# Protocol: A cluster randomised trial of text messaging reminders for influenza vaccine in patients under 65 in clinical risk groups in English primary care

## 1 Administrative information

### 1.1 Title

A cluster randomised trial of text messaging reminders for influenza vaccine in patients under 65 in clinical risk groups in English primary care.

### 1.2 Trial registration

Registered on clinicaltrials.gov.

### 1.3 Protocol version

Version 2.7, 11th February 2014

### 1.4 Funding

Wellcome Trust Senior Clinical Fellowship award.

### 1.5 Roles and responsibilities

Authors contributing to this protocol:


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Trial sponsor: LSHTM

### 1.6 Lay summary

Influenza causes a substantial burden to the NHS and the UK as a whole. Influenza vaccine is safe and effective but is required annually. In 2012, the UK government recommended that at least 75% of elderly people (aged 65+) and 75% people under 65 with certain chronic conditions (e.g. chronic heart disease, diabetes, asthma, etc) should be vaccinated. While primary care practices are achieving targets for the elderly, they are under-performing in patients with chronic conditions, missing a third of eligible patients in 2011/12. Therefore strategies to increase flu vaccine uptake in these patients are required.

Text messaging is already being used in some practices for flu vaccine reminders but there has been no trial assessing its effectiveness. Therefore, we propose a trial of a text message flu vaccine reminder in patients aged under 65 who have a chronic condition.

This study will randomise general practices to either standard care (seasonal flu campaign as planned), or to receive additional resources allowing them to send a targeted text messaging campaign to eligible patients aged under 65 and with a chronic condition. Vaccine uptake will be ascertained through the anonymised patient medical records.

## 1.7 Review by ethics committees

This protocol will be reviewed by:

- the London School of Hygiene and Tropical Medicine Ethics Committee;
- the Independent Scientific Advisory Committee at the Clinical Practice Research Datalink;
- the Research Projects Committee at ResearchOne, and
- the Surrey Borders National Research Ethics Committee.

# 2 Introduction

## 2.1 Background and rationale

### 2.1.1 Justification for a trial

Influenza morbidity and mortality causes a substantial financial burden to the NHS and to the UK as a whole. Influenza vaccine is safe and effective but is required annually because the circulating strain of virus changes each year. In the UK in 2012, the Chief Medical Officer (CMO) has recommended that at least 75% of elderly people (aged 65+) and 75% people under 65 with certain chronic conditions (e.g. chronic heart disease, diabetes, asthma, etc) should be vaccinated.

While primary care practices are achieving these targets for elderly patients, those set for patients with chronic conditions are not being met and have shown no substantial increases in the past decade[1]. Therefore strategies to increase flu vaccine uptake in these patients are required.

Several randomised trials have demonstrated the effectiveness of flu vaccine reminders delivered to patients by letter, postcard or telephone.[2, 3] However, use of text messaging in the NHS for appointment reminders is increasing as it is cheap, quick and effective. Text messaging is already used in roughly 30% of practices to remind patients about their flu vaccine[4] but there has been no trial addressing its effectiveness. Trials of text messaging in the US have shown some success as vaccine reminders, but whether there is an effect in UK primary care is unknown. Therefore, we propose a cluster randomised trial of a text messaging flu vaccine reminder in patients aged under 65 who have a chronic condition. We will randomise whole primary care practices to either standard care or a text messaging campaign to eligible patients.

## 2.2 Objectives

**Primary**

(i) To estimate the level of vaccine uptake in intervention and standard care groups
(ii) To evaluate the feasibility of recruiting and randomising practices to a text messaging intervention trial;
(iii) To evaluate the feasibility of practice delivery of a text message intervention to eligible patients within a primary care setting;
(iv) To evaluate the feasibility of ascertaining practice data regarding text message delivery and flu vaccine uptake.

**Secondary**

(v) To explore the acceptability of text messaging in a sample of patients

### 2.3 Trial design

A cluster randomised trial in three settings.

# 3 Methods

## 3.1 Participants, interventions and outcomes

### 3.1.1 Study setting

Three settings in UK primary care:

1. Practices contributing data to the ***Clinical Practice Research Datalink (CPRD)***, a primary care database;
2. Practices contributing data to ***ResearchOne***, a primary care database;
3. ***Practices in London using iPlato software***: Initially practices in Islington and Barnet, widening to all London boroughs to meet recruitment targets.

### 3.1.2 Eligibility criteria

Eligible practices will be those in one of the three settings described above that already use a text messaging system to communicate with patients about issues other than influenza vaccination. Within CPRD and practices in London, this system is iPlato[5]. Islington and Barnet have high iPlato coverage and therefore are ideal study settings. All practices within these boroughs will be targeted initially. We will then widen our recruitment to all iPlato practices to increase recruitment. Within CPRD, practices which have sent >100 text messages to patients for non-flu vaccine related issues will be identified and contacted (assuming other eligibility criteria are met). Within ResearchOne practices use TPP software, which has text messaging capability. Therefore all practices are automatically eligible. Practices using any other text messaging software will be excluded.

We will also exclude:

(i) Practices that used text messages for influenza vaccination reminders in the 2012/13 influenza season because their planned seasonal flu campaign is likely to include a text message to the target group. In CPRD and ResearchOne, this will be established by interrogating the practice medical records. In London practices using iPlato, the software company will provide this information.

(ii) Practices whose Clinical Commissioning Group (primary care trust) aims to send out a targeted text message campaign in all practices. The text messaging software company work with the seasonal influenza leads in each Clinical Commissioning Group and will be able to provide this information.

### 3.1.3 Interventions

This is a cluster trial[6, 7] in which whole general practices will be randomised to the intervention or control group.

Practices in the intervention arm will be asked to deliver a text message intervention to patients. Practices will receive additional support for this, comprising guidance notes regarding delivery of the message (content, timing, eligible patients) and payment for the time of a practice administrator to deliver the intervention.

The text message intervention will be an influenza vaccination reminder to patients who are under 65 in a clinical risk group (with chronic heart disease, chronic neurological disease, diabetes, chronic kidney disease, chronic liver disease, chronic respiratory disease, immunosuppression), as set out by the Chief Medical Officer. The Chief Medical Officer also recommends that pregnant women are vaccinated but due to difficulties in identifying pregnant women, and ethical issues regarding contacting them, we will not ask intervention practices to send a text message to them.

Practices will identify eligible patients based on their electronic medical records. Practices will have established systems for this using their practice software and we will not ask them to change this process.

The message content that practices will be asked to send is:

> "Hello *PATIENT NAME*, to reduce your risk of serious health problems from flu we recommend vaccination. Call *PRACTICE PHONE NUMBER* to book. *PRACTICE NAME*"

Intervention practices may be contacted up to three times during their flu season to remind and offer assistance from the text messaging software company with sending the text message to eligible patients.

**Practices in ResearchOne**: During the trial, ResearchOne collaborators will keep a record of intervention practices that have sent the text message, and will update the Chief Investigator fortnightly with this list. A named contact at practices that have not sent the message will be contacted by email by a member of the Trial Management Team up to three times to remind them to send the message. This will be done at weekly intervals from the start of the influenza campaign. Practices will be reminded that they can use the F1 help service in the TPP software for assistance in sending the message.

**Practices in CPRD or in London using iPlato**: During the trial, the iPlato software company will keep a record of intervention practices that have sent the text message, and will update the Chief Investigator weekly with this list. A named contact in practices that have not sent the message will be contacted by email by a member of the Trial Management Team up to three times to remind them to send the message. This will be done at weekly intervals from the start of the influenza campaign. Practices will be reminded that they can contact iPlato for assistance with sending the message.

An online or hard copy posted questionnaire will also be sent to practices in the intervention arm to ascertain feedback from practice staff about delivery of the intervention.

The comparison group will be asked to continue with their seasonal flu campaign as planned (standard care).

### 3.1.4 Sub-study for patient feedback

A small sub-study will also be conducted in 2 participating intervention practices. Each of these practices will send a short anonymous questionnaire to patients that were targeted in the seasonal influenza campaign. This questionnaire will be anonymised, with no personal identifiers and mailed back to the Chief Investigator in a stamped addressed envelope.

### 3.1.5 Outcomes

**Primary outcomes**

**Objective (i):** To estimate the level of vaccine uptake in intervention and standard care groups. We will measure:

- Influenza vaccine uptake, stratified by risk group;

**Secondary outcomes:**

**Objective (ii):** To evaluate the feasibility of recruiting and randomising practices to a text messaging intervention. We will measure:

- Practice recruitment rate;

**Objective (iii):** To evaluate the feasibility of practice delivery of a text message intervention to eligible patients within a primary care setting. We will measure:

- Extent that text messages are sent by practice to eligible patients;
- Practice acceptability of message, including aspects of delivery, content, results;
- Cost to practice of delivering intervention;

**Objective (iv):** To evaluate the feasibility of ascertaining practice data regarding text message delivery and flu vaccine uptake. We will measure:

- Availability of data to examine text message receipt in each risk group;
- Availability of data to examine vaccine uptake in each risk group;
- Time and cost required to gather data.
- Level of vaccine uptake in intervention and standard care groups;

**Objective (v):** Acceptability of text messaging to patients.

### 3.1.6 Practice timeline

The practice timeline is described in the table below.

| | Study period | | | | |
|---|---|---|---|---|---|
| | Enrolment | Allocation | Post allocation | | Closeout |
| Time point | Aug 2013 | Sept 2013 | Sep to Dec 2013 | Dec 2013 | Feb 2014 |
| **Enrolment:** | | | | | |
| Eligibility screen | X | | | | |
| Informed consent | X | | | | |
| Allocation | | X | | | |
| **Interventions:** | | | | | |
| Intervention | | | X | | |
| Control | | | X | | |
| **Assessments:** | | | | | |
| Practices complete questionnaire | | | | X | |
| Researchers extract relevant data from practice (age, sex, clinical risk group, influenza vaccination reminder types, vaccine uptake) | | | | | X |
| Questionnaire to patients in the substudy | | | | X | |

### 3.1.7 Sample size

At 90% power and 5% significance, we will require 180 practices to identify an increase in vaccine uptake from 54% to 57%. This 5.5% increase is a conservative estimate based on previous text messaging and vaccine reminder studies.[2] We have therefore chosen to recruit and randomise 200 practices with approximately 750 eligible patients per practice. This is based on a design effect of 0.02404; this was estimated based on clustering of influenza vaccine uptake in the 2011/12 influenza season for general practices in the CPRD.

### 3.1.8 Recruitment

#### *3.1.8.1 CPRD*

The Chief Investigator will identify eligible practices in the CPRD. The anonymised practice records of the CPRD will be interrogated to identify practice use of text messaging in the 2012/13 influenza season. Text messages to patients are recorded as Read codes. Any practice with >100 text message Read codes to patients will be defined as a frequent user of text messaging software. Practices that used text messaging for vaccination reminders in the 2012/13 influenza season will be excluded.

Eligible practices will be contacted by mail to ascertain their interest in the trial, to identify which software system is used and to establish whether the practice meets eligibility criteria.

Any interested practice that meets the eligibility criteria will be sent a consent form and further information regarding the study.

#### *3.1.8.2 ResearchOne*

All practices using TPP SystmOne software are potentially eligible for the trial as all have the facility to use the in-built text messaging software. Practices will be contacted by the Chief Investigator and asked for expressions of interest. At the time of expressing interest, practices will give consent for their anonymised records to be interrogated. Based on the practice records, the ResearchOne team will identify practices that sent a targeted text message campaign in the 2012/13 influenza season, and will also identify the CCG in which the practice sits. These data will allow eligibility criteria to be applied.

Any interested practice that meets the eligibility criteria will be sent a consent form and further information regarding the study.

#### *3.1.8.3 London practices using iPlato software*

Initially, practices in Islington and Barnet will be contacted via email for initial expressions of interest. Practices will be contacted by a member of Noclor, the North and Central London Research Consortium. Interested practices will be directed to the Chief Investigator or to a study website, where they will be able to access the practice information sheet and consent form. A formal letter of invitation, practice information sheet and consent forms will be sent to interested practices. To increase recruitment, we will also target practices using iPlato across other London boroughs.

#### *3.1.8.4 Recruitment to the sub-study*

After recruitment to the main study, practices in the intervention arm will be randomly selected for invitation to the sub-study. We aim to recruit two practices.

## 3.2 Assignment of interventions

### 3.2.1 Randomisation procedure

We will use block randomisation within each setting. In the CPRD and ResearchOne, we will stratify by region. In Islington and Barnet, we will stratify by borough.

We will randomise using random permuted blocks of size 2, 4 and 6. (Group 1 is the standard care, group 2 is intervention). 20% of blocks will be size 6, 50% of blocks size 4 and 30% of size 2. The randomisation will be blinded to practice name, and the study team will not see the randomisation list in advance.

## 3.3 Data collection, management and analysis

### 3.3.1 Data collection methods

#### *3.3.1.1 Recruitment rate*

We will record the number of practices approached, recruited and analysed.

#### *3.3.1.2 Data relating to intervention delivery from questionnaires*

Electronic questionnaires will be sent to all intervention practices in CPRD, ResearchOne and London-based practices.

#### *3.3.1.3 Data relating to measurement of exposure and outcome*

***CPRD***: In practices that contribute data to the CPRD, all exposure and outcome data will be ascertained through the anonymised electronic healthcare records, which are routinely uploaded by the practice into the database. We will collect data on age, sex, clinical risk group, vaccination reminder type (text, letter, phone call, face to face), vaccination uptake, death, transfer out of practice, flu and flu-like illness, and hospital admissions. Follow-up for practices will be complete using this method.

***ResearchOne***: In practices that contribute data to ResearchOne, all exposure and outcome data will be ascertained through the anonymised electronic healthcare records, which are routinely uploaded by the practice into the database. We will collect data on age, sex, clinical risk group, vaccination reminder (text, letter, phone call, face to face),vaccination uptake, death, transfer out of practice, flu and flu-like illness, and hospital admissions. Follow-up for all practices will be complete using this method.

For practices that do not join or withdraw from ResearchOne, we will approach the data provider (TPP SystmOne) directly to request a one-off data extract, or ask a practice administrator to extract the data for us. All data will be anonymised,

***Practices in London using iPlato software:*** Within London practices, ascertainment of exposure and outcome data will be tested through a number of methods because it is an objective of this trial to establish the best approaches for data collection based on ease of collection, cost and time. Approaches that we will use are:

(i) The GP extraction service;[8]
(ii) iPlato data collection;
(iii) Practice data interrogation by a member of research staff or practice administrator.
(iv) The EMIS data extraction service;
(v) The Vision data extraction service;
(vi) MIQUEST data extraction tool.

Data required are age, sex, clinical risk group, vaccination reminder (text, letter, phone call, face to face), vaccination uptake, death, transfer out of practice, flu and flu-like illness, and hospital admissions.

### 3.3.2 Data management

Data from the online questionnaires will be imported into a spreadsheet for analysis. These and all other practice electronic data will be stored inside a secure network at the London School of Hygiene and Tropical Medicine.

Trial consent forms, questionnaires and any correspondence with practices will be stored in locked filing cabinets at the Trial Coordinating Centre at the London School of Hygiene and Tropical Medicine. Only trial staff will have access to these.

### 3.3.3 Statistical methods

#### *3.3.3.1 Primary outcome*

We will compare vaccine uptake in the intervention and control groups using a t test.

A cluster-level analysis will be performed using practice specific proportions as observations. We will compare vaccine uptake in the intervention and standard care groups using a t test, with the size of clusters taken into account.

Although the study will be carried out in three settings, the analysis will not be stratified by setting. This is because the settings are identical in terms of the intervention used, the vaccine used and the vaccine targets. The only differences between the settings are the GP software system used by the practice. Since this will not influence vaccine uptake, there is no justification to stratify by setting.

#### *3.3.3.2 Secondary outcomes*

Across each of the three study settings, a series of descriptive statistics will be produced. Descriptive statistics will include:

- Recruitment rate:
- Number and proportion of patients within each risk group that were sent the text message;
- Proportion of practices experiencing difficulties sending the text message;
- Proportion of practices experiencing patient complaints;
- Proportion of practices describing the intervention as worthwhile;
- Proportion of practices open to participation in another text messaging trial;
- Average cost of delivering intervention;
- Cost and time required for ascertaining practice data;
- Proportion of patients who complained (sub-study data),

#### *3.3.3.3 Sensitivity and subgroup analyses*

Our primary analysis will be an intention to treat analysis. However, to account for any contamination between the standard care and intervention arms, we will carry out a per-protocol analysis.

Where available, we will also measure the difference in vaccine uptake, comparing practices that used the exact wording of the message in the study protocol with practices that used an alternative message. We hypothesise that practices using our message (based on behavioural theory) will have a higher uptake than an alternative designed by the practice. As this will be a non-randomised comparison, we will adjust for confounders.

Finally, we will compare the effectiveness of the text message based on the time of day that it was sent to patients. We hypothesise that messages sent in the late afternoon will have more effect that those sent at earlier times of day, when patients may not have the time to respond.

#### *3.3.3.4 Hawthorne effect*

The study design allows an evaluation of the generalisibility of the study population; practices that take part in the study can be compared to other practices outside of the trial that contribute data to ResearchOne and CPRD. We will test whether participation in the trial changes the behaviour of practices in their use of text messaging (Hawthorne effect).

This study will provide evidence regarding the effectiveness of text messaging reminders for influenza vaccine in patients under 65 with chronic conditions. The methodology here will be applied to future cluster randomised trials of text messaging interventions within electronic heath records.

### 3.3.4 Monitoring

The Trial Management Group will oversee the work of the coordinating centre and will meet regularly in person or by teleconference, to monitor the progress of the trial and to deal with any practical issues.

No Trial Steering Committee will be convened.

### 3.3.5 Data monitoring

An independent data monitoring and ethics committee (DMC) is not required for this trial.

### 3.3.6 Patient or usergroup involvement

We will consult with two lay members of the Steering Commitee of two CPRD trials that are currently underway.

# 4 Ethics and dissemination

## 4.1 Research ethics approval

The trial has research ethics committee approval for the UK and is gaining R&D approval from all sites. Potentially eligible practices will be provided with information about the trial to consider for up to one month. Informed consent will be sought prior to randomisation.

Approval has also been sought from the LSHTM ethics committee and the ResearchOne Projects Committee.

## 4.2 Protocol amendments

Any amendments will be submitted for approval to the appropriate bodies

## 4.3 Consent

Self-completion consent forms (attached in Appendix 5.1) will be mailed to practices, returnable to the Chief Investigator at the London School of Hygiene and Tropical Medicine.

## 4.4 Confidentiality

Patient and practice data will be stored as described in section 3.3.2. Any identifiable patient data will be anonymised and stored inside a secure network. Access to data will be controlled.

## 4.5 Declaration of interests

No competing interests declared.

## 4.6 Access to data

The data will be accessed by authorised persons from the London School of Hygiene & Tropical Medicine of research governance authorities to check that the study is being carried out correctly. All will have a duty of confidentiality and no data will be disclosed outside the research site. All patient- and practice-level information will be kept strictly confidential.

## 4.7 Dissemination policy

The results of the trial will be published in peer reviewed journals and a report will be disseminated to all participating practices.

# 5 Appendices

## 5.1 Informed consent materials

**Informed Consent Form for Practices**

Practice name: _____
Practice address:_____
_____
_____

Please could you provide the email address of practice member of staff who will take responsibility for the text message campaign?_____

Study Protocol Number: 2.4

Clinicaltrials.gov number:

Full Title of Project: *A cluster randomised trial of text messaging reminders for influenza vaccine in patients under 65 in clinical risk groups in English primary care.*

Name of Principal Investigator: Liam Smeeth

| | | **Please initial box** |
|---|---|---|
| 1. | I confirm that I have read and understand the practice information sheet dated 22/08/2013 (version 2.5) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered fully. | ☐ |
| 2. | I understand that my practice's participation is voluntary and we are free to withdraw at any time, without giving any reason, without our legal rights being affected. | ☐ |
| 3. | I understand that vaccine uptake data collected during the study may be looked at by responsible individuals from the London School of Hygiene and Tropical Medicine, from regulatory authorities or from the NHS Trust, where it is relevant to taking part in this research. I give permission for these individuals to access our practice records. | ☐ |
| 4. | I agree to our practice taking part in the above study. | ☐ |

_____ _____ _____

Name of Person giving consent Signature Date

1 copy for practice (original); 1 copy for Principal Investigator

# 6 References


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4. Dexter LJ, Teare MD, Dexter M, Siriwardena AN, Read RC. Strategies to increase influenza vaccination rates: Outcomes of a nationwide cross-sectional survey of uk general practice. *BMJ Open*. 2012;2
5. Iplato (www.Iplato.Net) accessed 17 april 2012.
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7. Weijer C, Grimshaw JM, Eccles MP, McRae AD, White A, Brehaut JC, Taljaard M. The ottawa statement on the ethical design and conduct of cluster randomized trials. *PLoS Med*. 2012;9:e1001346
8. General practice extraction service (http://www.Hscic.Gov.Uk/gpes) accessed 25 april 2012.

# 7 Read code lists

The following are Read code lists that we will use to ascertain text message exposure and vaccine uptake outcome data in the Clinical Practice Research Datalink and ResearchOne datasets.

## 7.1 Influenza vaccination

| Read code | Read term |
|---|---|
| 65E..00 | influenza vaccination |
| 65E2.00 | influenza vaccination given by other healthcare provider |
| 65E2000 | Seasonal influenza vaccination given by other healthcare provider |
| 65ED.00 | Seasonal influenza vaccination |
| 65ED000 | Seasonal influenza vaccination |
| 9OX8.00 | has influenza vaccination at work |
| ZV04800 | [v]influenza vaccination |
| ZV04811 | [v]flu - influenza vaccination |

In addition to these Read codes, influenza vaccination will be based on therapy codes using BNF codes 14.4.2 (Vaaccines and Antisera – influenza vaccines)

## 7.2 Text message vaccination reminder

| Read code | Read term |
|---|---|
| 9OXC.00 | influenza vaccination invitation sms text message sent |
| 9OXC100 | influenza vaccination invitation 1st sms text message sent |
| 9OXC200 | influenza vaccination invitation 2nd sms text message sent |
| 9OXC300 | influenza vaccination invitation 3rd sms text message sent |