PROTOCOL

STUDY SUMMARY

Study title	An improvement project to evaluate the effectiveness of different reminders designed to increase the University Hospitals Birmingham NHS Foundation Trust's staff uptake of the seasonal influenza vaccine
Short study title	An improvement project around staffs' influenza vaccine uptake
Chief Investigator's address and contact	Title / Name: Prof Richard J Lilford Post: Professor/CLAHRC-West Midlands Director Qualifications: PhD., FRCOG., FRCP., FFPH., DSc. (Hons) Employer: Warwick Medical School Address: Medical School Building University of Warwick, Coventry Post Code: CV4 7AJ Email: R.J.Lilford@warwick.ac.uk Phone: 02476575884
Collaborator's address and contact	Title / Name: Dr Kelly Ann Schmidtke Post: Research Fellow Address: Warwick Business School University of Warwick Scarman Road, Coventry CV4 7AL Email: Kelly.Schmidtke@wbs.ac.uk Phone: 07758933026 Title / Name: Prof Ivo Vlaev Post: Professor Address: Warwick Business School University of Warwick Scarman Road, Coventry CV4 7AL Email: Ivo.Vlaev@wbs.ac.uk Phone: 02476522945 Title / Name: Mr Lawrence Tallon Post: Director of Strategy, Planning and Performance Address: University Hospitals Birmingham NHS Foundation Trust Trust Headquarters Queen Elizabeth Medical Centre PO Box 9551 Main Drive, Edgbaston Birmingham B15 2PR Email: Lawrence.Tallon@uhb.nhs.uk Title / Name: Dr. Peter Nightingale Post: Statistician Address: Institute of Translational Medicine, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK, B15 2TH Email: peter.nightingale@uhb.nhs.uk

	Title / Name: Suzy Gallier Post: Clinical Business Development Lead Address: University Hospitals Birmingham NHS Foundation Trust Level 1 Queen Elizabeth Hospital Birmingham Mindelsohn Way, Edgbaston, Birmingham, B15 2GW Email: suzy.gallier@uhb.nhs.uk Title / Name: Katherine Reeves Post: Statistical Intelligence Analyst Address: University Hospitals Birmingham NHS Foundation Trust Level 1 Queen Elizabeth Hospital Birmingham Mindelsohn Way, Edgbaston, Birmingham, B15 2GW Email: Katherine.Reeves@uhb.nhs.uk
UHB Director of Communication's contact	Title / Name: Fiona Alexander Email: fiona.alexander@uhb.nhs.uk Phone: 0121 371 4325 0 797 386 9365
Sponsor's address and contact	Name of organization: University Hospitals Birmingham NHS Foundation Trust Name of person: Dr Chris Counsel Address: 1st Floor, Education Centre Queen Elizabeth Hospital Mindelsohn Way, Edgbaston Birmingham B15 2WB Email: chris.counsell@uhb.nhs.uk Phone: 01213714185
Funder	Collaboration for Leadership in Applied Health Research and Care - West Midlands University of Warwick Office Room A155 1st Floor Health Sciences Warwick Medical School University of Warwick Coventry CV4 7AJ
ClinicalTrials.gov Number	ClinicalTrials.gov Identifier: NCT03637036
Design	Randomized Controlled Trial. Participants randomized in equal proportions, stratified by site and job role
Participants	University Hospitals Birmingham NHS Foundation Trust staff eligible for the seasonal influenza vaccination
Sample size	Up to 18,000
Treatment duration	About 2-min
Project duration	5 months October 2018 to February 2019

Gantt Chart. Responsibility of:

University of Birmingham (UofB)	University of Warwick (UofW)	UofW and UHB

Stage 1

		Sep	Oct	Nov	Dec	Jan	Feb	Mar
Randomize participants to receive different letter types	UHB's Clinical Business Development Lead will create and send a data file to UHB's statistician that identifies each front line staff member, their worksite, and their job role.							
	UHB's statistician will randomize staff (stratified by worksite and job role) to groups that receive different letter types.							
Disseminate letters	UHB's communications team will disseminate the reminders according to the randomization schedule.							
	UHB Occupational Health Department will monitor vaccine uptake as per reporting protocols already in place.							
Retrieve data	UHB's Clinical Business Development Lead will create a data file to send UHB's statistician that describes: (1) the date each participant was vaccinated or no date – up to the 4th of January, (2) whether each participant indicated refusal to vaccinate, (3) whether each participant indicated receiving the vaccination elsewhere, and each participant's (4) group-assignment, (5) gender, (6) site, (7) job role.							
Analyze data	UHB's statistician will analyze the data.							
Write-up results	UHB's statistician and UofW's researchers will discuss the analyses interpret the findings.							
Write-up full reports	UofW's researchers will write-up the project for publication.							

Approvals being sought to conduct this study.

The decision as to whether the present study requires NHS-REC approval was decided using the Health Research Authority's tools: "Is my study research?" [1] and "Do I need NHS-REC approval?"[2] The outcomes provided by these tools are described in Table 1.

Table 1.

Is my study reseach?	Yes
Do I need NHS-REC approval?	No but may need other approvals, e.g., HRA and potentially site approvals.

Summary of study. (limit 300 words)

Seasonal vaccination against influenza is recommended for NHS staff.[3,4] To increase vaccination rates, NHS England put forth a Commissioning for Quality and Innovation goal for the 2018/2019 season of 75%.[5] University Hospitals Birmingham NHS Foundation Trust (UHB) wants its vaccination rate to surpass this target. Since staff get infected outside of the hospital and from patients staff vaccination does not provide significant 'herd immunity'

To reach past targets, every September UHB already invites staff to take up the vaccination, and regularly reminds staff that have not yet vaccinated to do so. The current protocol describes a randomized controlled trial (RCT) in which staff will be sent a different letter when first invited to receive vaccination, and we will compare the proportion of staff that go on to vaccinate after receiving each type of letter..

To conduct the RCT the research team will design four letter styles. One factor will emphasize an authority figure inviting staff to vaccinate (the Chief Executive, who is also a doctor). The other factor will emphasize a competitive social norm describing vaccination rates in peer hospitals, including Addenbrooke's, Cambridge University Hospitals (which has exemplary rates) see appendix A and across American hospitals (which also have high rates). Letters will be sent to staff in the last week in September by UHB's communications team and they will be disseminated in a randomized fashion.

The UoW's role in this study is to advise the study's design and write-up the project for publication. UHB will approve the reminders, send the reminders, retrieve the data, and analyse the data. No individual-level data will be transferred across organizations. All individual-level data will be managed by authorized UHB employees, e.g., a UHB statistician will randomize staff to receive different reminders and analyze the data, and UHB's communication team to disseminate the reminders.

Questions.		**Data/Outcomes.**	**Analyses.**
Primary:	Will the content of different wording on the letters requesting NHS staff to receive the seasonal influenza vaccination affect the rate at which those staff are vaccinated?	• Staff IDs- this is needed to randomize and send letters-Will be deleted after data collection ceases • Staff Name-this is needed to address letters, e.g., "Dear [name]" -Will be deleted after data collection ceases • Group Number (e.g., 0=letter version one, 1=letter version two, 2=) • Date of Vaccination at Trust (DD-MM-YYYY, or blank if the vaccination was never received), • Indicating Refusal to take up the vaccination (0=No, 1=Yes), • Indicating Vaccinating at non-Trust Location, e.g., general practice (0=No, 1=Yes)	The primary analysis will compare the proportions of staff that take up the vaccination in each group, where each group receives a different letter. The rates of vaccination will be analyzed with a binary logistic regression model including an interaction term and the two main effects. While all forms of wording will encourage uptake, we hypothesise that some will work better than others.
Secondary:	Will the effect sizes vary across different demographics?	There are no secondary outcome measures, but information related to the participants' worksite, job role and gender will be used as predictors in the secondary analyses. • Worksite (0=Queen Elizabeth, 1=Heartlands, 2=Solihull, 3=Good Hope), • Job role (1=Doctor, 2=Nurse, 3=Other-frontline), 4=Other-non-frontline), • Gender (0=Female, 1=Male, 2=Not indicated).	The secondary analysis will look for differences in the letter wording effectiveness related to sub-group demographics, i.e., worksite, job roles, and gender.
		Data retrieval will be facilitated by UHB's Clinical Business Development Lead from UHB's MyFluJab database, and from Occupational Health data systems.	Analyses will be conducted by a UHB statistician according to UHB's secure protocols.

Summary of main issues.

No significant ethical, legal, or management issues arise from this study.

The largest risk of this study is the opportunity for NHS staff data to be leaked. To minimize this risk, no individual-level data will be transferred across organizations. Rather all data will be retrieved and analyzed by authorized UHB staff.

Scientific Justification.

This research is worth doing because current vaccination rates among NHS staff remain lower than desired. The variation among NHS trusts' vaccination rates (from less than 40% to more than 80%)[6] suggests that some trusts' may doing something better. Unfortunately, reviews of past data do not easily indicate malleable factors as to why the rates differ. The current study will examine one malleable factor that may affect uptake rates, i.e., the content of letters asking staff to vaccinate.

Design and methodology.

Null Hypothesis: All the letters will similarly influence the rate at which staff take up the vaccination.
Alt Hypothesis: The letters will differently influence the rate at which staff take up the vaccination.

The RCT method was selected, because it is the most robust method through which to make causal inferences. The RCT method is feasible, because UHB already monitors whether each staff member receives the vaccination.

There will be no 'no-treatment' control group. All letters will non-coercively invite NHS staff to take up the vaccination, though we expect some reminders to work better than others.

Letter wordings are given Appendix A. One factor will emphasize an authority figure inviting staff to vaccinate. The other factor will emphasize a competitive social norm describing peer hospital performance. Letters will be sent both by e-mail and through the internal post.

UHB's Clinical Business Development Lead will send UHB's statistician a data file in mid-September containing information about staff who should be invited to have a vaccination:

(1) IDs-needed to randomize at an individual level
(2) Staff Name-needed to address reminders, e.g., "Dear [name]"
(3) Worksites-needed to stratify randomization, and
(4) Job Roles-needed to stratify randomization.

We expect this file to include up to 18,000 NHS staff members, and this number is more than sufficient for our primary comparison. UHB's statistician will randomize these staff to receive one of the letters and then will help UHB's communications team to disseminate the letters according to the randomized schedule.

In January UHB's Clinical Business Development Lead will send UHB's statistician a data file describing whether those staff randomized to receive a letter went on to get vaccinated by the 4th of January. The data will contain information describing each staff member's:

(1) ID,
(2) Worksite,
(3) Job Role,
(4) Gender,
(5) Group,
(6) Date vaccination was received at Trust, if ever,

(7) Whether the staff member indicated not intending to take up vaccination, and
(8) Whether the staff member has indicated receiving the vaccination from another source, e.g., general practice.

UHB's statistician will analyze the data and then interpret the findings with UoW's researchers. UoW's researchers will write-up the findings for publication.

Randomization Process.

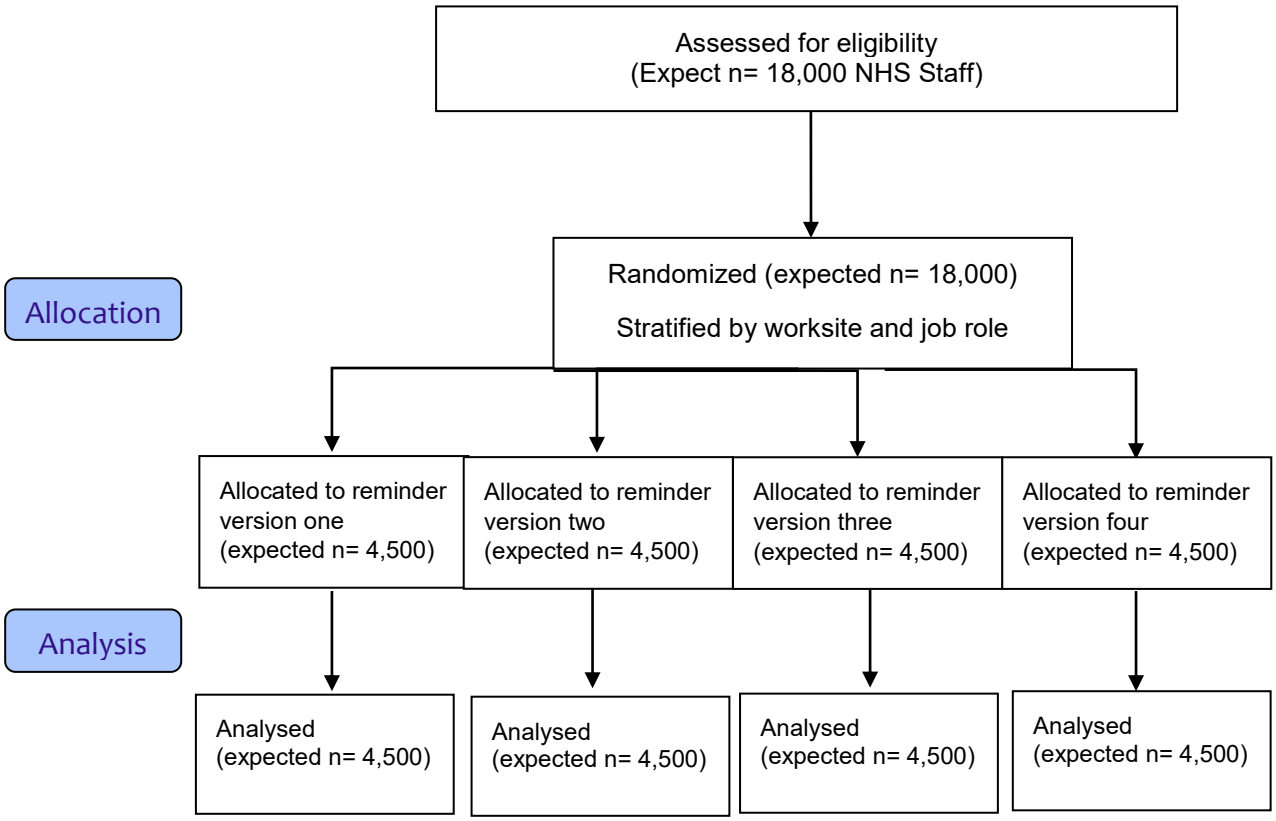
Yes.

Each NHS staff member will be randomized to one of the available groups, and each group will receive a different letter.

The randomization will be stratified by worksite and job role. The random number function RAND in Microsoft Excel will be used to generate random numbers and within each of the 12 strata the 25% of staff with the lowest values will be assigned to group 1, etc.

Participants.

Samples Size:	Up to 18,000
How was the sample size decided?	UHB aims to vaccinate approximately 18,000 NHS staff. The following sample-size calculations were performed (using an assumed alpha rate of 0.05 and a beta of 0.8) for a binary logistic regression model including an interaction term as well as two main effects. To detect an interaction such that the uptake is 40% in three of the groups and 50% in the other group will require a sample-size of at least 750 per group. Thus, we have a sufficient sample size to find a much smaller difference overall and differences in sub-groups.
Inclusion:	All UHB staff eligible for the seasonal influenza vaccination are eligible for this study.
Exclusion:	No patients will be excluded.
Duration in study:	NHS staff will be monitored in this study for approximately 4 months, i.e., from the date the letter is disseminated (near the end of September) through the 4th of January 2019. Note that our observations only involve recording when NHS staff receive the vaccination, and such data are already routinely recorded.
Risks:	There are no risks beyond standard practice. The largest risk regards NHS staff's personal data being leaked. To minimize the risk of data leaks, no data will be transferred across organizations. Rather data will be retrieved and analyzed by authorized UHB staff according to UHB's standard protocols.
Benefits:	NHS staff participants will contribute to our understanding of what types of reminders more effectively motivate NHS staff to vaccinate.


Assessed for eligibility
(Expect n= 18,000 NHS Staff)
Randomized (expected n= 18,000)
Stratified by worksite and job role
Allocation
Allocated to reminder version one (expected n= 4,500)
Allocated to reminder version two (expected n= 4,500)
Allocated to reminder version three (expected n= 4,500)
Allocated to reminder version four (expected n= 4,500)
Analysis
Analysed (expected n= 4,500)
Analysed (expected n= 4,500)
Analysed (expected n= 4,500)
Analysed (expected n= 4,500)

Participant Identification/Recruitment.

How will potential participants, records or samples be identified? Who will carry this out and what resources will be used?	UHB's Clinical Business Development Lead will identify NHS staff members who should be vaccinated using regularly collected information in UHB's Information Systems. We will be using the IT Flu Application developed in-house by UHB's Information Technology team from which UHB can extract staff level data indicating who has been vaccinated and their role. We will use similar systems at the other sites
Will the identification of potential participants involve reviewing or screening the identifiable personal information of patients, service users or any other person?	Yes. The identification of potential NHS staff members will involve reviewing the identifiable personal information. UHB's Clinical Business Development Lead will identify NHS staff members who are eligible to be vaccinated using regularly collected information in UHB's Information Systems.
Describe what measures will be taken to ensure there is no breach of any duty of confidentiality owed to patients, service users or any other person in the process of identifying potential participants.	To minimize the risk of data leaks, no data will be transferred across organizations. Rather data will retrieved and analyzed by authorized UHB staff according to UHB's standard protocols.
Will researchers or individuals other than the direct care team have access to identifiable personal information of any potential participants?	No
Will any participants be recruited by publicity through posters, leaflets, adverts or websites?	No
How and by whom will potential participants first be approached?	NHS staff participants will not be explicitly recruited, because their part in this study will be incidental as part of their normal staff experience. Recall that UHB already reminds staff to receive the vaccination and monitors whether those staff are vaccinated.
Will you obtain informed consent from or on behalf of research participants?	No. As stated above (for the How and by whom question), participants' part in this study will be incidental.
Will you recruit any participants who are involved in current research or have recently been involved in any research prior to recruitment?	Not known. No steps will be taken to find out whether the NHS staff are involved in other research, because (regardless of their involvement in other research) all staff are regularly reminded to

	take up the seasonal influenza vaccination.
Will you be undertaking any of the following activities at any stage (including in the identification of potential participants)?	Participants in this study are NHS Staff. The data collected are already regularly gathered and analyzed by UHB administrators for reporting.

Information about the data storage.

Please describe the physical security arrangements for storage of personal data during the study?	The data will be encrypted during transfer between authorized UHB staff over UHB network connections. No data will transfer outside of UHB. The data will be stored by UBS's statistician during the study in password protected files according to UHB's standard protocols.
How will you ensure the confidentiality of personal data?	No personal data will be stored after the data retrieval has ceased. Rather all personal data will be deleted and replaced with an anonymous ID.
Who will have access to participants' personal data during the study?	Only authorized UHB will have access to that data during the study.
Where will the data generated by the study be analyzed and by whom?	The data files used during this study will be created by UHB's Clinical Business Development Lead at UHB according to UHB's standard protocols. The data will be analyzed by a UHB statistician according to UHB's standard protocols.
Who will have control of and act as the custodian for the data generated by the study?	The data custodian will be a UHB statistician named in this protocol. If this UHB statistician is not able to fulfill this duty, an amendment will be submitted to replace the named statistician. The UHB statistician will conduct all analyses and no data will be transferred outside UHB.
For how long will you store research data generated by the study?	10-years
How long will personal data be stored or accessed after the study has ended?	No personal data will be stored after the study ends.
Please give details of the long term arrangements for storage of research data after the study has ended.	No identifiable data will be stored after data collection has ceased. The non-identifiable data will be stored on secure UHB servers in a password protected file. The statistician named on this protocol will have access to the data and will allow access to the data to regulators if requested.

Will you inform participants of the results?
The findings will be shared through the UHB's regular communication channels, e.g., the Trust's newsletter and all staff briefing.

Funder Responsibility.
CLAHRC money will be made available to cover 2.5% of Prof Richard Lilford's FTE salary over the duration of this project, i.e., approximately 4 hours per month. CLAHRC money will also be made available to pay for the dissemination materials if necessary, e.g., publication cost.

Conflicts of interest
Neither the participants nor the research team members will receive any payments (beyond typical salary) or other reimbursements for their part in this study.

Study Management.
The Study Management/Steering Committee will meet at the beginning of the study (October) the middle (December) and the end (March) to discuss the study and manage any concerns. Members are as follows:

- Prof Richard Lilford
- Dr Kelly Ann Schmidtke
- Prof Ivo Vlaev
- Mr Lawrence Tallon
- Peter Nightingale

Additional people may join the meeting upon as necessary to address issues as they arise.

Dissemination outside of UHB Authorship.
The findings will be written-up for an academic journal and may be presented at conferences/workshops. Any publication/presentation will acknowledge the funder's support.

All protocol contributors will be eligible for authorship. The author order and the addition of authors will be determined by the chief investigator.

Approvals to conduct.
The study described in this protocol will not be initiated before the protocol has received approval/favorable opinion from the Health Research Authority (HRA) and participating sites. If HRA deems that this study requires a sponsor, any consideration for amendments will immediately be given to the sponsor with a detailed justification. The sponsor will then decide whether such amendments constitute a non-substantial or substantial amendments. Amendments that require HRA approval will not be instituted until they received approval/favorable opinion from the HRA. Minor amendments may be implemented immediately, and the HRA will be informed.

The study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996,[7] the principles of Good Clinical Practice,[8] and the Department of Health Research Governance Framework for Health and Social Care, 2005.[9]

Appendix 1.

On the next page are four letter formats. One factor is the presence of an authority figure giving staff access to the vaccinations. The authority figure is Dr David Rosser, the Chief Executive and also a medical doctor. The other factor is the presence of descriptive norms describing the proportions of staff that have been vaccinated in peer hospitals.

Within the examples the highlighted areas indicate where these two factors are active.

GREEN = authority factor.
YELLOW = norms factor.

Emailed Letters.

Letter one

Dear colleague,

You are invited to take up your free flu jab this season to reduce your risk, and your patients' risk, of getting the flu.

Find out how to get your jab at the Trust, please visit the [_____] part of the Intranet or ask your line manager.

We appreciate your support in keeping colleagues and patients safe,

Occupational; Health Department

Letter two

Dear name,

I am inviting you to take up your free flu jab this season to reduce your risk, and your patients' risk, of getting the flu.

Last winter, the national expectation was for at least 70% of frontline staff to be vaccinated against seasonal flu. That was achieved at QEHB, with **71.6%**, and at Heartlands, Good Hope and Solihull with **73.5%**. This year, the national expectation is for 75% of frontline staff to be vaccinated.

However, we want UHB to be amongst the very best performers of similar hospitals, so that we maximise protection for our staff and patients. We know it is entirely achievable, with your support, for us to reach or surpass the levels of some of the best performers from last year:

Royal Liverpool & Broadgreen	**86.9%** of frontline staff vaccinated
Cambridge University Hospitals	**84.3%**
Birmingham Children's Hospital	**82.1%**
Leeds Teaching Hospitals	**80.8%**
Guy's and St Thomas's	**79.9%**

In the United States 92% of hospital staff receive flu vaccination.

Find out how to get your jab at the Trust, please visit the [_____] part of the Intranet or ask your line manager.

I appreciate your support in keeping colleagues and patients safe,

Kind regards

Occupational Health Department

Letter three

Dear colleague,

You are invited to take up your free flu jab this season to reduce your risk, and your patients' risk, of getting the flu.

Last winter, the national expectation was for at least 70% of frontline staff to be vaccinated against seasonal flu. That was achieved at QEHB, with **71.6%**, and at Heartlands, Good Hope and Solihull with **73.5%**. This year, the national expectation is for 75% of frontline staff to be vaccinated.

However, we want UHB to be amongst the very best performers of similar hospitals, so that we maximise protection for our staff and patients. We know it is entirely achievable, with your support, for us to reach or surpass the levels of some of the best performers from last year:

Royal Liverpool & Broadgreen	**86.9%** of frontline staff vaccinated
Cambridge University Hospitals	**84.3%**
Birmingham Children's Hospital	**82.1%**
Leeds Teaching Hospitals	**80.8%**
Guy's and St Thomas's	**79.9%**

In the United States 92% of hospital staff receive flu vaccination.

Find out how to get your jab at the Trust, please visit the [_____] part of the Intranet or ask your line manager.

We appreciate your support in keeping colleagues and patients safe,

Occupational; Health Department

Letter four

Dear name,

I am inviting you to take up your free flu jab this season to reduce your risk, and your patients' risk, of getting the flu.

Last winter, the national expectation was for at least 70% of frontline staff to be vaccinated against seasonal flu. That was achieved at QEHB, with **71.6%**, and at Heartlands, Good Hope and Solihull with **73.5%**. This year, the national expectation is for 75% of frontline staff to be vaccinated.

However, we want UHB to be amongst the very best performers of similar hospitals, so that we maximise protection for our staff and patients. We know it is entirely achievable, with

your support, for us to reach or surpass the levels of some of the best performers from last year:

Royal Liverpool & Broadgreen	**86.9%** of frontline staff vaccinated
Cambridge University Hospitals	**84.3%**
Birmingham Children's Hospital	**82.1%**
Leeds Teaching Hospitals	**80.8%**
Guy's and St Thomas's	**79.9%**

In the United States 92% of hospital staff receive flu vaccination.

Find out how to get your jab at the Trust, please visit the [_____] part of the Intranet or ask your line manager.

I appreciate your support in keeping colleagues and patients safe,

Kind regards

Dr Dave Rosser

Chief Executive

References.

[1] http://www.hra-decisiontools.org.uk/research/redirect.html
[2] http://www.hra-decisiontools.org.uk/ethics/
[3] England Public Health. (2016). Healthcare worker vaccination: Clinical evidence. London: PHE, 2016. http://www.nhsemployers.org/~/media/Employers/Publications/Flu%20Fighter/flu%20fighter%20clinical%20evidence%20Aug%202016.pdf [Accessed 20/05/2018
[4] Pereira, M., Williams, S., Restrick, L., Cuninon, P., Hopkinson, N. S., et al. (2017). Healthcare worker influenza vaccination and sickness absence: an ecological study, *Clinical Medicine*, *17*, 484-489.
[5] NHS England. (2018). NHS staff health & wellbeing: CQUIN 2017-19 Indicator 1 Implementation Support. https://www.england.nhs.uk/wp-content/uploads/2018/05/staff-health-wellbeing-cquin-2017-19-implementation-support.pdf [Accessed 20/05/2018]
[6] Public Health England. (2018). Seasonal influenza vaccine uptake amongst frontline healthcare workers (HCWs) in England. December Survey 2017/18. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/710531/Seasonal_influenza_vaccine_uptake_HCWs_winter_season_2017_to_2018.pdf
[7] https://www.wma.net/wp-content/uploads/2016/11/DoH-Oct1996.pdf
[8] https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/good-clinical-practice/
[9] https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/139565/dh_4122427.pdf

Statistical Analysis Plan

Version: 1
Date: 21-December-2018

Trial Title: An improvement project to evaluate the effectiveness of different reminders designed to increase the University Hospitals Birmingham NHS Foundation Trust's staff uptake of the seasonal influenza vaccine.

Authors:

- Schmidtke, Kelly (Kelly.Schmidtke@wbs.ac.uk, Research Fellow, University of Warwick)
- Nightingale, Peter (peter.nightingale@uhb.nhs.uk, Statistician, University Hospital Birmingham NHS Foundation Trust)
- Reeves, Katharine (katharine.reeves@uhb.nhs.uk, Statistical Intelligence Analyst, University Hospital Birmingham NHS Foundation Trust)
- Lilford, Richard (r.j.lilford@warwick.ac.uk, Professor, University of Warwick)

1. INTRODUCTION

The present Statistical Analysis Plan extends the outcome analyses previously stated in the protocol version 2.0 (ClinicalTrials.gov Identifier: NCT03637036) to clarify how we will handle more analyses and a protocol deviation that occurred during the randomization process.

2. DATA

Data collection is described in protocol (version 2, page 5). However, deviations from the protocol resulted in modifications to some of the data we will have available for the analyses. Table 1 describes the data contained in the data file.

The first deviation occurred because of the four worksites originally planned to be in the trial, three could not take part. This left one worksite in the trial, i.e. Queen Elizabeth Hospital.

The second deviation affects our plans for sub-group analyses. This occurred because the trust records describe job roles differently than stated in the protocol. So instead of the job roles stated in the protocol, staff were stratified by two Employment-Types and four Job-Types.

The third deviation occurred as 898 (10.6%) of the hospital's 8438 staff randomized were allocated to a fifth, no-letter, control group. The remaining 7,540 staff were randomized to the planned four groups in equal numbers (i.e., 1885 participants to each of four groups). We will analyse data in the four groups per the original protocol and this will be the primary analysis. However, we will also carry out a subsidiary analysis to compare the results of this no-letter control group to the letter groups, as described in the below section titled 'Supplementary Analysis'.

Table 1. Data in the project analysis file

Type	Name	Codes
Intervention	Group Number	0 = Standard, 1 = Social Norms, 2 = Authority 3 = Combined, and 4 = No Letter Control
Demographics	Gender	0 = Female, and 1 = Male
	Type of Employment	0 = Bank, and 1 = Substantive
	Job Type	0 = Healthcare assistants and other support staff, 1 = Medical and dental staff, 2 = Nursing, midwifery and health visiting staff, and 3 = Scientific, therapeutic and technical staff (for the analyses, groups 0 and 3 will be combined)
Primary Outcome	Date of vaccination at Trust	DD-MM-YYYY, or blank if the vaccination was never received
Other outcomes (formally self-reported)	Refusal to take up the Vaccination	0 = No, and 1 = Yes
	Vaccinating at a non-trust location	0 = No, and 1 = Yes

3. ANALYSIS OBJECTIVES

- Objective 1 is to assess the effects of the two intervention types (Social Norms and Authority) and any interaction effect of these interventions on the on-site vaccination rates by the end of the trial, i.e. 4th of January 2019.
- Objective 2 is to assess the effects of the interventions on subgroups of the study. We are most interested in comparisons across the above stated three job types, though we will also compare the effects across genders. We will not examine the type of employment because the bank sub-group is small, but we will report the proportion of staff taking up the vaccine in this subgroup.
- Objective 3 is to assess cumulative rates of vaccinations across each group by week from the beginning to the end of the study period.

4. GENERAL ANALYSIS CONVENTIONS

All descriptive statistics will be reported with 95% confidence intervals, and statistical analyses will be two-sided.

5. ANALYSES

Our primary analysis will be a binary logistic regression analysis with on-site vaccination (0=No, 1=Yes) as the outcome variable and the two main intervention effects, Social Norms (0=No, 1=Yes) and Authority (0=No, 1=Yes), and the interaction effect as explanatory variables. The no-letter control group will not be considered in this primary analysis.

Descriptively, a table (Table 2), will be created displaying the staff vaccination uptake for each group with the corresponding exact binomial 95% confidence interval.

Table 2. Staff onsite vaccination rates

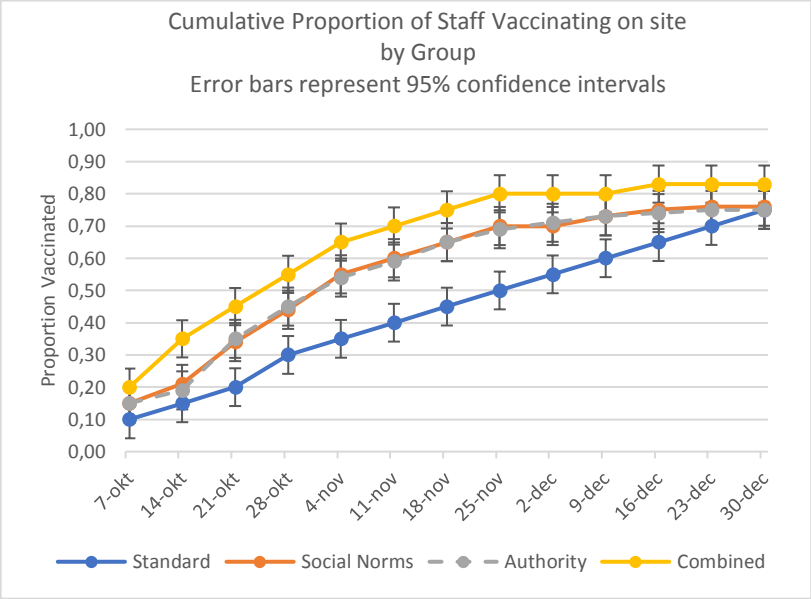
	Standard Group		**Norms Group**		**Authority Group**		**Combination Group**	
	n	**Uptake Proportion (95% Confidence Interval)**	**n**	**Uptake Proportion (95% Confidence Interval)**	**n**	**Uptake Proportion (95% Confidence Interval)**	**n**	**Uptake Proportion (95% Confidence Interval)**
Total	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Gender								
Female	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Male	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Employment-Type								
Bank	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Substantive	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Job-Type								
Medical and dental staff	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Nursing, midwifery and health visiting staff	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)
Healthcare assistants, other support staff Scientific, therapeutic and technical staff	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)	#	0.__ (0._, 0.__)

In addition to the primary analysis, a binary logistic regression analysis will be used to predict staff on-site vaccination rate (0 = No, 1= Yes) using all of the following variables: the two main intervention effects (Social Norms and Authority) and their interaction effect, Employment-type (0=Bank, 1=Substantive), Job-Type (1=Medical and dental staff, 2=Nursing, midwifery and health visiting staff, and 4= a combined group composed of Healthcare assistants, other support staff and Scientific, therapeutic and technical staff), Gender (0=Female, 1=Male) and any of the following interactions that are significant: Social Norms x Job type; Social Norms x Gender; Authority x Job type; Authority x Gender; Social Norms x Authority x Job type; and Social Norms x Authority x Gender. (If either of the three-way interactions is included, all the constituent two-way interactions will also be included.)

To achieve Objective 3, secondary analysis will assess the effects of the interventions over time, to examine the hypothesis that the benefits of the interventions may be greater nearer the beginning of the trial than nearer the end.

This effect will initially be assessed by visually examining a time-series chart, such as represented in Figure 1. We will also estimate the time to vaccination within each group to reach 70% vaccination. To do so, Kaplan–Meier rates of survival (i.e. non-vaccination) will be derived, with confidence intervals based on the exponential Greenwood formulation of the standard error. We selected 70% because this was the vaccination target and was achieve by the hospital over the 2017-2018 vaccination season. If a rate of 70% is not achieved in all four groups we will estimate the time to reach 10m%, where m is the largest integer such that the rate in all four groups is at least 10m%. The proportional hazards assumption will be tested by including interactions of each term (the two main intervention effects and their interaction) with log of time since 00:00 on 4th October 2018 in a Cox proportional hazards model.

Figure 1. Time series chart



6. COLLECTION AND ENDPOINTS

The outcome data are being collected in real-time and stored by UHB's team (not the research team) between the day the letters were sent out, the 4th of October 2018, until data-lock at 12:00 AM on the 4th of January 2019. The research team's statistician, Dr Peter Nightingale, will receive the outcome data on the 4th of January 2019 between 8:00 and 13:00 Greenwich Mean Time.

7. DATA NOT CONSIDERED IN STATISTICAL ANALYSES

The other outcomes (refusal to vaccinate and vaccinating at another site) will not be considered in statistical analyses for two reasons. First, participants are required to self-report this information through an online system that was not encouraged by our interventions. Second, these numbers are typically too small to impact our planned analyses, i.e. typically less than 2.5% of participants.

These outcomes will be reported descriptively for each group in the final report. For example: *Of the total number of participants ## refused to take up the vaccination, of which ## were sent the standard letter, ## were sent the social norms letter, ## were sent the authority letter, and ## were sent the combined letter.*

8. HANDLING OF MISSING VALUES

The outcome data will not have missing values as onsite staff vaccinations, the primary outcome, are all recorded routinely at the time of the vaccination. The denominator will comprise all front-line staff working in the hospital on the day of randomization, the 24th of September 2018. Self-reported refusals and self-reported vaccinations at another site are not the primary outcome data but are recorded on the system when available.

No attempt will be made to include staff joining the hospital after the randomization on the 24th of September 2018.

9. SUPPLEMENTARY ANALYSIS

Unknown to the University team who registered the trial and obtained ethical approval, for operational reasons the hospital members of the research team created a fifth group of participants who were sent no letter (n = 898).

A further analysis will be performed to utilize data collected in response to this protocol deviation. Using the information collected because of this deviation, we will compare the uptake of staff in this group to the amalgamation of those who were sent any of the four letters. This will be done by comparing the vaccination rates in these two groups using Fisher's exact test and also by binary logistic regression analysis with the outcome on-site vaccination (0 = No, 1= Yes) and the following explanatory variables: whether letter sent (0 = No, 1= Yes), Employment-type (0=Bank, 1=Substantive), Job-Type (1=Medical and dental staff, 2=Nursing, midwifery and health visiting staff, and 4= a combined group composed of Healthcare assistants, other support staff and Scientific, therapeutic and technical staff), Gender (0=Female, 1=Male) and any of the following interactions that are significant: Social Norms x Job type; Social Norms x Gender; Authority x Job type; Authority x Gender; Social Norms x Authority x Job type; and Social Norms x Authority x Gender. (If either of the three-way interactions is included, all the constituent two-way interactions will also be included.)