Health Economic Modelling Of blood donation strategies for maintaining the supply of safe blood (HEMO): Study protocol for survey of blood donors previously enrolled in the INTERVAL trial (Donor Preference Survey)

Project overview

The Health Economic Modelling Of blood donation strategies for maintaining the supply of safe blood (HEMO) project is funded for 2 years by the National Institute for Health Research (NIHR) Health Services and Delivery Research programme. HEMO is a collaboration between health economists and statisticians from the London School of Hygiene and Tropical Medicine (LSHTM), INTERVAL trialists based at the University of Cambridge, and policy-makers at National Health Service Blood and Transplant (NHSBT). This protocol has been jointly developed by these three groups and informed by the views of blood donors and public representatives.

The purpose of this protocol is to outline the design and analysis of a survey of whole-blood donors previously enrolled in the INTERVAL trial (REC reference 11/EE/0538). A similar survey of blood donors who did not participate in the INTERVAL trial has already been carried out as part of the HEMO research project (REC reference 16/YH/0023 & minor amendment 1).

Section 1: Summary of Research

The aim of the HEMO research project is to identify cost-effective strategies for maintaining the future supply of whole-blood to the NHS. One such strategy could be to reduce the minimum inter-donation intervals between whole-blood donations, an approach which is under investigation in the INTERVAL trial. Other possible strategies include extending the opening times for blood collection centres to include opening in the evenings or at weekends, or introducing a donor health report to give donors some basic information about their health at the time of donation (e.g. cholesterol levels and blood pressure). The survey outlined in this protocol will elicit the preferences of donors for these alternative strategies. This survey will only include donors who participated in the INTERVAL trial to complement the previous stated preference survey carried out as part of HEMO, which was administered to donors who did not participate in the INTERVAL trial. The previous survey provided estimates of donors' willingness to donate whole-blood at different frequencies, as well as donors' relative preferences for potential future changes to the blood collection service.

The rationale for this new survey is that INTERVAL donors differ from the non-trial participants in two important ways; first they are more reliable and more frequent donors and second they have given blood in fixed (as opposed to mobile) donor centres. Fixed donor centres are of strategic importance for NHSBT as they offer many advantages for the service over blood collection at mobile sites. It is anticipated that changing the form of the blood donation service could have an effect on donors' willingness to give blood. In order to maintain the future supply of whole-blood to the NHS, it is important to understand how donors might respond to potential changes to the blood service. These preferences will be

estimated from our survey and will feed into our decision model[1]. The results of the model will allow us to report the relative costs and consequences of alternative strategies (such as extending the opening hours at blood collection sites) for maintaining the future supply of whole-blood to the NHS.

Objectives:

1. To investigate the frequency with which former INTERVAL participants are willing to donate whole-blood according to potential future changes to the blood collection service.
2. To estimate the cost-effectiveness of alternative minimum inter-donation intervals between whole-blood donations.
3. To estimate the cost-effectiveness of alternative strategies for maintaining the supply of whole-blood to the NHS.

Overview of the INTERVAL trial

INTERVAL is a randomised controlled trial to determine whether the minimum interval between blood donations can be safely and acceptably decreased to optimise blood supply. Participants were recruited over a 2-year period (June 2012 – June 2014) and were randomised to give blood at specific donation intervals for a period of two years. Men were randomised to either 8, 10 or 12-week intervals and women to 12, 14 or 16-week intervals. All participants completed their 2-year involvement in the study between June 2014 and June 2016; those completing before January 2016 were invited to continue donating at their randomised interval for a longer period up until June 2016 (this additional period is known as INTERVAL Phase II). Data collection was complete for the 2-year study in July 2016 and will be completed for Phase II in September 2016, with some questionnaire data to follow. Further details about the INTERVAL trial protocol can be found in Moore et al.(1)

We will invite all donors recruited and subsequently randomised to INTERVAL to take part in the HEMO survey with the exception of those who have withdrawn permission for future contact and future use of their data collected during INTERVAL. We will also exclude participants who meet the specific exclusion criteria for the HEMO study (see section 2A).

Overview of methods

The HEMO research project includes two surveys designed to investigate donors' willingness to donate whole-blood under future changes to the blood collection service. The first survey, a stated preference survey of donors who did not participate in the INTERVAL trial, was successfully completed in July 2016. Only 10% of donors in this sample attended a fixed blood donation centre at their last donation. The survey consisted of several background questions followed by six stated preference questions. Donors were asked to state how often they would give blood, given the scenario described (including the option to state they would probably not donate). This method of eliciting preferences allowed us to directly

[1] The decision model was outlined in the protocol for the survey of donors who did not participate in the INTERVAL trial (REC reference 16/YH/0023)

estimate frequency as well as willingness to give blood under different configurations of the blood collection service. The second survey, the subject of this protocol, will be administered to former INTERVAL trial participants, all of whom have attended fixed blood collection centres. It will consist of the same stated preference survey previously used, but will also include a Discrete Choice Experiment (DCE) consisting of 7 questions. The DCE is a commonly used method of eliciting preferences; donors will be presented with two alternative blood collection services with slightly different features, and asked to choose which service they prefer. The rationale for including a DCE as well as the Stated Preference survey, is that it will allow the study to test whether blood donors revealed preferences differ according to the form of survey (stated preference survey versus DCE).

This survey will provide new evidence about donor's preferences from the DCE questions as well as their predicted donation frequency from the stated preference questions, both in response to possible future changes to fixed blood collection centres which is of prime policy interest to NHSBT (*Objective 1*). For example, the survey proposed will allow us to estimate donors' relative preferences for shorter minimum intervals between blood collection, versus changes to fixed donor centre opening hours. We will also compare stated donation frequency from donors' responses to this stated preference survey, versus the corresponding frequencies from the earlier survey of donors who were not in the INTERVAL trial, and mainly attended mobile blood collection sites.

We will develop a decision model to compare the costs and consequences of strategies to reduce the minimum interval between blood donations with alternative changes to the blood collection service. INTERVAL trial data will be used to populate the decision model, to estimate the effect of different minimum inter-donation intervals on the frequency of attending a whole-blood donation session, donors' quality of life (QoL), and costs (*Objective 2).* The decision model will also incorporate the findings from both surveys, together with data from the INTERVAL trial and PULSE, the national donor register, to predict the costs and consequences of alternative blood collection strategies. We will report the relative costs and consequences of alternative changes to the blood service, overall and for donor subgroups, for example according to gender, age, and blood type (*Objective 3*).

Objective 1: To investigate the frequency with which former INTERVAL participants are willing to donate whole-blood according to potential future changes to the blood collection service.

The survey of former INTERVAL participants will provide estimates of their willingness to donate whole-blood under the outlined alternative future changes to the blood service. The current and future maximum number of whole-blood donations per year for men (4, 5 and 6 times per year) are different to those for women (3 and 4 times per year). We will recognise these differences by administering a gender-specific survey.

Responses to the survey will be linked to data collected at an individual level for the INTERVAL trial (including employment status and responses to study specific questionnaires) as well as data derived from PULSE (such as age, sex, ethnicity). This will be supplemented with data on donor's donation history from PULSE, which has not been incorporated into the INTERVAL database, in concordance with agreed data sharing agreements (see Section 3).

The survey responses from former INTERVAL participants will be compared with those of the non-trial participants from our first survey (n=24,000 responders), before and after adjusting for differences between the donors and the settings (e.g. type of donation centre). We will report residual differences in predicted annual donation frequencies between former INTERVAL participants and donors who have not taken part in the INTERVAL trial. We will interpret the reasons for any residual differences between the INTERVAL and non-INTERVAL settings, which may reflect for example, unobservable differences as well as differences in donor preferences.

Objective 2: To estimate the cost-effectiveness of alternative minimum inter-donation intervals between whole-blood donations (the INTERVAL trial strategies)

The INTERVAL trial will estimate the relative effect of different minimum inter-donation intervals (12 vs 10 vs 8-week for men; 16 vs 14 vs 12-week for women) on donation frequency. The results of the trial will be particularly relevant for policy-making due to its pragmatic design with broad inclusion criteria and the large sample size (n=45,263) which includes pre-specified subgroups of policy relevance. But even following the publication of the INTERVAL trial results, it will be unknown whether increasing the maximum number of donations per year is effective and cost-effective in routine practice. Importantly for considerations of cost-effectiveness, the measurement of resource use and donors' health have also been recorded over time. Hence the trial-based economic evaluation will provide NHSBT with a precise, accurate estimate of the short-term cost-effectiveness of alternative minimum recall intervals, initially over the 24-month trial follow-up, for the donors and settings represented by the INTERVAL trial.

Objective 3: To estimate the cost-effectiveness of alternative strategies for maintaining the supply of whole-blood to the NHS

An economic evaluation based solely on whole-blood donors' behaviour observed within the INTERVAL trial setting is insufficient for informing future investment decisions by NHSBT. Donors' willingness to give blood may change over the longer term, in particular according to their relative preferences for other potential changes to the blood collection service, beyond changing the minimum donation interval. Our initial research identified the strategic initiatives that could help NHSBT meet its objective of reducing costs while maintaining the blood supply. These initiatives were identified through a review of NHSBT documents describing future strategies and policies, a review of the results of market research, an informal review of relevant published literature, consultation with NHSBT colleagues, and insights from preliminary qualitative research undertaken with INTERVAL donors (part of the INTERVAL study) and a public representative on our project team.

The strategic initiatives of interest for this evaluation are:

a) Extension of opening times of whole-blood collection sites
b) Provision of health reports for all whole-blood donors
c) Increase in the maximum number of whole-blood donations per year per donor, pending the results of INTERVAL.

To evaluate these strategies, we will need to make some assumptions about their implementation, as summarised in Table 1.

Table 1: Summary of strategic options, specific service reconfigurations, and relevant donor experience attributes

Broad Strategy	Possible Service changes	Relevant donor experience attribute
1. Extension of opening times	All venues to open evenings/weekends	Opening Times
		Appointment availability
		Travel time
2.Provision of health reports	Provision of health report to all donors	Availability of health report
		Total donation time
3.Increase maximum number of donations per year	Pending the results from the INTERVAL trial, donors have the opportunity to increase the maximum number of donations per year.	Maximum number of donations per year

While the survey of whole blood donors not included in the INTERVAL trial will provide some information on donors' relative preferences, the majority (90%) of the donors who responded to this survey had not attended permanent (fixed) donation sites. Fixed centres are of prime policy relevance for NHSBT who plan to expand the proportion of blood donations rather than at mobile sessions.

Section 2: Survey design

A. Survey administration and consent process

The administration of the survey of former INTERVAL participants will mirror the survey already successfully carried out with donors who did not take part in the trial. The online survey will be administered by NHSBT. Invited donors will be selected according to the following selection criteria:

Inclusion criteria:

i. Donors who gave consent to participate in INTERVAL and were randomised to an arm of the trial
ii. Donors for whom the last procedure code was whole-blood donation
iii. Donors who have an email address held by NHSBT
iv. Donors who reside in mainland England

Exclusion criteria:

i. Donors who have been reported as deceased
ii. Donors who have withdrawn consent for both contact by the INTERVAL trial team, and for the future use of their data collected during the trial
iii. Donors who are temporarily suspended from giving blood (e.g. donors who have had a tattoo recently)
iv. Donors who are identified on the NHSBT database as unwilling to participate in surveys

v. Female donors with AB+ blood (who have recently been asked by NHSBT not to give blood as their blood is not needed)

Invited donors will receive an email invitation from Dr Gail Miflin, Associate Medical Director, NHSBT. The email invitation will provide a weblink to the online survey within which information about the survey will be provided. Following the standard NHSBT process, the email invitation, information sheet, consent form and the survey questions will only be made available in English. The online information sheet (displayed over two screens) will make clear that the research team will access the INTERVAL trial data, and existing data held by NHSBT on each participant's donation history. Donors will be offered the opportunity to call the NHSBT helpline, if they require further information on the study, who will provide contact details of a named researcher working on the HEMO project at LSHTM.

The online information provided at the commencement of the survey will:
- Include details of the study, including information about confidentiality and data security
- Explain that participation is entirely voluntary
- Provide details of the number to call if they have any concerns or queries (the NHSBT call centre)

Donors will be asked to provide opt-in consent. Consent is mandatory, donors will not be able to start the survey until they have answered the consent question. In giving consent donors will be stating that they have read the online information provided and that they consent:

- to the use of their responses to the survey, in the described research
- for their survey responses to be linked to data held on the INTERVAL database collected as part of the trial, and for this to be shared this with researchers at the London School of Hygiene and Tropical Medicine in anonymised form.
- for NHSBT to link their survey responses to data held on the PULSE database about their donation history and their characteristics, and to share this with researchers at the London School of Hygiene and Tropical Medicine.

Those donors who consent to participate will begin the online survey, powered by Fluid Surveys (or similar survey software). If invited, donors who do not wish to participate in the survey will be able refuse consent. If consent is not given, participants will not be able to complete the survey. They will be reminded that the blood donation service they receive will not be affected in any way and will also be reminded of the NHSBT call centre phone number to call in case of any queries. As participants of INTERVAL, donors may be used to calling the trial telephone helpline. If donors call the INTERVAL helpline about the HEMO survey, they will be given basic information about the survey and directed to the NHSBT call centre if required.

Invited donors who neither provide nor refuse consent to take part in the survey will be sent one reminder email from NHSBT, 72 hours later. This reminder email will again include a weblink to the online information about the survey. Those invited donors who do not respond after this reminder email will not be sent further invitations to do so. The weblink

for completing the survey will be available for a maximum of 6 days (72 hours after the reminder email).

B. Survey content

Once consent is established, donors will be able to take part in the survey. We anticipate the survey will take donors up to 10 minutes to complete. Donors will be asked to provide basic information about the last time they gave blood, e.g. travel time and total donation time and several other background questions. The purpose of these questions is to supplement information available on individual donors within the PULSE database and recorded by INTERVAL necessary for the model-based analysis. For example, it will be necessary to establish from where donors travel to give blood and how long it takes them to arrive at the blood donation site.

The survey then asks donors six stated preference questions. Each question will contain a table showing a different set of blood donation service characteristics (see table 2). The pre-amble to the questions will provide lay definitions of what is meant by each attribute.
It is anticipated that changing the form of the blood donation service could have an effect on donors' willingness to give blood. The choice of attributes and levels used in the stated preference questions in the survey were determined following a process of rapid literature review, preliminary findings from qualitative research with participants of INTERVAL and input from policy makers at NHSBT. Once the possible future service changes were defined, we identified a series of attributes that relate to those aspects of the blood donors experience which may be affected by the proposed changes (see table 2). The appropriate levels for each attribute were then defined according to summary estimates from the PULSE database, discussion with NHSBT and initial findings from qualitative research undertaken with INTERVAL participants (see summary in Table 2)

Table 2: Summary of relevant donor experience attributes and associated levels in the survey

Relevant patient experience attribute	**Attribute levels**
Travel time	• Your typical travel time[§] • 10 minutes longer than your typical travel time • 20 minutes longer than your typical travel time • 30 minutes longer than your typical travel time *[§] In questions that relate to "the last place you gave blood" this is the only level considered for this attribute*
Appointment availability	• Every day (Monday – Sunday) • Every weekday (Monday – Friday) • 1 day every 2 months (Monday – Friday) • 1 day every 2 months (Saturday or Sunday)
Opening times	• 9am-12pm and 2pm-5pm • 9am - 5pm • 9am - 8pm • 2pm - 8pm

Relevant patient experience attribute	**Attribute levels**	
Health report	• Yes, after each donation • No	
Maximum number of donations per year	FEMALES • 3 donations per year (current max.) • 4 donations per year (pending INTERVAL)	MALES • 4 donations per year (current max) • 5 donations per year (pending INTERVAL) • 6 donations per year (pending INTERVAL)

The responder will be asked to state how many times per year they would donate blood under a particular type of blood service. First donors are asked about their likely annual donation frequencies when faced with a scenario that describes a blood donation service located at the place where they last gave blood (x 2 questions). Donors are then asked to suppose they were asked to donate blood at a different place. They will be offered a scenario describing the features of that blood donation service, upon which they will be asked how many times per year they would give blood (x 4 questions).

As so far described, the proposed survey replicates the survey that was successfully administered to donors who did not take part in the INTERVAL trial. However, we will also ask former INTERVAL participants to complete a discrete choice experiment (DCE). The DCE is an alternative, and arguably more established, method of eliciting preferences. The purpose of including both DCE and stated preference elements in this survey is to test whether estimates of donor preferences about different types of blood service, differs according to the choice of survey (DCE versus stated preference survey). DCE choices are easier to answer than stated preference choices (since the respondent indicates which of two options they prefer rather than indicating their preferred annual frequency of donation). However, the information generated regarding how donors trade-off different aspects of the opportunity to donate is comparable and thus by collecting preference data using two distinct methods we can increase the robustness of our analysis. The responses will be used to provide estimates of donation frequency that will inform the modelling of the cost-effectiveness of alternative blood collection strategies.

The DCE consists of the final seven questions of the survey. These questions present similar information using a discrete choice experiment to elicit donor preferences. Donors are shown two alternative blood donation services located at the place where they last gave blood, and are asked to express whether they prefer service A or service B (x 2 questions). Donors are then shown another pair of alternative blood donation services, located at a different place to where they last gave blood (x 5 questions). Again, donors are asked to express a preference for service A or service B.

More questions are required about giving blood at a different place to where the donor last gave blood since in these scenarios travel time to the new blood donation site is varied, whereas when donors are asked to think about the place they last gave blood, travel time does not change. This results in four times the number of stated preference scenarios, and 16 times the number of DCE choice pairs. We therefore require one additional "different place" questions to ensure a sufficient number of responses to each possible blood service configuration, particularly for the DCE questions.

Sample size

Sample size calculations for stated preferences surveys are not straightforward. Judging whether a difference in preferences between donors is of material difference is problematic and will depend on factors that are currently unknown, including the expected coefficients associated with each attribute and the subsequent regression model (described in section 4). In addition, the response rate of donors is uncertain; the INTERVAL trial participants have high questionnaire response rates (e.g. 70% response to the 2-year INTERVAL questionnaire) while routine NHSBT surveys achieve response rates of 10% to 25% and the HEMO survey of non-trial participants had a 25% response rate. We therefore anticipate the response rate for this survey to be between 20% and 50%.

NHSBT will invite all donors who satisfy the inclusion and exclusion criteria to participate in the **survey. Of the 45,263 donors randomised to an arm of the INTERVAL trial, it is estimated that around 25,000 donors** will satisfy these criteria and be eligible at the time of survey initiation. Given the likely response rates (20% to 50%) the expected number of responders is between 5,000 to and 12,500. These projected sample sizes are sufficient to report two-way interactions between relative preferences for combinations of attributes, and also to investigate the heterogeneity of donor preferences according to subgroup (according to sex, whether the donor gave blood at the INTERVAL donation site prior to the trial, the arm of the INTERVAL trial and whether the donor is in the INTERVAL continuation study).

To avoid burdening the respondents we have designed the survey in order to ensure the likely time to complete the questionnaire is 10 minutes.

Section 3: Data linkage, transfer and storage

The INTERVAL trial data manager will identify INTERVAL participants who were randomised to an arm of the trial. The donor ID of donors who have been reported as deceased and donors who have since withdrawn both consent to be contacted from the INTERVAL trial team and for the future use of their data collected during the INTERVAL trial will be removed from this list. The remaining donor IDs will be transferred to NHSBT according to agreed data transfer protocols. NHSBT will then apply the remaining inclusion and exclusion criteria to this list of donors to identify those eligible for the survey.

Identifiable personal information of donors will not inform the identification of potential participants, but once the sample is generated by the database, personal email addresses will be visible to the NHSBT staff sending out the links to the survey. These will only be

visible to staff who would ordinarily have access to the information, under the existing Terms of Use for Users of the Online Blood Donor Register.

Anonymisation of data will be carried out by NHSBT; each participant will be allocated a unique HEMO 'study ID'. This study ID, based on the donor ID, is embedded in the weblink to the online survey provided in the email invitation. NHSBT will retain a link of study IDs to donor IDs but LSHTM researchers will only access the HEMO study IDs. Responses to the survey will be linked to two existing datasets using the HEMO study ID; the INTERVAL database and the PULSE database.

To facilitate the linking of data outlined below, a Data Transfer Agreement has been agreed between NHSBT and LSHTM, between NHSBT and the University of Cambridge. A Data Transfer Agreement will be put in place between the University of Cambridge and LSHTM to establish procedures for the secure transfer of data from the INTERVAL trial to LSHTM. No personally-identifiable data will be shared with LSHTM researchers. Data will be held and used in accordance with Information Security Policies and Procedures at NHSBT, LSHTM and the University of Cambridge.

Linking to INTERVAL data

NHSBT will provide the INTERVAL trial data manager with the NHSBT PULSE ID and (psuedonymised) HEMO study ID of all those to be invited to the survey. The INTERVAL data sharing manager will ordinarily have access to this information, as set out in the INTERVAL trial protocol (REC reference 11/EE/0538). The INTERVAL data manager will retrieve the relevant data and share the psuedonymised linked INTERVAL dataset with named researchers at LSHTM.

Linking to PULSE data

NHSBT will link the survey responses to donor's details, including their donation history and other data held in the PULSE database, via the HEMO study ID. Patient characteristics including age, sex, ethnicity, blood group, total number of donations, number of donations within the past two years, donor reliability score, duration of donor career, usual blood donation panel visited, characteristics and frequency of availability of usual donation venue and distance from usual blood donation panel visited to home postcode, and home postcode 'sector' (not considered personally-identifiable) will be made available to LHSTM researchers as per the data transfer process outlined below. Data collected from the stated preference survey and DCE will also be linked to future donation behaviour.

The data outlined will be transferred from the University of Cambridge to NHSBT, from NHSBT to LSHTM, and from University of Cambridge to LSHTM, in accordance with NHSBT procedures for transferring data securely in encrypted form (*NHSBT Encrypting Personal Data*). In summary:

- the files will be zipped and encrypted (the encryption method will be 256-Bit AES encryption (stronger))
- it will be sent by email and marked as confidential; this means it will be held on a secure server until it is retrieved

- the password will be immediately provided over the phone and the phone call will not end until the file is unzipped by the recipient and it is confirmed as the correct file.

Dr Gail Miflin, at NHSBT will have control of and act as the custodian for the data generated by the study (responsible for the use, security and management of all data generated by the study). Within LSHTM, Richard Grieve as Principal Investigator will act as Data Custodian for the research data.

Within NHSBT, data will be handled under the existing Terms of Use for Users of the Online Blood Donor Register, in accordance with the NHSBT Information Security Policy, whereby manual files are stored in locked drawers in locked NHSBT buildings, and personal data is held on secure servers rather than stored locally on computers, and is only accessible by authorised individuals.

At LSHTM:

- Research data linked to the HEMO study ID will be held on a server on the University Network and will only be accessible to the authorised researchers in anonymous form.
- Manual files will be stored in locked drawers in locked University buildings.
- The information management and security policy of the London School of Hygiene and Tropical Medicine is to retain research data for 20 years, after which it will be deleted in accordance with University policy by the Archivist.

Section 4: Proposed analysis

We will analyse the resulting choice data from the survey responses with a suitable regression model, such as a generalised mixed logit model. Such a regression model will account for heterogeneity in respondents' preferences in reporting the marginal rate of substitution (MRS) across each potential pair of blood collection service attributes, and will include donor characteristics, history and randomised arm as independent variables. For instance, we will report the extent to which donors are willing to reduce the minimum interval between donations, in exchange for receipt of a donor health report. The initial regression models will be applied solely to the former INTERVAL sample. We will report MRS overall and according to donor subgroup, in particular according to whether or not blood donors attended INTERVAL sites prior to enrolment in the trial.

We will then contrast the estimates of the MRS between the former INTERVAL participants and donors who did not take part in the trial. The regression models will include dummy variables for whether or not the donor participated in INTERVAL.

We will handle missing data either from non- or incomplete response by multiple imputation, apply the regression models to each of the imputed datasets, and combine the resultant estimates with Rubin's formulae.

The analysis of the SP survey will provide estimates of the predicted frequency of blood donation. For attributes pertaining to current blood collection service provision we will report the proportion of respondents who state that they would be willing to donate whole-

blood within a particular time period (e.g. 4 months). We will then estimate the effect of marginal changes to the blood collection service (e.g. weekend opening), as the change in the proportion of respondents who say they will donate within that time period (say within 4 months).

The validity of the resultant predicted probabilities assumes that *stated* preferences translate into *revealed* preferences; i.e. the frequency with which whole blood donors attend donation sessions is predicted by their responses to the hypothetical questions raised by the survey. The validity of the predictions will be tested by contrasting predicted probabilities to observed donation rates for:

i) former INTERVAL donors from the control arm (*baseline event* rate, trial)
ii) non-INTERVAL donors in the PULSE dataset (*baseline event* rate, current practice)
iii) former INTERVAL donors intervention versus control arm (*relative* event rate, trial)

This validation exercise will initially set characteristics in the survey to those observed in the validation dataset (INTERVAL or PULSE). The validation will then estimate the residual mean differences between predicted versus observed donation frequencies overall, and by donor subgroups. These residual differences will reflect discrepancies between revealed versus stated donor preferences, and measures of the likely biases from using the survey responses to predict the effect of future changes to the blood collection service on the frequency of whole-blood donation. The subsequent cost-consequence analysis (objective 3) will use predicted probabilities after correcting for these biases, when estimating the relative cost-effectiveness of alternative minimum donation intervals, alongside future changes to the blood collection service.

The analysis will report

i) The marginal rate of substitution (MRS) between attributes of the blood collection service, including different intervals between whole-blood donations
ii) The marginal effect of future changes to the blood collection service on the probability of whole- blood donation within a particular time period
iii) The mean differences in the MRS and the predicted probabilities of future donation for whole-blood donors who participated in INTERVAL versus those who did not
iv) A comparison of the MRS estimated using the SP and DCE methods within the INTERVAL population

Anticipated outputs

The results of the survey will provide estimates of **predicted frequencies of intended whole blood donation** for different minimum recall periods in the INTERVAL trial together with other potential future changes to the blood collection service. These estimates will allow for a broader assessment of the relative costs and consequences of reducing the minimum recall interval for blood donation alongside other potential future changes to the blood donation service. The surveys will also provide estimates of the relative preferences of alternative changes to the blood service for INTERVAL participants versus non-participants.

This evidence can inform the decision as to whether and how the INTERVAL strategies should be 'rolled out' to donors outside the setting of the INTERVAL trial

- to subgroups of donors under-represented in the INTERVAL trial
- to mobile blood donation sites

The results from the survey of former INTERVAL trial participants will then be used in the general decision model estimating the relative costs and consequences of alternative future changes to the blood service (objective 3). The results of the two surveys will also offer insights into the extent to which different preference elicitation methods generate similar measures of donor preferences.

Section 5: Dissemination, projected outputs, knowledge mobilisation

To help maximise the research impact, policy-makers at NHSBT and donors have driven the choice of objectives, the research design and will continue to be involved at each stage of the research process. Early findings will be disseminated through NHSBT, INTERVAL and project specific websites, and through conference presentations. We will run two translation workshops to present preliminary findings to donors, and local blood collection service providers. The final results will be published in open-access peer-reviewed journal publications.

The study will provide NHSBT with evidence on donors' preferences for, and the cost-effectiveness of, alternative strategies for sustaining the blood supply. This evidence can help NHSBT personalise donation strategies, according to donors' characteristics and donation history. This study can help NHSBT maintain the blood supply and ensure that future patients achieve health gains from interventions that require blood and blood products.

The findings of the proposed study will be disseminated alongside those of the INTERVAL trial, and will be given a high-profile. The results from these two studies will be major determinants of future NHSBT policy. The co-applicants from NHSBT (GM, CW) all sit on the Blood Donation Research Strategy Group (chaired by GM), and will ensure the findings at each stage are discussed with colleagues to inform both NHSBT research and the Blood Donation Strategy and signed off by the Blood Supply Senior Management Team. Thus the results will inform future NHSBT strategy on the organisation of blood collection services, and future research priorities.

Findings will be presented at appropriate national and international conferences, including the International Society for Blood Transfusion conference, the Health Services Research Network symposium, the Health Economists' Study Group, and the annual conference of the Society for Medical Decision Making. The LSHTM media department will help ensure that the study findings will be available to the broader public via popular and donor-related media (e.g. donor magazine), through relevant websites (e.g. INTERVAL study website, NHSBT website, and a new project-specific website), and where appropriate, wider media outlets.

A full and complete account of the research, reviewed by NHSBT and the INTERVAL study group, will be made available by open access as a publication in the NIHR HS&DR Journal. Research papers arising out of the study will be published in peer-reviewed journals.

Section 6: Project management

Richard Grieve will take overall responsibility for project delivery (20% WTE); he will supervise the Research Fellow, Silvia Perra (SP) / Assistant Professor of Health Economics, Zia Sadique (ZS) (100% WTE) and the Research Fellow Sarah Willis (SW) (RF, 40% WTE) and will be assisted by the senior project manager Jennifer Turner (JT), in managing the budget, monitoring progress against timelines and leading the study management group. JT will co-ordinate activity across the three institutions, organise the translation workshops, schedule and plan input from collaborators including donor and public representatives, and update materials for the project website. The study management group will meet fortnightly (by teleconference or in person) and will report to the study advisory group which will have an independent chair – Professor Janet Powell, Imperial College).

Neil Hawkins (NH) will be responsible for the development and analysis of the decision model, and John Cairns for the surveys; they will provide SP/ZS with specialist guidance on these aspects. RG, Mark Pennington (Lecturer, now at King' College London) and Crispin Wickenden (CW) will guide SP in the analysis of the survey data. SW will co-ordinate the administration of the survey, overseen by CW. Laura Hontoria del Hoyo and Gail Miflin will guide the costing of future changes to the blood collection service and the implications of the study findings for NHSBT strategy.

Section 7: Public and patient involvement

The views of blood donors and public have informed the research design. Members of the Oxford donor panel and the Cardiac Division and Thoracic Public Involvement Panel, reviewed an initial draft of the full funding application, and the proposal was refined accordingly. Comments by a public representative (Peter Zollman), improved the language and clarity of the revised lay summary, and emphasised that the survey of donor views should be given greater prominence. The views of blood donors have already informed the design of the proposed donor surveys by suggesting that the aspects of the service that might be important should include total donation time, and blood centre opening times. Blood donors have also identified attributes that should not be included (e.g. financial payment for donating blood). The questionnaire design has also been informed by findings from qualitative research on blood donors' views. In addition to the piloting and administration of the stated preference survey to donors who had not participated in the INTERVAL trial, the wording and form of the background questions, the stated preference and discrete choice experiment questions were informally checked with a sample of whole blood donors attending a permanent (fixed) blood collection centre. These donors also reported no significant problems with answering any of the questions.

The proposed research requires input from whole-blood donors and Public representatives to inform the approach taken for eliciting donors' views, the range of themes to explore in the survey, how best to undertake the subsequent analysis, and how to interpret the results. Members of the Oxford panel have reviewed the wording of the draft donor questionnaires in meetings with the research team before and after the questionnaire was piloted. The proposed research will also elicit donors' views to help our understanding of why questionnaires may not be returned, and why responses may be incomplete. This research will help future studies make full use of the data from representative samples of patients, and improve on existing approaches.

The views of blood donors have informed the knowledge mobilisation strategy, which will include a number of translation workshops targeted towards blood donors as well as local blood service providers. Donors' views will inform the project website design, and the programmes for the translation workshops. Blood donors will advise on how best to communicate the study findings to a broad audience. In particular, donors have agreed to help edit presentation slides for workshops, and lay summaries that will be posted on the project website. It is not anticipated that donors will require specific training for providing the required input. The expenses and time of blood donors and the Public Representative that the research will require has been fully costed as per INVOLVE guidelines.

Section 8: Funding and insurance

The National Institute for Health Research Health Services & Delivery Research Programme has funded the study for 2 years (Project 13/54/62. Funded to £297,281.00). NHSBT and the INTERVAL trial were co-applicants for the grant.

The risks associated with the study are considered to be very low. As an NHS sponsored project, the NHS Indemnity Scheme will apply to meet the potential legal liability of the sponsor(s) for harm to participants arising from the research.

References

1. Moore C, Sambrook J, Walker M, et al. "The INTERVAL trial to determine whether intervals between blood donations can be safely and acceptably decreased to optimise blood supply: study protocol for a randomised controlled trial." *Trials*. 2014;15:363.