

PRINCIPLE TRIAL: TEXT MESSAGE INFORMATION FOR PARTICIPANTS

This is a message from Dr XX at XX Medical Practice. A clinical trial exploring treatment for the COVID-19 virus is taking place. If you experience **a new or worsening continuous cough and/or a high temperature** and have had it for **less than 14 days and are not starting to feel better**, please click [here](#) to find out more. Please call the Trial Team if you have any questions or do not have access to online systems: 0800 138 0880

PRINCIPLE TRIAL: TEXT MESSAGE INFORMATION FOR PARTICIPANTS (SHORT VERSION)

This is from Dr xxxxxxxx at XX re COVID-19. If you currently feel unwell with a **new/worsening cough or high temp** or develop these symptoms later, and would like to know about a clinical trial you could participate in click [HERE](#) or call the Trial Team 0800 138 0880.

NHS 111 London Ambulance – Email for eligible patient containing link to online consent form

Dear XXXXX,

Thank you for your recent call to the NHS 111 service and your interest in the PRINCIPLE trial. The symptoms you have described suggest you may be able to join this trial, which is testing possible treatments for COVID-19.

To find out more and to complete your registration into the trial please follow the link provided below:

<Link here>

If you have any questions or are having difficulty accessing our online systems, please call: 0800 138 0880. The 111 service has no further information regarding this trial.

Kind regards,

The PRINCIPLE trial team

NHS 111 London Ambulance - Email for non-eligible patient thanking them for their time completing screening over the phone

Dear XXXXXXXX

Thank you for completing the screening for the PRINCIPLE trial.

Unfortunately, you are not eligible to take part in the study.

We very much appreciate you taking the time to complete the screening process.

Kind regards,

The PRINCIPLE trial team

PRINCIPLE – Text message for Daily Diary

Daily Diary – days 1-7

Hello, this is the PRINCIPLE trial team. Please complete today's daily diary even if you feel better. If you have trial medication please remember to take the full course. If you have any questions or there is a problem please call trial team on XXXXXXXX. Thank you for your time. To opt out of these messages send 'PRINCIPLE STOP' to XXXX.

Daily Diary – days 8-27

Hello, this is the PRINCIPLE trial team. Please complete today's daily diary even if you feel better. Thank you for your time. To opt out of these messages send 'PRINCIPLE STOP' to XXXX.

Daily Diary – day 28

Hello, this is the PRINCIPLE trial team. Please complete the last daily diary. We may call you within the next 1 – 3 days to collect some final trial data. Thank you for your participation in the PRINCIPLE trial, your time has helped to contribute to this important research.

NHS 111 National - TEXT MESSAGE INFORMATION FOR PARTICIPANTS

This is a message from the NHS 111 service on behalf of the PRINCIPLE clinical trial team in relation to the COVID-19 outbreak. The symptoms you have described suggest you may be able to join the trial which is testing possible treatments. If you would like further information about the PRINCIPLE Trial, please [click here](#). Please call the Trial Team if you have any questions or cannot access online systems: 0800 138 0880. The 111 service has no further information regarding this trial.



Radcliffe Observatory Quarter, Woodstock Road, Oxford. OX2 6GG
Tel: 0800 138 0880 • principle@phc.ox.ac.uk • www.phc.ox.ac.uk/ctu

Date:

Dear Dr _____,

Name of patient:

Patient's date of birth:

This patient was entered into the PRINCIPLE trial on (insert date): _____

Further information about PRINCIPLE is available on the attached sheet or at

<https://www.phctrials.ox.ac.uk/principle-trial>

A copy of your patients consent form is attached. **Please retain the consent form, along with this letter, in your patient's medical record.** Please note that your patient has given consent for us to gather information from their medical notes.

The treatment your patient has been randomised to receive is:

Trial Treatment: _____

For patients in the active treatment arm, please put the drug details as an 'outside' prescription in your clinical record so that it is visible in the Emergency Care Summary if the patient contacts NHS24 or is admitted to hospital.

Please report any Serious Adverse Events (SAEs) other than hospitalisation or death due to COVID-19 infection to the Scottish trial team within 24 hours.

PRINCIPLE Trial details

Site ID:

Local trial team contact details:

PRINCIPLE Patient ID:

Many thanks.

The PRINCIPLE team

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Tel: 0800 138 0880 • principle@phc.ox.ac.uk • www.phc.ox.ac.uk/ctu

What is the PRINCIPLE trial?

The PRINCIPLE trial is one of three UK-wide COVID-19 trial platforms (the other two are in hospitals). It will evaluate a series of drugs which are potential treatments for COVID-19. The first drug evaluated is hydroxychloroquine, and the second drug will be azithromycin. The primary outcome is hospital admission with COVID-19 or death within 28 days of randomisation.

What do I have to do?

The Oxford and local trial teams will manage trial medication prescribing and dispensing and core data collection. You may be asked to help with eligibility screening and with follow-up data extraction (these will be done by the trial team for most patients, but it is important that we get complete data on death and hospital admission for patients who are lost to follow-up). We would also like you to report any adverse events which come to your attention.

What are Serious Adverse Events (SAEs) and how do I report them?

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening at the time of the event
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above. Hospitalisation and death due to COVID-19 are our trial primary outcomes so do not need reporting as SAEs. Please report SAEs to the **Scottish Trial contact listed on the patient notification**. The Trial Team will need to know the PRINCIPLE Patient ID, and a brief description of when the SAE happened and what it consisted of. The trial team is responsible for assessing if the adverse event is likely related or not to the trial medication, and for reporting to regulators.

Please report SAEs using the SAE form provided, which contains date of birth, but no other personal identifiable information.

Can I refer patients to the trial?

Yes. If you see a patient who you think is likely to have COVID-19, then you can tell them to get in touch with the Oxford trial team to find out more. They can do this by any of:

Website: www.principletrial.org
Tel: 0800 138 0880
email: principle@phc.ox.ac.uk

To be eligible patients have to be within 14 days of symptom onset AND:

1. Be aged 65 years and over
- OR



Radcliffe Observatory Quarter, Woodstock Road, Oxford. OX2 6GG
Tel: 0800 138 0880 • principle@phc.ox.ac.uk • www.phc.ox.ac.uk/ctu

2. Be aged 50-64
years and also

have one or more of high blood pressure, heart disease, diabetes (but *not* on insulin),
asthma or lung disease, stroke or neurological problems, immunodeficiency or
immunosuppression, or mild-moderate liver disease.

The Oxford trial team will then fully screen them for eligibility.



Website Trial Advert

Join a COVID-19 clinical trial

The PRINCIPLE trial aims to find treatments that reduce hospital admission and improve symptoms for people with COVID-19. You could be eligible to join if

- You have had these symptoms for fewer than 15 days:
 - a continuous new or worsening cough
 - a high temperature
- You are aged 50 to 64 with a pre-existing illness
- You are aged 65 and above
 - **Find out more**

IRAS PROJECT ID 281958, REC Reference 20/SC/0158 Confirmation of favourable opinion for substantial amendment

berkshire.rec@hra.nhs.uk <noreply@harp.org.uk>

Mon 5/4/2020 12:48

To: Christopher Butler <christopher.butler@phc.ox.ac.uk>; CTRG Sponsorship Correspondence <ctr@admin.ox.ac.uk>
Cc: nhsg.nrspcc@nhs.net <nhsg.nrspcc@nhs.net>; Hannah Swayze <hannah.swayze@phc.ox.ac.uk>

1 attachments (96 KB)

IRAS 281958 SL32_Favourable_opinion_of_a_substantial_amendment-1.pdf;

Dear Dr Butler

IRAS project ID:	281958
REC reference:	20/SC/0158
Short Study title:	PRINCIPLE
Date complete amendment submission received:	01 May 2020
Amendment No./ Sponsor Ref:	SA4
Amendment Date:	30 April 2020
Amendment Type:	Substantial
Outcome of HRA Assessment	This email also constitutes HRA and HCRW Approval for the amendment, and you should not expect anything further.

I am pleased to confirm that this amendment has been reviewed by the Research Ethics Committee and has received a Favourable Opinion. Please find attached a copy of the Favourable Opinion letter.

HRA and HCRW Approval Status

As detailed above, **this email also constitutes HRA and HCRW Approval for the amendment**. No separate notice of HRA and HCRW Approval will be issued. You should implement this amendment at NHS organisations in England and/or Wales, in line with the conditions outlined in your categorisation email.

- If this study has HRA and HCRW Approval, this amendment may be implemented at participating NHS organisations in England and/or Wales once the conditions detailed in the categorisation section above have been met
- If this study is a pre-HRA Approval study, this amendment may be implemented at participating NHS organisations in England and/or Wales that have NHS Permission, once the conditions detailed in the categorisation section above have been met. For participating NHS organisations in England and/or Wales that do not have NHS Permission, these sites should be covered by HRA and HCRW Approval before the amendment is implemented at them, please see below;
- If this study is awaiting HRA and HCRW Approval, I have passed your amendment to my colleague and you should receive separate notification that the study has received HRA and HCRW Approval, incorporating approval for this amendment.

User Feedback

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: <http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/>.

If you require further information, please contact [amendments@hra.nhs.uk]amendments@hra.nhs.uk

20/SC/0158/AM05 Please quote this number on all correspondence

Kind regards

Alison Doherty

Approvals Administrator

Health Research Authority

Bristol REC Centre | Whitefriars | BS1 2NT

T. 020 7104 8049

E. berkshire.rec@hra.nhs.uk

W. www.hra.nhs.uk

Sign up to receive our newsletter [HRA Latest](#).

IRAS 281958. Amendment confirmation of REC Validation, categorisation and implementation information

Berkshire <berkshire.rec@hra.nhs.uk>

Tue 5/5/2020 15:16

To: Christopher Butler <christopher.butler@phc.ox.ac.uk>; CTRG Sponsorship Correspondence <ctrgrg@admin.ox.ac.uk>

Cc: Hannah Swayze <hannah.swayze@phc.ox.ac.uk>

 1 attachments (127 KB)

IRAS 281958 SL27_Acknowledgement_of_a_valid_notice_of_a_substantial_amendment.pdf;

Reissued 05 May 2020

Amendment Confirmation of REC Validation, Categorisation and Implementation Information

Dear Dr Butler,

IRAS Project ID:	281958
Short Study Title:	PRINCIPLE
Date complete amendment submission received:	01 May 2020
Amendment No./ Sponsor Ref:	SA4
Amendment Date:	30 April 2020
Amendment Type:	Substantial
Outcome of HRA and HCRW Assessment	HRA and HCRW Approval for the amendment is pending. HRA and HCRW Approval for the amendment will be separately confirmed by email.
Implementation date in NHS organisations in England and/or Wales	2 days from date amendment information together with this email, is supplied to participating organisations (provided HRA and HCRW Approval for the amendment is in place and conditions are met)
Implementation date in NHS/HSC organisations in Northern Ireland and/or Scotland	5th June 2020 (providing conditions are met)
For NHS/HSC R&D Office information	
Amendment Category	A

Thank you for submitting an amendment to your project. We have now categorised your amendment and please find this, as well as other relevant information, in the table above.

Please also find attached a copy of the REC validation letter for the submitted amendment.

What should I do next?

Please read the information in [IRAS](#), which provides you with information on how and when you can implement your amendment at NHS/HSC sites in each nation, and what actions you should take now.

If you have participating NHS/HSC organisations in any other UK nations that are affected by this amendment please note that **we will** forward the amendment submission to the relevant national coordinating function(s).

If not already provided, please email to us any regulatory approvals (where applicable) once available. Your amendment will be reviewed by the REC, as per the attached letter.

When can I implement this amendment?

You may implement this amendment in line with the information in [IRAS](#). Please note that you may only implement changes described in the amendment notice.

Information relating to the addition of new sites.

This amendment also adds new participating NHS/HSC organisations to the study. The 35 day implementation date does not apply to the new sites. Please set up new sites as detailed below (as processes change from time to time, we recommend that you refer to the most up to date guidance about site set up, found within [IRAS](#)).

If your study is supported by a research network, please contact the network as early as possible to help support set up of the new site(s).

For new sites in Northern Ireland and/or Scotland:	Please start to set up your new sites. Sites may not open until a REC Favourable Opinion and NHS/HSC management permission is in place.
For new sites in England and/or Wales:	<p><u>For studies which already have HRA and HCRW Approval:</u> HRA and HCRW Approval for the amendment is pending. You can start the process of setting up the new site but cannot open the study at the site until HRA and HCRW Approval for the amendment is in place and the site has confirmed capacity and capability (where applicable).</p> <p><u>For studies which do not yet have HRA and HCRW Approval:</u> HRA and HCRW Approval for the <u>initial application</u> is pending and you will receive this in due course. You can start</p>

	the process of setting up the new site but cannot open the study at the site until HRA and HCRW Approval is in place and the site has confirmed capacity and capability (where applicable).
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Who should I contact if I have further questions about this amendment?

If you have any questions about the ethical review of this amendment, please do not hesitate to contact me.

If you have any other questions about this amendment please contact the relevant national coordinating centre for advice:

- England – amendments@hra.nhs.uk
- Northern Ireland – research.gateway@hscni.net
- Scotland – nhsg.NRSPCC@nhs.net
- Wales – HCRW.amendments@wales.nhs.uk

Additional information on the management of amendments can be found in the [IRAS guidance](#).

Please do not hesitate to contact me if you require further information.

Kind regards

Alison Doherty
Approvals Administrator
Health Research Authority

Ground Floor | Skipton House | 80 London Road | London | SE1 6LH

E. amendments@hra.nhs.uk

W. www.hra.nhs.uk

Sign up to receive our newsletter [HRA Latest](#).

This message may contain confidential information. If you are not the intended recipient please inform the sender that you have received the message in error before deleting it. Please do not disclose, copy or distribute information in this e-mail or take any action in relation to its contents. To do so is strictly prohibited and may be unlawful. Thank you for your co-operation..

FW: PRINCIPLE Substantial Amendment 4 EudraCT: 2020-001209-22

Elaine Chick <elaine.chick@admin.ox.ac.uk>

Fri 5/1/2020 12:16

To: Hannah Swayze <hannah.swayze@phc.ox.ac.uk>

Cc: rpm@oxfordjro.org <rpm@oxfordjro.org>; Emma Ogburn <emma.ogburn@phc.ox.ac.uk>

Dear Hannah

I can confirm that the above referenced substantial amendment has been reviewed in CTRG and we are happy for it to be submitted to the relevant organisations for approval. This email can be forwarded as confirmation of sponsor approval for the amendments as required.

- Email documents to the REC that originally reviewed the study. The REC will review the amendments and categorise it. If necessary, they will transfer the amendments internally to HRA for them to review as well.

- o If the amendment does not require HRA review, the REC will state this in their categorisation letter.

- o If it is sent on to the HRA, the HRA will advise you when you can send final REC and HRA approved documents to your local sites.

- Copy in CTRG generic email address (<mailto:ctrig@admin.ox.ac.uk>) so the sponsor has final documents and is included in subsequent correspondence

Please send a copy of the approval letters to the CTRG generic email address (<mailto:ctrig@admin.ox.ac.uk>) once you have received them. Please do not implement your amendments until all approvals are in place.

Best wishes

Elaine

<https://www.ox.ac.uk/>

Elaine Chick

Deputy Head CTRG, Research Services

University of Oxford

Boundary Brook House, Headington, OX3 7LQ Tel: 01865 616481

<mailto:Elaine.chick@admin.ox.ac.uk>

<https://researchsupport.admin.ox.ac.uk/ctrig>

PID14903-A004-SP001-AC001

South Central - Berkshire Research Ethics Committee

Bristol REC Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

04 May 2020

Christopher Butler
University of Oxford
Radcliffe Observatory Quarter, Woodstock Road
Oxford
OX2 6GG

Dear Dr Butler

Study title: Platform Randomised trial of Interventions against COVID-19 In older peoPLE
REC reference: 20/SC/0158
Protocol number: PRINCIPLE
EudraCT number: 2020-001209-22
Amendment number: SA4
Amendment date: 30 April 2020
IRAS project ID: 281958

Thank you for submitting the above amendment, which was received on 01 May 2020. I can confirm that this is a valid notice of a substantial amendment and will be reviewed by the Sub-Committee of the REC at its next meeting.

Documents received

The documents to be reviewed are as follows:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Annex 2: Notification of Amendment [AmendmentFormMHRAEudract_ReadyForSubmission (1)]	SA4	30 April 2020
Copies of advertisement materials for research participants [PRINCIPLE Website Advert v1.0 01.05.20]	1.0	01 May 2020
Cover Letter [REC SA4 cover letter 01.05.20]		01 May 2020
GP/consultant information sheets or letters [PRINCIPLE GP Letter Scotland v1.0 01.05.20]	1.0	01 May 2020
Letter from sponsor [SA4 Sponsor Approval 01.05.20]		01 May 2020
Other [PRINCIPLE_Text Message Info (National 111)_v1.2_01.05.20_Clean]	1.2	01 May 2020
Other [PRINCIPLE_Text Message Daily Diaries 3.0 01.05.20_Clean]	3.0	01 May 2020
Other [PRINCIPLE TRIAL - Text Message Info v2.0 01.05.2020_Clean]	2.0	01 May 2020

Other [PRINCIPLE TRIAL - Text Message Info v2.0 01.05.2020_tracked]	2.0	01 May 2020
Other [PRINCIPLE_Email_London Ambulance 111_v1.0_01.05.20]	1.0	01 May 2020
Other [PRINCIPLE_Text Message Info (National 111)_v1.2_01.05.20_tracked]	1.2	01 May 2020
Sample diary card/patient card [PRINCIPLE_Text Message Daily Diaries 3.0 01.05.20_tracked]	3.0	01 May 2020

Notification of the Committee's decision

The Committee will issue an ethical opinion on the amendment within a maximum of 35 days from the date of receipt.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval for the research.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: <https://www.hra.nhs.uk/planning-and-improving-research/learning/>

20/SC/0158:

Please quote this number on all correspondence

Yours sincerely



Alison Doherty
Approvals Administrator

Email: berkshire.rec@hra.nhs.uk

Copy to: N/A N/A CTRG

South Central - Berkshire Research Ethics Committee

Bristol REC Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

04 May 2020

Christopher Butler
University of Oxford
Radcliffe Observatory Quarter, Woodstock Road
Oxford
OX2 6GG

Dear Dr Butler

Study title: Platform Randomised trial of Interventions against COVID-19 In older peoPLE
REC reference: 20/SC/0158
Protocol number: PRINCIPLE
EudraCT number: 2020-001209-22
Amendment number: SA4
Amendment date: 30 April 2020
IRAS project ID: 281958

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

<i>Document</i>	<i>Version</i>	<i>Date</i>
Annex 2: Notification of Amendment [AmendmentFormMHRAEudract_ReadyForSubmission (1)]	SA4	30 April 2020
Copies of advertisement materials for research participants [PRINCIPLE Website Advert v1.0 01.05.20]	1.0	01 May 2020
Cover Letter [REC SA4 cover letter 01.05.20]		01 May 2020
GP/consultant information sheets or letters [PRINCIPLE GP Letter Scotland v1.0 01.05.20]	1.0	01 May 2020
Letter from sponsor [SA4 Sponsor Approval 01.05.20]		01 May 2020
Other [PRINCIPLE_Text Message Info (National	1.2	01 May 2020

111)_v1.2_01.05.20_Clean]		
Other [PRINCIPLE_Text Message Daily Diaries 3.0 01.05.20_Clean]	3.0	01 May 2020
Other [PRINCIPLE TRIAL - Text Message Info v2.0 01.05.2020_Clean]	2.0	01 May 2020
Other [PRINCIPLE TRIAL - Text Message Info v2.0 01.05.2020_tracked]	2.0	01 May 2020
Other [PRINCIPLE_Email_London Ambulance 111_v1.0_01.05.20]	1.0	01 May 2020
Other [PRINCIPLE_Text Message Info (National 111)_v1.2_01.05.20_tracked]	1.2	01 May 2020
Sample diary card/patient card [PRINCIPLE_Text Message Daily Diaries 3.0 01.05.20_tracked]	3.0	01 May 2020

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

Working with NHS Care Organisations

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

Statement of compliance

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities— see details at: <https://www.hra.nhs.uk/planning-and-improving-research/learning/>

20/SC/0158:	Please quote this number on all correspondence
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Yours sincerely
PP



Mr David Carpenter
Chair

E-mail: berkshire.rec@hra.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *N/A N/A CTRG*

South Central - Berkshire Research Ethics Committee

Attendance at Sub-Committee of the REC meeting in correspondence

Committee Members:

<i>Name</i>	<i>Profession</i>	<i>Present</i>	<i>Notes</i>
Mr David Carpenter	Retired Social Scientist	Yes	
Mike Proven		Yes	

Also in attendance:

<i>Name</i>	<i>Position (or reason for attending)</i>
Alison Doherty	Approvals Administrator

Sharon Tonner

From: Hannah Swayze
Sent: 27 May 2020 09:05
To: Sharon Tonner
Subject: Fw: PRINCIPLE SA4 Update
Attachments: SA4 REC.zip

Follow Up Flag: Flag for follow up
Flag Status: Flagged

Emily sent 2&3

From: Hannah Swayze <hannah.swayze@phc.ox.ac.uk>
Sent: Monday, May 4, 2020 17:13
To: vicki.clatworthy@oxfordhealth.nhs.uk <Vicki.Clatworthy@oxfordhealth.nhs.uk>
Cc: Helen Collins <helen.collins@nihr.ac.uk>; PRINCIPLE Study <principle@phc.ox.ac.uk>
Subject: PRINCIPLE SA4 Update

Dear Vicky,

We have just received approval for Substantial Amendment 4, details given below. The protocol wasn't updated this time and so sites won't be disrupted - this will just be for information and was mainly to allow set-up of Scotland and 111 services. All amended/new docs listed below. Are you able to disseminate to the other CRNs? Also, please can you confirm that SA3 was disseminated?

Thanks,

Hannah

- 1. Text message invite (PRINCIPLE Text Message Info, v2.0, 01.05.20)**
A short version of the text invite has been included as some GP Practices are restricted to a character count for texts **(provided to sites by CTU when given the green light)**
- 2. Daily diary reminder texts (PRINCIPLE Text Message Daily Diaries, v3.0, 01.05.20)**
The texts have been updated for clarity. **(sent out from CTU only)**
- 3. NHS 111 (National) Invitation letter (PRINCIPLE_Text Message Info (National 111), v1.2, 01.05.20)**

The trial invite will be used for patients calling NHS 111 to signpost potentially eligible patients to the Principle trial. The text has been updated to meet the requirements of NHS 111.

- 4. NHS London Ambulance 111 Invitation letter (PRINCIPLE_Email_London Ambulance 111, v1.0 01.05.20)**

London Ambulance 111 will act as a Trial Site. Clinicians at London Ambulance 111 will assess eligibility of patients for the trial. The invitation email will be used to invite these patients to the trial and if not eligible patients will be informed using the text provided.

5. GP Letter for GPs in Scotland (GP Letter Scotland, v1.0 01.05.20)

The GP letter has been updated to meet the requirements of the Health Boards in Scotland.

6. Website Advert (PRINCIPLE Website Advert, v1.0, 01.05.20)