ethnicity as a separate family of hypothesis tests in which each arm is compared to the control with a maximum false discovery rate of 5%.

EXTENSION

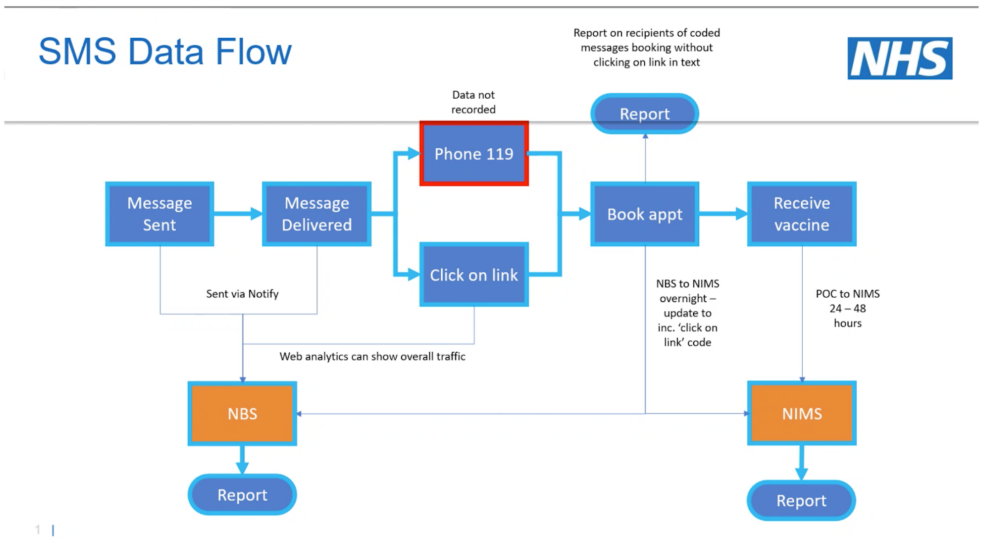
The analysis will follow the same strategy of the main experiment, but it will include one additional secondary outcome - booking rate within 14 days from being sent the message.

Statistical packages

Researchers at BIT will use Rstudio1.2 & R3.6.0 and Stata 16th Edition statistical packages to analyze the results.

6 STUDY SETTING

Data will be collected through the National Immunization Management Service (NIMS) system. NIMS will pull data from different sources, including 119 and the NHS official vaccination booking website. Details of the data flow is illustrated in the figure below:



7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

Participants will be adults aged between 40 and 49 residing in England who are eligible to get an NHS COVID-19 vaccine and who haven't been invited by the National Immunisation Management Service (NIMS) system.

7.1.1 Inclusion criteria

- Registered in the NHSEI system with a mobile phone number;

- Aged between 40-49 (particularly those between 40 to 44) who are eligible for COVID-19 vaccination;

- Haven't received an NHS COVID-19 SMS invitation via the national immunisation management service system.

EXTENSION

- Aged between 18-29 (most likely 29-26) who are eligible for COVID-19 vaccination;

- Registered in the NHSEI system with a mobile phone number;

- Haven't received an NHS COVID-19 SMS invitation via the national immunisation management service system.

7.1.2 Exclusion criteria

- Adults not in the specified age band or not a resident in England;

- Adults residing in England who have already received or been invited for the NHS COVID-19 vaccine via the national immunisation management service system;

- Adults residing in England who have not registered with the NHS or are not reachable by the NHS via SMS.

7.2 Sampling

7.2.1 Size of sample

Estimated size of the **40 - 49 years old cohort** (data source: NIMS):

- 5.44 million in total
- 544,000 per year group

Expected **sample size** for this study:

- We expect to send the SMS invitations to 3 year groups (42, 43, 44), i.e. 1.63 million participants in total
- The actual sample size will depend on vaccine supply and vaccination capacity

EXTENSION

Estimated size of the **18 - 29 years old cohort** (data source: NIMS):

- 8 million in total
- 670,000 per year group

Expected **sample size** for this study:

- We expect to send the SMS invitations to 4 year groups (26, 27, 28, 29), i.e. 2.88 million participants in total
- The actual sample size will depend on vaccine supply and vaccination capacity

7.2.2 Sampling technique

We will use a stratified sampling technique to select participants. Eligible participants will be stratified by age, and we will send text messages starting with older year groups and progressing to younger ones according in line with their eligibility. The rationale of the sampling strategy is that vulnerability to the coronavirus increases with age, thus older people have priority over younger people.

7.3 Recruitment

7.3.1 Sample identification

NHSEI will identify eligible participants using the NIMS system and pull the data from the National Booking System and NIMS system. SMS invitations will be sent to all eligible participants according to year group, starting with the oldest cohort eligible at the time of the study. There are no costs involved for participants to participate in this study.

7.3.2 Consent

We are not seeking consent for this trial for six reasons:

- Participants will have already consented to receive SMS communication from the NHS. However, we recognise that this consent does not imply that the patient has consented to be part of this research study.
- The intervention itself does not affect the treatment being provided to the patient by the NHS.
- Seeking informed consent could lead to observer or "Hawthorne" effects. That is, patients' knowing they are part of a trial may influence their behaviour and affect the external validity of the trial.
- Seeking informed consent could also lead to selection effects whereby those that opt into the trial may be different from the wider population of interest. This would affect the robustness of any findings, since results in the study may not be replicated in the wider patient population.
- Seeking informed consent would have added an additional burden both to participants and to the service as it would require an additional contact point to seek consent. There is also no existing way in the National Immunisation Management System (NIMS) to record this consent, therefore technical changes would have to be made by NIMS to allow this. We felt that this was an unnecessary burden for the already stretched NIMS.
- Only pseudonymised data will be transferred to BIT and NHSEI researchers for analysis.
- There are precedents for not seeking informed consent for text messaging trials. For example, an earlier trial (17/YH/0264) involving text messages interventions received NHS REC approval.

8 ETHICAL AND REGULATORY CONSIDERATIONS

The aim of the intervention is to encourage recipients to receive their COVID-19 vaccine, which will lower their risk from COVID-19. Overall we believe this will have health benefits for recipients and the risk is minimal.

Potential risks

One risk of SMS interventions is that the BI messages might not work equally well for everyone. This

may result in some groups of participants being encouraged to book a vaccine, but might inadvertently discourage some other groups from booking it. This risk has been minimised by developing the messages based on evidence available in the literature, as well as input from experts at BIT, NHS and PHE. In addition, to further minimise this risk, messages have been pre-tested using an online panel, excluding any message performing worse than the business as usual message.

Potential benefits
For participants less motivated to get a COVID-19 vaccine, the messages might motivate or simply prompt them to get one, lowering their risk of severe outcomes from COVID-19 infection. Therefore we believe this will have health benefits for participants.

Potential ethical concerns
There is an ethical issue that some patients will get messages that are more effective than others, even if there is no backfire effect. However, we cannot know in advance of the trial which message will be most effective, so ex-ante participants all have an equal chance of getting the most effective one. However, no participants will receive a text message who would not otherwise have received one and all messages will contain the same information for booking appointments. There is no additional booking burden for intervention recipients; they will simply receive a different invitation message directing them to book a vaccination appointment in the usual way.

8.1 Assessment and management of risk

One risk is that the behaviourally-informed messages have an unintended **backfire effect** and reduce vaccination uptake in some groups. This risk has been minimised by developing the messages based on the evidence available from related research, as well as input from experts at the Behavioural Insights Team (BIT), NHS England and NHS Improvement (NHSEI), and Public Health England (PHE). To further mitigate this risk, messages have been pre-tested with an online panel and messages leading to a significant decrease in intention to get vaccinated have not been included in the trial. In addition, all participants who haven't booked an appointment within two weeks will receive a reminder delivered via post, further mitigating the risk of potential message backfiring.

Mitigation strategies:
If backfire occurs for any BI message or for any ethnicity group, we propose the following mitigation strategy: **every participant** who hasn’t booked an appointment will be sent the default reminder letter in **14-16 days** (the status quo being 14-21 days) after they receive the SMS invitation.

Definition of backfire: Any BI message arm whose corresponding booking rate within 72 hours is equal to or more than **2** percentage points lower (and the effect is **significant**) compared to the business-as-usual message (either for all sample or for any of the 6 specific ethnic groups). It’s worth noting that if the negative effects are ***not statistically significant***, or if the magnitude of negative effects is ***less than 2 percentage points***, we won’t classify them as backfire.

8.2 Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the study, a favourable opinion for the study protocol will be sought from the Cornwall and Plymouth REC.

- Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site.
- All correspondence with the REC will be retained.
- It is the Chief Investigator's responsibility to produce the annual reports as required.
- The Chief Investigator will notify the REC of the end of the study.
- An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended.
- If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination.
- Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

Amendments

If the sponsor wishes to make a substantial amendment to the REC application or the supporting documents, the sponsor will submit a valid notice of amendment to the REC for consideration.

The sponsor does not anticipate wishing to make a substantial amendment. However, in case this changes, the following process would be followed:

- The Chief Investigator, Michelle Kane, would be responsible for the decision to amend the protocol and for deciding whether an amendment is substantial or non-substantial. She would be advised by the study steering group.
- Substantive changes would be communicated to the REC through submission of a valid notice of amendment.
- The amendment history will be tracked through version numbering of the trial protocol.

8.3 Peer review

This research project and research protocol has been reviewed by the following groups:

The Behavioural Insights Team's Director of health and education Hugo Harper, chief scientist Alex Sutherland, and head of quantitative research James Lawrence have reviewed the project through a health policy lens and a research lens, giving critical feedback on the research methods.

Dale Weston from PHE and Simon Enright from NHSEI have reviewed the design of behaviourally-informed messages.

Robert Scott from NHSEI has reviewed the data flow and power calculations.

8.4 Patient & Public Involvement

The public are involved in three stages of research: Design of the research, Undertaking the research, and Dissemination of findings

We have involved some members of the public to pre-test the content of the coronavirus vaccine SMS invitation. The COVID-19 vaccine SMS invitation will be sent to eligible population cohorts. We will share the research findings with the public via blogs, reports, or other media.

8.5 Protocol compliance

We will document protocol deviations, non-compliances, or breaches which are departures from the approved protocol.

- Accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.
- We will adhere to the protocol as much as possible and preempt frequent deviations from the protocol.

8.6 Data protection and patient confidentiality

- The physical security arrangements for storage of personal data during the study

As part of the BAU processes for sending the invitation SMS, Microsoft Azure cloud hosting is established for processing purposes and the contract in place is GDPR compliant with appropriate controls in place to secure infrastructure.

For the purpose of this study, researchers will receive pseudonymised data. These data will be stored encrypted on BIT and NHSEI servers and access will be password-restricted on a need-to-know basis.

All researchers' laptops have anti-virus applications installed and encrypted hard-drives to protect data stored locally.

- Limiting access to the minimum number of individuals necessary for quality control, audit, and analysis.

The data will only be assessed by a limited number of individuals. NHSE staff will have access to patients' phone numbers (in line with BAU processes) to send text messages to patients.

The research team will receive pseudonymised information (and will not have access to a linking key) to conduct data analysis in order to answer the research questions. We are not planning on seeking consent for this study, as outlined above.

- How the confidentiality of data will be preserved when the data are transmitted to sponsors and co-investigators

For the purpose of this study, researchers will receive pseudonymised data only. Patients will be assigned unique numbers (different from NHS or hospital identifiers) and researchers at BIT and NHSEI (who will analyse the data) will not have access to the linking key (which will also be securely deleted once all data have been transferred to the researchers).

All personal data collected as part of the study will be treated with the strictest confidence and processed only in accordance with the requirements of the GDPR and the Data Protection Act 2018.

BIT and NHSEI will take reasonable steps to protect personal information and follow procedures designed to minimise unauthorised access, alteration, loss or disclosure of personal information hosted by them.

BIT and NHSEI ensure that those who have temporary or regular access to personal data, or that are involved in the processing of personal data, are trained and informed of their duties and responsibilities when processing personal data. BIT and NHSEI provide such access on

a need-to-know basis, and have measures in place which are designed to remove that access once it is no longer required.

Physical personal devices used by BIT and NHSEI are encrypted to protect personal data. BIT and NHSEI have put in place procedures to deal with any suspected personal data breach and will notify any applicable regulator of a breach where we are legally required to do so.

Data will be transmitted via a secure service for sharing large data files; this is most likely to be Quatrix or possibly Vitru.

- How long the data will be stored for.

Personal data be stored or accessed for 6 – 12 months after the study has ended for secondary analysis and publication's purpose.

- Who is the data custodian?

Kevin Willis will be the data custodian. His contact details are as follows:
Post: Data Protection Officer and Solicitor at NHS Digital
Work Address: Skipton House 80 London Road London SE1 6LH
Email: kevin.willis@nhs.net

8.7 Indemnity

1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the sponsor(s) for harm to participants arising from the management of the research?

   NHS indemnity scheme will apply (as this study is sponsored by the NHS).

2. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of the sponsor(s) or employer(s) for harm to participants arising from the design of the research?
   NHS indemnity scheme will apply (protocol authors with NHS contracts only)

3. What arrangements will be made for insurance and/ or indemnity to meet the potential legal liability of investigators/collaborators arising from harm to participants in the conduct of the research? Note that if the study involves sites that are not covered by the NHS indemnity scheme (e.g. GP surgeries in primary care) these investigators/collaborators will need to ensure that their activity on the study is covered under their own professional indemnity.

   NHS indemnity scheme or professional indemnity will apply (participants recruited at NHS sites only)

4. Has the sponsor(s) made arrangements for payment of compensation in the event of harm to the research participants where no legal liability arises?

   No

5. If equipment is to be provided to site(s) for the purposes of the study, the protocol should describe what arrangements will be made for insurance and/ or indemnity to meet the potential legal liability arising in relation to the equipment (e.g. loss, damage, maintenance responsibilities for the equipment itself, harm to participants or site staff arising from the use of the equipment)

   No

8.8 Access to the final study dataset

The anonymised final data set will be analysed by the research team at BIT (Dr Giulia Tagliaferri, Dr Lev Tankelevitch and other members of BIT's research team, if required) and NHSEI (Robert Scott and Rachel Rosen).

All researchers will be physically located in the United Kingdom. Given continuing government advice to work from home where possible, researchers will be following this guidance and conducting the analysis on secure encrypted organisational network drives, accessed remotely by their NHSEI or BIT laptops.

EXTENSION
The anonymised final data set will be analysed by the research team at BIT (Sarah Merriam, Pujen Shreshta and other members of BIT's research team, if required) and NHSEI (Robert Scott and Rachel Rosen).

These researchers will be physically located in the United Kingdom.

9 DISSEMINATION POLICY

9.1 Dissemination policy

We intend to disseminate the findings from this study in the following forms:

- Peer reviewed scientific journals (TBD)
- Conference presentations (TBD)
- Internal reports
- Publication on organisational websites
- Blog posts
- Other publications and media

Final decision on publication rests with the study sponsor.

9.2 Authorship eligibility guidelines and any intended use of professional writers

We will abide by the NHS authorship guidelines when deciding authorship.
Broadly speaking, authorship will be given to individuals who have contributed meaningfully in the inception, design, implementation, analysis, and manuscript drafting stages.

10 REFERENCES

References have been hyperlinked throughout the manuscript.

11. APPENDICES

11.1 Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	1.2	27/5/2021	Hannah Behrendt	The research will be extended to test whether behaviourally-informed (BI) text messages can increase the likelihood of booking and receiving COVID-19 vaccination among a cohort of individuals, aged 18-29. Inclusion criteria will be extended to

				include individuals aged 18-29 who are eligible for COVID-19 vaccination. The remaining inclusion and exclusion criteria will still apply. Methods, randomisation procedures and data handling will remain the same as in the first experiment among the cohort aged 40-49. The following sections of the trial protocol have been updated - all update are under the heading "EXTENSION" ● Key study contacts ● Study summary ● Funding and support in kind ● Study flow chart ● Intervention messages ● Background ● Rationale ● Objectives ● Outcome ● Research question/aims ● Study design ● Data analysis ● Inclusion criteria ● Size of sample ● Access to the final study dataset