

# Health Economics MOdelling (HEMO) for maintaining the supply of blood

## Study protocol

### Summary of Research

The aim of this 24-month study is to identify cost-effective strategies for maintaining the future supply of whole-blood to the NHS. The study will estimate the cost-effectiveness of alternative minimum inter-donation intervals that are permitted. The study will investigate whole-blood donors' willingness to donate at alternative frequencies in the context of anticipated future changes to the blood collection service. We will also report the relative cost-effectiveness of alternative future strategies for sustaining the blood supply (e.g. extending venues' opening hours for blood collection), for a population of whole-blood donors representative of routine blood collection practice.

#### *The objectives of the study are*

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

#### *Overview of Methods*

We will use INTERVAL trial data 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. We will develop a decision model to extrapolate the cost-effectiveness of alternative minimum permitted donation intervals over 5 years. We will access data from PULSE, the NHSBT national donor database, on donor characteristics and donation history. These PULSE data will be used to define the target population, and to estimate long-term rates of donation, under *current* minimum permitted recall intervals, and characteristics of the blood collection service. We will conduct a stated preference (SP) survey to investigate donors' willingness to donate whole-blood under *future* changes to the blood collection service. Our cost analysis will take an NHSBT perspective, and estimate the relative costs of the alternative proposed changes to the blood service. The cost-effectiveness analysis (CEA) will use the findings from the SP survey, together with those from the re-analyses of INTERVAL and PULSE data, in a decision model, to predict the costs and cost-effectiveness of alternative blood collection strategies over a 5 year time horizon for a representative population of whole-blood donors. We will report the relative costs and cost-effectiveness overall and for donor subgroups, for example according to gender, age, and blood type.

A subsequent research protocol will be submitted that relates to economic evaluation of the interventions considered in the INTERVAL trial (objective 1). This protocol focuses on the research methods that will be required to address objectives 2 and 3. This protocol therefore defines the broad blood service changes that the evaluation will consider, provides an overview of the main features of the SP survey, outlines why and how PULSE data will be used, and explains how data management and research governance issues will be addressed.

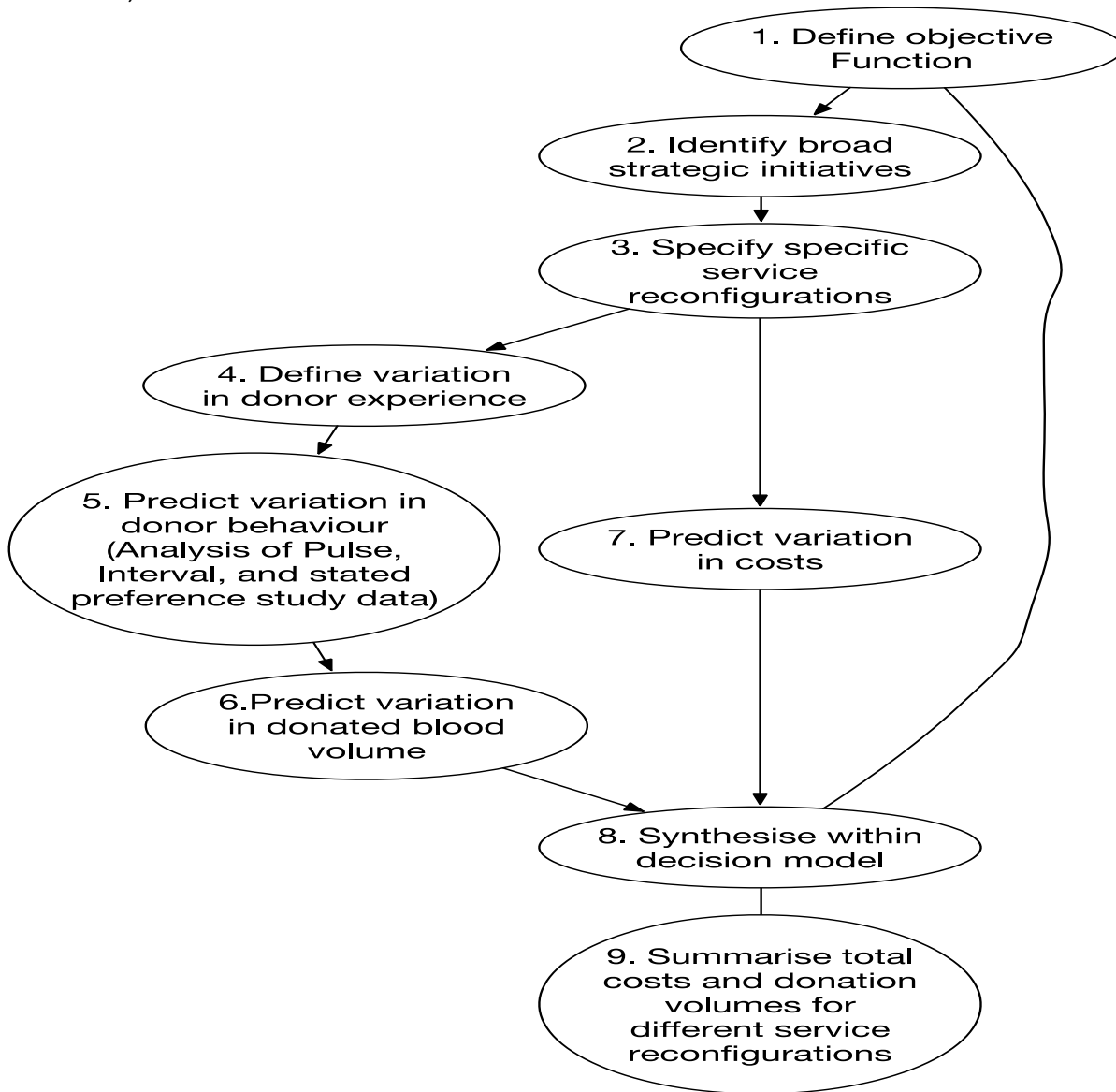
## **Project overview**

This research project is funded by the NIHR health services research and development programme. The remit of this funder emphasises that the scope, design, conduct and interpretation of the research should be informed by the relevant health service decision-makers and managers, and also have significant input from relevant public representatives. Hence, the proposal and accompanying protocol have been jointly developed with colleagues at NHSBT, and have also been informed by the views of blood donors.

The overall project structure is given in Figure 1, and associated commentary follows, starting with the definition of NHSBTs relevant objective (subsection 1). The objective shapes the choice of strategic initiatives that this study will evaluate (2), and possible changes to the blood collection service that they imply (3). The SP survey is designed to predict the likely effects of these possible service changes on aspects of donor experience (4), and the ensuing impact on donation frequency (5). The relationship between changes to the blood service and donation frequency, will be estimated both directly and indirectly. This relationship can be estimated directly when there are data on both the changes to the blood collection service (e.g. extended opening hours) and donation rates in the PULSE or INTERVAL data sets. When these data are not available in PULSE or INTERVAL, these relationships will be estimated indirectly by estimating the effect of service changes on the donor experience, and the relationship between the donor experience and donation rates. These indirect relationships will be estimated from responses to the SP survey, and through analyses of the linked PULSE and INTERVAL data.

The donor experience attributes of interest will be identified by considering the likely effects of the potential changes in blood service identified in the strategy review. In addition, the wider literature, NHSBT surveys, and donor panel will be consulted to characterise the potential impact of alternative changes to the blood service, and other potential donor experience attributes that might influence donation rates. In turn, consideration of this wider set of donor experience attributes may suggest further strategic changes to the blood service. The direct and indirect relationships estimated from the three sources will be synthesised, and the potential impact of the alternative service configurations on the costs and volumes of donated blood will be estimated using a decision analytic model.

The sequence of steps required in the study are defined in Figure 1, and summarised briefly below.



**Figure 1: Requisite Study Steps**

**1. Definition of the relevant objective function for the study**

NSHBT’s objective is defined as being: to meet the short-term demand for blood at the lowest cost, whilst maintaining donor well-being.<sup>1</sup> For this study, we define the decision-maker’s objective as minimising the cost of collecting the current volume of blood. This is a more appropriate objective than that of minimising the cost per unit of blood collected, or maximising the supply of blood given a maximum cost per unit. The former objective could be achieved simply by closing donation venues in descending order of their individual cost per unit blood collected. However, this would lead to an inadequate supply of blood. It is also a more appropriate objective than that of maximising supply as the current supply is adequate and demand is decreasing. Therefore, the study will not consider strategies which may have a longer term impact, such as changing the levels of investment in strategies to

<sup>1</sup> “Keeping the blood price flat or lower than £122 a unit in the face of falling demand and increasing costs.” From *Blood 2020 A strategy for the blood supply in England and North Wales*.

attract new donors. Neither will the study consider day-to-day operational issues for NHSBT, nor specific policies of high relevance to a particular locality (e.g. closure of particular - named - donation venues).

## **2. Definition of broad strategic initiatives for evaluation**

Strategic initiatives that could help the organisation meet the above objective were identified through a review of NHSBT documents describing future strategies and policies, 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. The strategic initiatives identified as being of potential interest for the evaluation were:

- a) Closure of all 3- and 6- bedded sites for whole-blood collection
- b) Extension of opening times for both permanent and temporary sites collecting whole-blood
- c) Provision of health reports for all whole-blood donors
- d) Increase in the number of maximum number of whole-blood donations per year, pending the results of the INTERVAL trial
  
- e) Reduction in the time taken for booked appointments to one hour (“one hour pledge”)
- f) Reimbursement of parking charges
- g) Extension of the provision of Wi-Fi
- h) Refurbishment of donation venues
- i) Elimination of walk-in appointments
- j) Provision of online check-in and completion of pre-donation questionnaire
- k) Provision of a non-invasive HB test

Of those, the selection of strategies for evaluation was according to the following criteria:

- The strategy can be defined as a distinct series of service changes, with attributable costs and consequences that can be estimated
- The strategy is anticipated to have an effect on important attributes of the donor experience
- NHSBT decisions on whether to adopt a particular strategy could be informed by evidence from the study
- It was necessary to include a strategy that related directly to the results of the INTERVAL trial
- There was a limit to the number of strategies under consideration, to ensure the survey had a manageable number of attributes (maximum of 7).

Based on the criteria above, the following strategies were excluded from further consideration within this project:

- e) ‘One Hour pledge’: it was not feasible to define the service changes required for NHSBT to meet this pledge, and so the costs and effects of introducing this strategy will not be modelled. The importance of total donation time to donors is recognised and so to improve the face validity of the survey this attribute will be included (see next section).
- f) Extension of reimbursement of parking charges, these have already been introduced in some sites (both temporary and permanent).
- g) Provision of Wi-Fi: alternative forms of mobile internet access are likely to become increasingly available and the cost of Wi-Fi provision is likely to decline. h) Refurbishment of donation venues: it was not possible to objectively describe the scope and outcomes of these refurbishments for inclusion in either the decision model or stated preference survey.
- i) Elimination of walk-in appointments: evidence from the study would not be anticipated to inform a future decision.

- j) Provision of online check-in and completion of pre-donation questionnaire: these strategies are already planned.
- k) Provision of a non-invasive HB test: this was judged unlikely to have a substantial impact on costs or donation frequency

### **3. Definition of specific changes to the service for evaluation**

Hence the following strategies are proposed for evaluation:

- a) Closure of all 3- and 6- bedded temporary sites for whole-blood collection**
- b) Extension of opening times for both permanent and temporary sites collecting whole-blood**
- c) Provision of health reports for all whole-blood donors**
- d) Increase in the number of maximum number of whole-blood donations per year, pending the results of the INTERVAL trial**

To evaluate the above strategies we will need to make some assumptions around implementation.

For strategy a) we will assume that all 3- and 6- bedded temporary sites will be closed and donors redirected to their next nearest donation venue, which will usually be a 9-bedded temporary site, but could be a 12- bedded site, or a permanent site. Where donors are redirected to a temporary site we will consider scenarios where the number of available sessions increases in proportion to the additional number of donors. Where donors are redirected to a fixed site we will assume the venue has sufficient spare capacity to accommodate them.

For strategy b) we will consider a change in working hours of temporary site staff to allow the site to run sessions in the evening and/or at weekends. We will assume no change in staff remuneration pro rata for evening sessions, but that staff will receive the usual overtime payment for weekend sessions.

For strategy c) In the future if a health report were to be provided it might give the results of information on blood pressure and cholesterol . The tests would typically be undertaken by an independent provider.

For strategy d) we assume that if the INTERVAL trial reports that reducing the minimum donation interval is safe and efficacious, NHSBT would be interested in evaluating the potential effects of 'rolling out' the INTERVAL 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, 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. Hence, we consider strategies of increasing the maximum number of whole-blood donations per year. It should be recognised that the current and future maximum number of whole-blood donations per year for men (4 and 5) are different to those for women (3 and 4). We will recognise these differences by gender, in administering a gender-specific survey (see later section).

It was recognised that in keeping with NHSBT's objective, it would be necessary to combine some of the above strategies to avoid increasing overall costs. So for example, a strategy for closing all 3- and 6- bedded temporary sites could be combined with extended opening hours in all 9-bedded sites and in all permanent sites.

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

<b>Broad Strategy</b>	<b>Possible Service changes</b>	<b>Relevant donor experience attribute</b>
1. Closure of all 3- and 6-bedded temporary sites	Donors offered opportunity to donate at next nearest blood donation venue, which will usually be a 9-bedded temporary site. These larger sites may offer extra sessions to cater for the additional donors within their catchment areas.	Usual venue
		Travel time
		Appointment availability
		Opening times
2. Extension of opening times	All venues to open evenings/weekends	Opening Times
		Appointment availability
		Travel time
3. Provision of health reports	Provision of health report to all donors	Availability of health report
		Total donation time
4. 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

#### **4. Definition of donor experience attributes and levels to capture potential changes to the blood collection service**

Following the definition of the possible service changes, we have defined a series of attributes for the SP survey, that relate to those aspects of the blood donors experience, which may be affected by the proposed changes to the blood donation service.

So for example, if 3- and 6-bedded temporary sites are closed, then it would be anticipated that donors will be invited to donate at a different venue, and this could imply changes to the donor experience with regard to,

- i) donating at a different venue; ii) an increase in travel time; iii) a change in appointment availability and
- iv) a change in opening times .

It is therefore anticipated that by changing the donors' experience, these service changes could have an effect on the donors' willingness to donate blood at particular frequencies.

The appropriate levels for each attribute have been defined according to summary estimates from the PULSE database, discussion with NHSBT informants, consultation with blood donors, and initial findings from qualitative research undertaken with INTERVAL participants (see summary in Table 2). Since donating at one's usual donation venue is related to other attributes (travel time, opening times) we will ask donors to respond to two scenarios; at the last place of donation and at a different place. This will be included as part of preamble to the scenario, rather than as an attribute.

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

Relevant patient experience attribute	Attribute levels	
1. Donors <i>travel time</i> to blood donation venue	<ul style="list-style-type: none"> <li>Your typical travel time</li> <li>10 minutes longer than your typical travel time</li> <li>20 minutes longer than your typical travel time</li> <li>30 minutes longer than your typical travel time</li> </ul>	
2. <i>Appointment availability</i>	<ul style="list-style-type: none"> <li>Every day (Monday – Sunday)</li> <li>Every weekday (Monday – Friday)</li> <li>1 day every 2 months (Monday – Friday)</li> <li>1 day every 2 months (Saturday or Sunday)</li> </ul>	
3. <i>Opening times</i>	<ul style="list-style-type: none"> <li>9am-12pm and 2pm-5pm</li> <li>9am – 5pm</li> <li>9am – 8pm</li> <li>2pm - 8pm</li> </ul>	
	<ul style="list-style-type: none"> <li></li> </ul>	
4. Availability of <i>health report</i>	<ul style="list-style-type: none"> <li>Yes, after each donation</li> <li>No</li> </ul>	
5. Maximum number of donations per year	FEMALES <ul style="list-style-type: none"> <li>3 donations per year (current max.)</li> <li>4 donations per year (pending INTERVAL)</li> </ul>	MALES <ul style="list-style-type: none"> <li>4 donations per year (current max)</li> <li>5 donations per year (pending INTERVAL)</li> <li>6 donations per year (pending INTERVAL)</li> </ul>

**5. Variation in donor behaviour regarding differences in willingness to donate whole-blood at alternative frequencies according to alternative changes to the blood service**

The purpose of the SP survey is to predict the frequency of whole-blood donations according to the alternative proposed changes to the blood service. The SP survey will be designed and analysed in conjunction with data from PULSE and the INTERVAL trial to provide accuracy predictions of donation frequency for a representative sample of current whole-blood donors in England. The data sources for the levels for each attribute are shown in Table 3.

**Table 3: Data sources for estimating the impact of changes in donor experience attributes on predicted frequency of whole-blood donation**

Donor Experience Attributes	Data Sources		
	SP survey	PULSE dataset	INTERVAL trial

1.Usual donation venue	X		
2.Travel time/distance	X	X	
3.Opening times	X	X	
4. Appointment availability	X	X	
5.Donor health report	X		
6.Maximum number of donations per year	X		X

### Inclusion and exclusion criteria for the SP survey

Eligible donors will be randomly selected from eligible whole-blood donors registered in the PULSE dataset. Eligibility to participate in the SP survey will be according to the following inclusion criteria, which will be applied at study initiation (e.g. 1.1.2016) (see below)

- i. Age 17-70 years old (inclusive) at the time of study initiation
- ii. Have successfully donated a unit of whole-blood at least once in the past 12 months
- iii. Last procedure code was whole-blood donation
- iv. Have an email address held by NHSBT
- v. Reside in mainland England

Donors will be excluded from the SP survey if they:

- i. Are temporarily suspended from giving blood (e.g. donors who have had a tattoo recently)
- ii. Are identified on the NHSBT database as unwilling to participate in surveys
- iii. Have received any survey or request to participate in research from NHSBT in the six months preceding the study initiation date
- iv. Have participated in the INTERVAL trial
- v. Are females with AB+ blood

### Sample size and piloting

Sample size calculations for SP surveys are not straightforward. While we have pre-specified the number of attributes (5), the number of levels of each attribute (2 to 4), and the number of questions presented to each respondent (6), other aspects that will influence the proposed sample size are currently unknown, including the expected coefficients associated with each attribute, and the subsequent econometric model. A further issue is that even following the pilot study (see next section), response rate of donors for the full survey is uncertain; previous NHSBT surveys have reported response rates of 10% to 20%. The proposed sample size is required to be 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.

We propose that NHSBT invites a total of 100,000 donors to participate in the study. In discussion with the NHSBT co-applicants, it is envisaged that issuing email invitations to 25,000 donors per month for four months would not lead to a noticeable additional burden for NHSBT helpdesks, nor reduce the pool of donors eligible for routine NHSBT surveys. It is envisaged that the eventual sample size will be between 10,000 (10% response rate) and 20,000 (20% response rate).

Before we administer the SP survey we will undertake an extensive piloting exercise, to provide an accurate assessment of the likely response rate, the time taken and burden to donors in completing the questionnaire, the 'face validity' of the questionnaire, and also the practicalities of the survey administration. For the pilot study, NHSBT will therefore issue 5,000 email invitations to eligible donors, which we would anticipate to yield between 500 and 1,000 responses. It is envisaged that this pilot exercise will provide sufficient information to guide the final choice of sample size, choice of attributes and levels for the SP survey, and resolve any logistical issues concerning the survey administration.

Update after the pilot survey:
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5,016 email invitations were issued and a response rate of 25% was achieved. The mean time to complete the whole survey was just under 6 minutes (5 mins 47 secs). No calls relating to our pilot survey were logged at the NHSBT call centre.

When validating the pilot survey results with data from PULSE, we found that even our baseline scenario (e.g. your typical travel time, Monday-Friday 9am-12pm and 2-5pm, a long blood duration, no health report and the current maximum permitted number of donations) did not capture constraints to donation at some mobile centres, specifically in terms of the availability of appointments. The design of the final survey recognises this constraint to donors by including an additional attribute ('appointment availability'). The 'opening times' attribute has been simplified to only include the times at which sites are open. The definition of the attributes and levels are applicable to donation visits at both temporary (mobile) and fixed (permanent) sites. Total duration time was removed as an attribute since recent information from NHSBT showed that most donor donation visits were less than one hour in accordance with NHSBT policy.

For the main survey we anticipate that the response rate will be similar to the pilot survey but this is still uncertain. The choice of scenarios offered in the pilot survey was informed by an efficient design based on the need to estimate only main effects. The main survey design will be based on the need to report two-way interactions between relative preferences for combinations of attributes, and also to investigate the heterogeneity of donor preferences according to subgroup.

We design of the final survey also recognises that, pending the results of the INTERVAL trial, men may be permitted in future to give blood up to 6 times a year. This third attribute level means there are twice as many version of the survey than for women (For women: 32 sets of 2 LP questions, 64 sets of 4 DP questions = 2,048 possible versions; For men: 48 sets of 2 LP questions and 96 blocks of 4 DP questions = 4,608 possible versions). Therefore to achieve our target sample size, we will invite twice as many men as women to complete the survey; (roughly 66,667 and 33,333 male and female donors = 100,000 total invited population).

As no calls relating to the pilot survey were received by NHSBT call centre, the survey will be administered in 2 batches of 50,000 donors, not 4 as previously anticipated. This means that the survey is still on target to be complete by end of June.

### **Survey administration and consent process**

This online SP survey will be administered by NHSBT. The email invitation will be from Dr Gail Miflin, Associate Medical Director, NHSBT (see separate attachment). The email invitation will provide a weblink to the online survey which will include the information and an online consent question for study participation (see attachment). Consent is required before respondents are able to see the first question of the online survey. Following the standard NHSBT process, the email invitation, information sheet, consent form and also the survey will only be made available in English. The information sheet will make clear that the research team will also access existing data 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.

Therefore, the online information sheet at the commencement of the survey will:

- Provide 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 requested to provide consent (opt-in consent) by clicking the box on the web link, and in giving consent they will be stating that they have read the online information sheet and that they are consenting:

- to the use of their responses to the stated preference survey, in the described research
- 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.

If invited donors do not wish to participate in the survey, they will be able to click on a link to express this refusal of consent. If consent is not given, participants will not be offered an opportunity to complete the survey. They will also be reminded of the NHSBT call centre phone number to call in case of any queries.

Those donors who consent to participate in the survey, will be directed by weblink to the online survey, powered by Fluid Surveys. The survey will require donors to provide basic information about the last time they donated blood, e.g. travel time and total donation time, and then ask donors to complete the survey. Full information and examples on how to complete the survey will be provided (see attachment).

Invited donors who do not indicate whether or not they give consent, will be sent one reminder email from NHSBT 72 hours later. The reminder email will again include a weblink to the information sheet and consent form. Those invited donors who still do not respond will not be sent further invitations to participate in the SP survey. The weblink for completing the survey will be available for a maximum of 6 days (72 hours after the reminder email is sent).

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.

#### **Example of the SP survey and numbers of questions**

Each donor who provides informed consent will be asked to complete the SP survey. The responder will be asked to state how many times per year they would donate blood under a particular type of blood service. The descriptions of the blood service will be in line with the potential service changes described above. Each survey would consist of 6 questions, each containing different set of service characteristics. The pre-ambule to the questions will provide lay definitions of what is meant by each described attribute. An example of a question for the SP survey given in Table 4, below:

**Table 4: Example of a question for the SP survey.**

**Each respondent will receive 6 questions asking them to state their willingness to donate at alternate frequencies according to different blood service characteristics. These descriptions will cover questions that define service characteristics that relate to:**

- donors' last blood donation venue, which imply the same travel times that donors currently experience.
- alternative blood donation venues, which can imply additional travel time

**A preamble to each question will make plain that these are not necessarily current service options, or those experienced by the individual donor.**

Description of Service
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Travel time	Your typical travel time
Appointment availability	Every Monday – Friday
Opening times	9 am – 5pm
Health report provided	No
Maximum number of donations per year (women)	3 donations per year

***In this scenario, how many times a year would you give blood?***

<input type="checkbox"/>	I would probably not donate
<input type="checkbox"/>	Once a year
<input type="checkbox"/>	Twice a year
<input type="checkbox"/>	Three times a year
<input type="checkbox"/>	Four times a year

**Data linkage**

Anonymisation of data will be carried out by NHSBT; each participant will be allocated a unique ‘study ID’. This study ID, based on the donor’s NHSBT ID, is embedded in the weblink to the online survey provided in the email invitation. This will be used by NHSBT to link the survey responses to the donor’s details, including donation history and other data held on the PULSE database. NHSBT will retain a link of study IDs to donor IDs but LSHTM researchers will only access the study IDs. 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 will also be linked to future donation behaviour.

**Proposed analysis of the SP survey**

The SP survey will be used to provide estimates of the frequency of whole-blood donation according to the alternative changes to the blood collection service defined above (for example the introduction of donor health reports vs current practice). Preliminary plots and classic statistical tests will be employed to assess the mathematical relationship between the stated frequency of donation and the SP attributes. Next the most suitable regression models will be used to analyse the responses from the SP survey and to estimate the impact of the alternative proposed changes to the blood service on the frequency of donation. The validity of the resultant predicted probabilities from the SP survey 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 from the survey will be tested by contrasting predicted probabilities from the survey responses to the survey attributes that define current practice to the observed donation rates donors from the PULSE dataset. 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-effectiveness model (see below) will use predicted probabilities from the survey after correcting for these biases, when estimating the relative cost-effectiveness of the alternative strategies.

## ***6. Predicted volumes of whole-blood donated***

The predicted volumes of blood donated over 5 years according to the alternative strategies will be estimated by combining the predictions from the SP survey with PULSE data on volumes of whole-blood donated over time. The PULSE data will be linked to the sample of donors considered for the stated preference survey. The PULSE data will be used to define the target population, as a national sample of current whole-blood donors, and to estimate rates of whole-blood donation over 5 years. Analysis of the PULSE data will require access to the following types of variables:

- 1) donor level variables (for example age, sex, postcode 'sector', blood group, distance from local panels, donation history)
- 2) panel level variables (for example opening hours, availability of health report, number of beds).

The precise fields and variables required will be defined in conjunction with NHSBT. The study will not require access to particularly sensitive data including the results of tests of donated blood. PULSE data will be analysed to quantify patterns of donation by donor subgroup, rates of no-show for appointments, and deferral rates. We will also analyse, where possible, the impact on donation frequency and donor retention of recently implemented changes to the service such as the closure of panels (donation venues), changes in the frequency of attendance at temporary sites, and changes in the opening times of donation venues. These predicted volumes, along with the cost of implementing changes in service configurations (see section 7) will be combined in a decision analysis model to estimate the cost-effectiveness of different alternative service configurations (section 8).

## ***7. Costs of the alternative changes to the blood collection service***

The accompanying investment required to make the proposed changes to the blood collection service will be costed from internal NHSBT finance records according to the minimum levels of investment required. For example, an initiative to extend blood donation venues' opening times would require centre staff to work additional shifts, which will be costed on the median pay-scale for each grade of staff required, and will include any additional salary and associated on-costs for weekend opening together with appropriate apportionment of additional transport costs, overheads and capital costs (permanent sites). An initiative to reimburse donor expenses, such as parking costs will be based on a sample of parking charges in the locality of the blood donation venues, and would be according to the median total time for blood donation including waiting time.

## ***8. Decision model, combining both predicted costs and volumes for alternative strategies***

The decision model will use predictions from the SP and PULSE database on donation frequency, together with estimates of the relative costs of alternative changes to the blood service to provide predictions of the relative volumes of whole-blood, costs and cost-effectiveness of the alternative strategies. Specifically we will provide estimates of the relative cost-effectiveness of closing smaller mobile units, alternative opening times (e.g. weekend opening), providing free donor health checks and increasing the maximum number of donations allowed per year. We will consider each of these strategies, alone and in combination. In contrasting possible service changes, the model will draw on the estimates from the SP, for example the effect of a change in travel time (e.g. increase of 30

minutes) on the predicted probability of attendance within 6 months (e.g. change from 0.75 to 0.50), after adjusting for the estimated discrepancies between stated and revealed preferences.

For each strategy, the model will report costs, and units of whole-blood supplied over 5 years, overall and by donor subgroup. The probabilistic sensitivity analysis will report the relative probability that each strategy is the most cost-effective at alternative levels of willingness to pay for an additional unit of whole-blood donated. The structural sensitivity analysis will use alternative approaches to allow for discrepancies between the frequencies of blood donation predicted by the SP survey versus those observed in practice.

## **Project Outputs**

The project outputs will address the study objectives listed above by providing

1. Predicted costs, volumes of whole-blood donated, and cost-effectiveness of alternative strategies such as closing 3- and 6- bedded temporary units, extending opening hours, or investing in free donor health checks (each strategy alone and then in realistic combinations with other strategies)
2. Recommendations about which changes to future blood collection strategies are most cost-effective, overall and for donor subgroups (e.g. gender, age, new versus existing donors, baseline levels of iron, ethnicity, blood type and according to donation history e.g. duration of whole-blood donation).
3. Recommendations about how whole-blood collection strategies can be personalised to the requirements of individual donors.
4. A decision model that can be used in the future to assess the cost-effectiveness of new strategies for sustaining the supply of whole-blood.
5. Identification of which areas of further research would be most valuable for informing future NHSBT strategy.

## **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, the development of the study protocol and will 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 three 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.

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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.

## Research governance

Approval for the study as outlined in this protocol, including both the pilot and full stated preference survey will be sought from:

- The NHS Research Ethics Committee (using the Integrated Research Application (IRAS) system)
- The NHSBT R&D Office (this can be done through the same application, through IRAS)
- The LSHTM Research Ethics Committee.

Separate applications, if necessary, will be considered at a later stage, for the objective related to the INTERVAL trial. Therefore, the current applications to the research ethics committees will focus on study objectives two and three: to investigate the frequency with which donors are willing to donate whole-blood according to alternative future changes to the blood collection service; and, to estimate the cost-effectiveness of alternative strategies for maintaining the supply of whole-blood to the NHS. The applications for ethical approval will consider the potential issues associated with this research, including consent and confidentiality, information security, sampling and recruitment of donors, and any issues of sensitivity. Where the pilot survey results in significant changes to the study, amendments to the original applications will be submitted for further approval.

## Data storage and transfer

The data outlined will be transferred from NHSBT 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.

An Information Sharing Protocol will be agreed between NHSBT and LSHTM. It is not intended for any personally-identifiable data to be shared with LSHTM researchers. Data will be held and used in accordance with Information Security Policies and Procedures at NHSBT and LSHTM.

Dr Gail Mifflin, 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.

- Research data linked to 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.
- Research data will be held for 10 years in line with LSHTM policy for retention of research data, after which it will be deleted in accordance with University policy by the Archivist.

## **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 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). The meetings of the study advisory group will be in months 1, 6, 11 and 22, timed so that the advisory group can help ensure that each key study component is delivered on time.

Neil Hawkins (NH) will be responsible for the development and analysis of the decision model, and John Cairns for the SP survey; they will provide SP / ZS with specialist guidance on these aspects. RG and Crispin Wickenden (CW) will guide Mark Pennington (lecturer, LSHTM), and SP, in the analysis of the PULSE data. CW will oversee the administration of the SP survey. Laura Hontoria del Hoyo and Gail Mifflin will guide the costing of future changes to the blood collection service and the implications of the study findings for NHSBT strategy.

## **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.

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 SP survey, how best to undertake the subsequent analysis, and how to interpret the results. Members of the Oxford panels are reviewing the wording of the draft donor questionnaires in meetings with the research team before and after the questionnaire is 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 three 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

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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.