Appendix: Example survey questions

Example question from the pilot survey

Thinking of the place where you *usually* donate blood, imagine the service is like this:

	Description of Service
Travel time	Your usual travel time
Opening times	Monday-Friday (day time only)
Total time of the visit	120 minutes
Health report provided	No
Maximum number of ***donations*** per year	3 donations per year

In this situation, how many times a year would you donate blood?

Please select one of the boxes below:

Never, I would stop donating	Once a year	Twice a year	Three times a year
☐	☐	☐	☐

Non-INTERVAL donors

Version 1.2, 13 May 2016

Note: This is a representation of an electronic survey that appeared over multiple screens. It was preceded by information for donors (screens 1-2) and a consent question (screen 3), which are available on the project website.

SCREEN 4:

Question 1: How many times **did you give** blood in the last 12 months?

If you can't remember, please give your best guess.

- I did not give blood in the past 12 months
- Once
- Twice
- Three times
- Four times
- More than four times (please specify)

Question 2: How many times did you **want to give** blood in the last 12 months?

This answer may differ from your answer to question 1 for many reasons. For example, you could not attend your appointment because you had to care for a sick child, or you wanted to give blood but the waiting time was too long.

- I did not give blood in the past 12 months
- Once
- Twice
- Three times
- Four times
- More than four times (please specify)

The following questions ask about **the last time you gave blood**.

Question 3: When you last gave blood, where did you travel from?

If you can't remember, please give your best guess.

- Your home
- Your workplace
- Somewhere else
- Question 4: Roughly how far did you travel to the place where you last gave blood?
- *If you can't remember, please give your best guess.*
- Less than 2 miles
- 2-4 miles
- More than 4 miles
  Please tell us to the nearest mile (response limited to 3 integers)

Question 5: How did you travel to the place where you last gave blood?

Please choose the answer that applies to the longest part of your journey.

- Walk
- Cycle
- Car
- Public transport (e.g. bus, tube, train or tram)
- Question 6: How long did it take you to travel to the place where you last gave blood?
- *If you can't remember, please give your best guess.*
- Less than 10 minutes
- 10-30 minutes
- 30-60 minutes
- More than 60 minutes
  Please tell us how long *in minutes* _ _ _(answer limited to 3 integers)

Question 7: Roughly how long did your last blood donation visit take?

From your scheduled appointment time, to the time you arrived at the tea table and were free to leave (including waiting time).

- 1 hour or less
- More than 1 hour

Question 8: What prompted you to make your last appointment to give blood?

Please choose the answer that best applies to you.

- I booked at a previous blood donation visit
- I received an invitation letter
- I received an email, phone call or text message
- I saw an advert, publicity or campaign
- I booked without being prompted
- I did not make an appointment
- Other

Question 9:

[Question not asked if respondent answers “I did not make an appointment” to question 8] Are you able to book appointments to give blood as often as you would like, at a day and time that suits you?

- Yes, easily
- Yes, but with some difficulty or delay
- No, it is very difficult

SCREEN 5:

The next 6 questions will ask **how often** you would donate blood under different scenarios. The scenarios describe a service with different features that are described in the table below. Each scenario is a little different but it would always take around **1 hour** from your appointment time to the time you arrive at the tea table and are free to leave (including waiting time).

Travel time to the place where you donate blood	This is the time it would take you to travel to the place where you donate blood. Travel time in the scenarios may range from 10 minutes shorter than your typical travel time, up to 30 minutes longer than your typical travel time.
Appointment availability	These are that days the appointments are available for donors to give blood. Options include: 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	These are the times of the day, when you can give blood. Possible opening times include: 9am-12pm and 2pm-5pm 9am-5pm 9am-8pm 2pm-8pm
Health report provided	A health report is not currently provided. In the future if a health report were to be provided it might give measurements such as your blood pressure and cholesterol.
Maximum number of ***donations*** per year	This is the maximum number of times each year that you are allowed to give blood in the UK for health and safety reasons. Currently this is 3 times a year for women and 4 times a year for men. A clinical trial is looking at the impact of donors giving blood more often. Depending on the results of the trial, donors might be allowed to give blood more often in future. Women may be permitted to give blood up to 4 times a year. Men may be permitted to give blood up to 6 times a year.

For each question please pick a single answer. **There are no right or wrong answers, we are just interested in your views.** If you are not sure, please give us your best guess.

SCREEN 6:

Scenario 1:

At the place where you *last gave* blood, suppose the service is like this:

	Description of Service
Travel time	Your typical travel time
Appointment availability	Every weekday (Monday-Friday)
Opening times	9am-12pm and 2pm-5pm
Health report provided	No
Maximum number of ***donations*** per year	3 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

In this scenario, how many times a year would you give blood? [Answer is mandatory]

- ☐ *I would probably not donate*
- ☐ *Once a year*
- ☐ *Twice a year*
- ☐ *Three times a year*
- ☐ *Four times a year*

SCREEN 7:

Scenario 2:

At the place where you *last gave* blood, suppose the service is like this:

	Description of Service
Travel time	Your typical travel time
Appointment availability	1 day every 2 months (Monday – Friday)
Opening times	2pm-8pm
Health report provided	No
Maximum number of ***donations*** per year	4 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

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

[Answer is mandatory]

- [ ] *I would probably not donate*
- [ ] *Once a year*
- [ ] *Twice a year*
- [ ] *Three times a year*
- [ ] *Four times a year*

SCREEN 8:

The next four scenarios ask you to imagine giving ***blood at a different place.***

SCREEN 9:

Scenario 3:

At a different place to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	15 minutes longer than your typical travel time
Appointment availability	1 day every 2 months (Saturday or Sunday)
Opening times	9am-8pm
Health report provided	Yes, after each donation
Maximum number of ***donations*** per year	3 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

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

[Answer is mandatory]

- ☐ *I would probably not donate*
- ☐ *Once a year*
- ☐ *Twice a year*
- ☐ *Three times a year*
- ☐ *Four times a year*

SCREEN 10:

Scenario 4:

At a <u>different place</u> to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	30 minutes longer than your typical travel time
Appointment availability	Every day (Monday – Sunday)
Opening times	9am-8pm
Health report provided	Yes, after each donation
Maximum number of ***donations*** per year	3 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

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

[Answer is mandatory]

- ☐ *I would probably not donate*
- ☐ *Once a year*
- ☐ *Twice a year*
- ☐ *Three times a year*
- ☐ *Four times a year*

SCREEN 11:

Scenario 5:

At a <u>different place</u> to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	10 minutes shorter than your typical travel time
Appointment availability	Every day (Monday – Sunday)
Opening times	2pm – 8pm
Health report provided	No
Maximum number of ***donations*** per year	3 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

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

[Answer is mandatory]

- [ ] *I would probably not donate*
- [ ] *Once a year*
- [ ] *Twice a year*
- [ ] *Three times a year*
- [ ] *Four times a year*

SCREEN 12:

Scenario 6:

At a different place to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	30 minutes longer than your typical travel time
Appointment availability	1 day every 2 months (Monday – Friday)
Opening times	9am-12pm and 2pm-5pm
Health report provided	No
Maximum number of ***donations*** per year	4 donations per year

[Definitions of each attribute are available as "tool tips" by hovering over the left hand column with a mouse]

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

[Answer is mandatory]

- ☐ *I would probably not donate*
- ☐ *Once a year*
- ☐ *Twice a year*
- ☐ *Three times a year*
- ☐ *Four times a year*

SCREEN 13:

Thank you for taking the time to complete the survey. Your responses have been submitted.

We are currently working in collaboration with researchers from London School of Hygiene and Tropical Medicine, University of London to review and improve the service we offer to our donors.

We would like to re-iterate that the scenarios in this survey are hypothetical. For more information on the guidelines around blood donation, including permitted frequency, please visit our website (https://www.blood.co.uk/who-can-give-blood/).

Thank you for your continued support and generosity.

Dr Gail Miflin

Associate Medical Director, Blood Supply, NHS Blood and Transplant

Ex-INTERVAL donors

Version 1.1, 24 September 2016

Note: This is a representation of an electronic survey that appeared over multiple screens. It was preceded by information for donors (screens 1-2) and a consent question (screen 3), which are available on the project website.

SCREEN 4:

Question 1: How many times **did you give** blood in the last 12 months?

If you can't remember, please give your best guess.

- I did not give blood in the past 12 months
- Once
- Twice
- Three times
- Four times
- More than four times (please specify)

Question 2: How many times did you **want to give** blood in the last 12 months?

This answer may differ from your answer to question 1 for many reasons. For example, you could not attend your appointment because you had to care for a sick child, or you wanted to give blood but the waiting time was too long.

- I did not give blood in the past 12 months
- Once
- Twice
- Three times
- Four times
- More than four times (please specify)

The following questions ask about **the last time you gave blood**.

Question 3: When you last gave blood, where did you travel from?

If you can't remember, please give your best guess.

- Your home
- Your workplace
- Somewhere else

Question 4: Roughly how far did you travel to the place where you last gave blood?

If you can't remember, please give your best guess.

- Less than 2 miles
- 2-4 miles
- More than 4 miles

  Please tell us to the nearest mile (response limited to 3 integers)

Question 5: How did you travel to the place where you last gave blood?

Please choose the answer that applies to the longest part of your journey.

- Walk
- Cycle
- Car
- Public transport (e.g. bus, tube, train or tram)

Question 6: How long did it take you to travel to the place where you last gave blood?

If you can't remember, please give your best guess.

- Less than 10 minutes
- 10-30 minutes
- 30-60 minutes
- More than 60 minutes

  Please tell us how long *in minutes* _ _ _(answer limited to 3 integers)

Question 7: Roughly how long did your last blood donation visit take?

From your scheduled appointment time, to the time you arrived at the tea table and were free to leave (including waiting time).

- 1 hour or less
- More than 1 hour

Question 8: What prompted you to make your last appointment to give blood?

Please choose the answer that best applies to you.

- I booked at a previous blood donation visit
- I received an invitation letter
- I received an email, phone call or text message
- I saw an advert, publicity or campaign
- I booked without being prompted
- I did not make an appointment
- Other

Question 9:

Are you able to book appointments to give blood as often as you would like, at a day and time that suits you?

- Yes, easily
- Yes, but with some difficulty or delay
- No, it is very difficult

SCREEN 5:

The next 6 questions will ask **how often** you would donate blood under different scenarios. The scenarios describe a service with different features that are described in the table below. Each scenario is a little different but it would always take around **1 hour** from your appointment time to the time you arrive at the tea table and are free to leave (including waiting time).

Travel time	This is the time it would take you to travel to the place where you donate blood. Travel time in the scenarios may range from 10 minutes shorter than your typical travel time, up to 30 minutes longer than your typical travel time.
Appointment availability	These are that days the appointments are available for donors to give blood. Options include: 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	These are the times of the day, when you can give blood. Possible opening times include: 9am-12pm and 2pm-5pm 9am-5pm 9am-8pm 2pm-8pm
Health report	A health report is not currently provided. In the future if a health report were to be provided it might give measurements such as your blood pressure and cholesterol.
Maximum number of donations per year	This is the maximum number of times each year that you are allowed to give blood in the UK for health and safety reasons. Currently this is 3 times a year for women and 4 times a year for men. The INTERVAL trial is looking at the impact of donors giving blood more often. Depending on the results of the trial, donors might be allowed to give blood more often in future. Women may be permitted to give blood up to 4 times a year. Men may be permitted to give blood up to 6 times a year.

For each question please pick a single answer. **There are no right or wrong answers, we are just interested in your views.** If you are not sure, please give us your best guess.

SCREEN 6:

Scenario 1:

At the place where you *last gave* blood, suppose the service is like this:

	Description of Service
Travel time	Your typical travel time
Appointment availability	Every weekday (Monday-Friday)
Opening times	9am-12pm and 2pm-5pm
Health report	No
Maximum number of donations per year	3 donations per year

In this scenario, how many times a year would you give blood? *[Answer is mandatory]*

- [ ] I would probably not donate
- [ ] Once a year
- [ ] Twice a year
- [ ] Three times a year
- [ ] Four times a year

SCREEN 7:

Scenario 2:

At the place where you *last gave* blood, suppose the service is like this:

	Description of Service
Travel time	Your typical travel time
Appointment availability	1 day every 2 months (Monday – Friday)
Opening times	2pm-8pm
Health report	No
Maximum number of donations per year	4 donations per year

In this scenario, how many times a year would you give blood? *[Answer is mandatory]*

- [ ] I would probably not donate
- [ ] Once a year
- [ ] Twice a year
- [ ] Three times a year
- [ ] Four times a year

SCREEN 8:

The next four scenarios ask you to imagine giving ***blood at a <u>different place</u>.***

SCREEN 9:

Scenario 3:

At a <u>different place</u> to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	15 minutes longer than your typical travel time
Appointment availability	1 day every 2 months (Saturday or Sunday)
Opening times	9am-8pm
Health report	Yes, after each donation
Maximum number of donations per year	3 donations per year

***In this scenario, how many times a year would you give blood*?** [Answer is mandatory]

- [ ] I would probably not donate
- [ ] Once a year
- [ ] Twice a year
- [ ] Three times a year
- [ ] Four times a year

SCREEN 10:

Scenario 4:

At a <u>different place</u> to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	30 minutes longer than your typical travel time
Appointment availability	Every day (Monday – Sunday)
Opening times	9am-8pm
Health report	Yes, after each donation
Maximum number of donations per year	3 donations per year

In this scenario, how many times a year would you give blood? *[Answer is mandatory]*

☐	I would probably not donate
☐	Once a year
☐	Twice a year
☐	Three times a year
☐	Four times a year

SCREEN 11:

Scenario 5:

At a <u>different place</u> to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	10 minutes shorter than your typical travel time
Appointment availability	Every day (Monday – Sunday)
Opening times	2pm – 8pm
Health report	No
Maximum number of donations per year	3 donations per year

In this scenario, how many times a year would you give blood? *[Answer is mandatory]*

- [ ] I would probably not donate
- [ ] Once a year
- [ ] Twice a year
- [ ] Three times a year
- [ ] Four times a year

SCREEN 12:

Scenario 6:

At a different place to where you last gave blood, suppose the service is like this:

	Description of Service
Travel time	30 minutes longer than your typical travel time
Appointment availability	1 day every 2 months (Monday – Friday)
Opening times	9am-12pm and 2pm-5pm
Health report	No
Maximum number of donations per year	4 donations per year

In this scenario, how many times a year would you give blood? *[Answer is mandatory]*

- [ ] I would probably not donate
- [ ] Once a year
- [ ] Twice a year
- [ ] Three times a year
- [ ] Four times a year

FINAL SCREEN

We are currently working in collaboration with researchers from London School of Hygiene and Tropical Medicine, University of London to review and improve the service we offer to our donors.

Would you be happy to be contacted in future about this research?

☐ Yes

☐ No

We would like to re-iterate that the scenarios in this survey are hypothetical. For more information on the guidelines around blood donation, including permitted frequency, please visit our website (https://www.blood.co.uk/who-can-give-blood/).

Thank you for your continued support and generosity.

Dr Gail Miflin

Medical and Research Director, NHS Blood and Transplant

SCREEN 21

Thank you for taking the time to complete the survey. Your responses have been submitted.

Thank you for your continued support and generosity.

Dr Gail Miflin MA FRCP FRCPath

Medical and Research Director, NHS Blood and Transplant

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RESEARCH PAPER COVER SHEET

Please note that a cover sheet must be completed for each research paper included within a thesis.

SECTION A – Student Details

Student ID Number	1406820	**Title**	Ms
First Name(s)	Kaat Lieve An		
Surname/Family Name	De Corte		
Thesis Title	An approach to stated preference surveys for reducing hypothetical bias and predicting the effects of alternative policy changes: the case of blood donation		
Primary Supervisor	Professor Richard Grieve		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Transfusion Medicine		
When was the work published?	2018		
If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

*If yes, please attach evidence of retention. If no, or if the work is being included in its published format, please attach evidence of permission from the copyright holder (publisher or other author) to include this work.

SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	

Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I contributed to the overall design of the study, the data collection, and preference prediction analysis for the cost-effectiveness analysis. Sarah Willis analysed the cost data and led the drafting of the manuscript. I contributed to the writing and review of the manuscript. The other co-authors advised on the project and reviewed the manuscript.

SECTION E

Student Signature	Kaat De Corte
Date	22 October 2022

Supervisor Signature	Richard Grieve
Date	23 October 2022

TRANSFUSION MEDICINE
Official Journal of the British Blood Transfusion Society
British Blood Transfusion Society
Transfusion Medicine | ORIGINAL ARTICLE

Cost-effectiveness of alternative changes to a national blood collection service

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SUMMARY

Objectives: To evaluate the cost-effectiveness of changing opening times, introducing a donor health report and reducing the minimum inter-donation interval for donors attending static centres.

Background: Evidence is required about the effect of changes to the blood collection service on costs and the frequency of donation.

Methods/Materials: This study estimated the effect of changes to the blood collection service in England on the annual number of whole-blood donations by current donors. We used donors' responses to a stated preference survey, donor registry data on donation frequency and deferral rates from the INTERVAL trial. Costs measured were those anticipated to differ between strategies. We reported the cost per additional unit of blood collected for each strategy versus current practice. Strategies with a cost per additional unit of whole blood less than £30 (an estimate of the current cost of collection) were judged likely to be cost-effective.

Results: In static donor centres, extending opening times to evenings and weekends provided an additional unit of whole blood at a cost of £23 and £29, respectively. Introducing a health report cost £130 per additional unit of blood collected. Although the strategy of reducing the minimum inter-donation interval had the lowest cost per additional unit of blood collected (£10), this increased the rate of deferrals due to low haemoglobin (Hb).

Conclusion: The introduction of a donor health report is unlikely to provide a sufficient increase in donation frequency to justify the additional costs. A more cost-effective change is to extend opening hours for blood collection at static centres.

Key words: blood donation, cost-effectiveness analysis, stated preferences.

The World Health Organisation (WHO) and the International Federation of Red Cross and Red Crescent Societies (IFRC) set out a shared global vision for a self-sufficient blood supply by 2020 (WHO and IFRC, 2010). This framework for action called on blood supply agencies to encourage more frequent donation from current whole-blood donors, such as by making blood donation more convenient. However, there is little evidence about the effect that changes to the blood collection service have on the frequency and costs of whole-blood donation.

Blood supply agencies require evidence on the relative costs and effectiveness of alternative strategies, whether they are required to increase, decrease or maintain the current levels of whole blood supplied. In England, the overall demand for whole blood is falling, but there is increased demand for the universal blood type O negative (O−) as well as A negative (A−), B negative (B−) and rare blood subtypes more common in Black, Asian and minority ethnic (BAME) donors (e.g. Ro). A key challenge is to identify changes to the blood service that increase donation frequency for those donors whose blood type is in relatively high demand at low additional cost.

The Health Economics Modelling of alternative blood donation strategies (HEMO) study aimed to assess the cost-effectiveness of strategies to maintain the blood supply in England (Grieve *et al.,* 2017, in press). The study estimated the frequency with which existing donors would be willing to donate whole blood following changes to the current blood collection service. This paper reports the essential features of the cost-effectiveness analysis (CEA) and its implications for policymakers.

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Table 1. Overview of the cost-effectiveness analysis

Strategy	Target population	Attribute levels with status quo	Attribute levels with new strategy
Provision of health report for all donors	All donors who gave blood in last year.	Health report not provided	Health report provided
Weekend opening at static donor centres	All donors who gave blood in the last year at a static donor centre that is not routinely open at weekends.	Appointment availability *Every weekday Monday–Friday*	Every day: Monday–Sunday
Weekday evening opening at static donor centres	All donors who gave blood in the last year at a static donor centre that did not remain open until 20·00 on weekdays.	Current opening hours	Opening hours 09·00–20·00
Weekend opening of mobile sessions	All donors who gave blood in the last year at a mobile session that is not routinely open at weekends.	Appointment availability *1 day every 2 months: Monday–Friday*	Appointment availability *1 day every 2 months: Saturday or Sunday*
Weekday evening opening of mobile sessions	All donors who gave blood in the last year at a mobile sessions that is not routinely open until 20·00 on weekdays.	Current opening hours	Opening hours 14·00–20·00
Shorter minimum interval between donations for both men and women	All donors who gave blood in the last year at a static donor centre.	Maximum number of donations: Males four times per year and Females three times per year	Maximum number of donations: Males six times per year; Females four times per year

MATERIALS AND METHOD

Strategies for the CEA

In England, the NHS Blood and Transplantation (NHSBT) strategy emphasised the need to improve the donation experience for existing donors (NHS Blood and Transplant, 2015). The HEMO study therefore considered alternative service changes for increasing donation frequency for current whole-blood donors; strategies to attract new donors were outside the study scope. The service changes of interest were identified through a review of NHSBT strategy documents, the results of market research, an informal review of relevant published literature, consultation with policymakers and insights from preliminary qualitative research with donors. The six strategies considered were the provision of a donor health report (at all blood collection venues), offering weekend and evening donation opportunities at either static centres or mobile sessions and reducing the minimum interval between donations for donors at static centres (see Table 1).

Each strategy involved a single change to the blood collection service compared to the current service experienced by whole-blood donors. The strategies are not mutually exclusive and are not 'scalable' to the same degree, so we made a series of pairwise comparisons for each potential change compared to the current service provision. A 1-year time horizon was adopted as the longer-term demand for blood is unknown, and the shorter-term effects of the alternative strategies on the volume and type of blood collected were considered more relevant for future policy.

Health report

Several European blood supply agencies provide information about donors' own health to incentivise blood donation (Marantidou *et al.,* 2007). A health report provides donors with information about their own health from data routinely collected during blood donation, and sometimes from additional tests. The policy is controversial; blood supply agencies are not providers of healthcare, and evidence of its effectiveness in increasing the blood supply is mixed (Goette *et al.,* 2009). The HEMO study defined a health report as information provided to a donor on their blood pressure taken prior to donation and a cholesterol test taken from the blood sample after each donation. The analysis excluded any longer-term sequelae following the health report.

Session opening times

Holding sessions at evenings and weekends may make blood donation more convenient and increase donation frequency. To investigate realistic changes to opening times at static centres, we assumed that providing sessions at weekends or during weekday evenings would be *additional* to those provided during current opening hours. For mobile sessions, it was more realistic to assume that weekend or weekday evening sessions would *substitute* daytime sessions. In 2016, 86% of blood donations were made at a mobile session. In total, 23 000 mobile sessions were held in England for whole-blood donation, of which only 10 % were open until 20:00 and only 4 % at weekends. Donors can also visit 1 of 24 permanent static centres where blood collection

is offered in the same venue several days a week. Of the static donor centres, 15 were routinely open at weekends in 2016, and 5 offered sessions until 20:00 on weekday evenings.

Inter-donation interval

INTERVAL, a large multicentre, randomised, controlled trial, provided evidence on whether reducing inter-donation intervals in all static centres in England would increase donation frequency without compromising donor safety (Di Angelantonio *et al.,* 2017; Moore *et al.* 2014). The trial reported that donors randomised to the shorter minimum donation interval (8 weeks for men, 10 weeks for women) successfully donated more whole blood on average compared to those randomised to the current minimum donation intervals (12 weeks for men, 16 weeks for women). Higher rates of deferral were recorded in the shorter donation interval randomised arms.

The HEMO study assessed the cost-effectiveness of the shortest minimum inter-donation interval adopted in the INTERVAL trial for men and women donating at static donor centres versus current minimum donation intervals.

Stated preference survey

The CEA required predictions of the effects of alternative changes to the blood service on the frequency of blood donation. In England, these potential service changes have either not been implemented at all (e.g. the donor health report) or have only been implemented in some venues (e.g. weekend opening). We therefore needed to understand how donors might respond to these changes to the service without first experiencing them. Formal methods to elicit choices under hypothetical conditions, known as stated preferences, are used extensively in transport, environmental and health economics when information on actual choices, known as revealed preferences, are not available. We conducted a large stated preference survey of donors who had donated whole blood at least once in the previous year.

The stated preference survey was designed iteratively, incorporating the views of NHSBT policymakers and donors. The survey was revised following a large pilot study (De Corte *et al.,* 2016). The final survey included five attributes that described those characteristics of the blood service that were liable to be modified following proposed changes to the blood service. The chosen attributes were: donor travel time to the blood donation venue; the opening hours for blood collection; and the availability of appointments for blood donation, provision of a health report and the maximum number of whole-blood donations permitted in a year. For each attribute, alternative levels were defined according to current and future service provision; e.g. for the health report attribute, two levels were defined according to whether or not a health report was provided.

Figure 1 presents an example question from the survey. Respondents were asked to state the frequency with which they would be willing to donate blood according to the

At the place where you ***last gave blood***, suppose the service is like this:

	Description of Service
Travel time	Your typical travel time
Appointment availability	Every weekday: Monday - Friday
Opening times	9am-12pm and 2pm-5pm
Health report provided	Yes, after each donation
Maximum number of donations per year	3 times per year

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

☐ I would probably not donate

☐ Once a year

☑ Twice a year

☐ Three times a year

☐ Four times a year

Fig. 1. An example of a question from the stated preference survey.

Table 2. Background characteristics of the population and respondents to the stated preference survey

		Donors who responded to the survey ($N = 23\,981$)		All donors in March 2016 extract of PULSE database ($N = 781\,028$) who had donated in the last 12 months	
		N	%	*N*	%
Age group	17 – 30	3 309	13·80	188 744	24·17
	31 – 45	5 774	24·08	205 505	26·31
	46 – 60	9 824	40·97	267 856	34·30
	60+	5 073	21·15	118 923	15·23
Blood type	High demand	2 472	10·31	111 948	14·33
	Standard demand	21 509	89·69	669 080	85·67
Ethnicity	White	22 339	93·15	724 880	92·81
	Black/mixed Black	201	0·84	8 315	1·06
	Asian/mixed Asian	562	2·34	21 727	2·78
	Other or not stated	879	3·67	26 106	3·34
'Nursery' donor	Yes	6 566	27·38	283 502	36·30
	No	17 415	72·62	497 526	63·70
Session type	Static centre	2 053	8·53	107 811	13·80
	Mobile session[1]	21 928	91·44	673 217	86·20
Number of donations in last 12 months	1	7 148	29·81	317 266	40·62
	2	8 063	33·62	245 984	31·49
	3	7 267	30·30	183 211	23·46
	4	1 454	6·06	29 460	3·77
	5	40	0·17	3 450	0·44
	6	9	0·04	1 657	0·21

[1] A session is an organisational feature of NHSBT that can be understood as a single effort to collect blood on one particular day, by a particular team, in a particular location. For example, even if the same team collects blood at the same location for two consecutive days, this would be considered two sessions.

alternative attributes and levels offered in different scenarios. We hypothesised that donors would state a higher frequency of donation if they were offered an incentive to donate, such as a health report, or if donation was made more convenient, e.g. by providing opportunities to donate at weekends or in the evening.

The survey received ethical approval from both NHS (reference 16/YH/0023) and LSHTM (reference 10 384) Research Ethics Committees. A total of 100 000 donors were randomly selected to be sent an email inviting them to take part in the online survey if they met the following inclusion criteria: 17 – 70 years old, donation of at least one unit of whole blood in the past 12 months, email address held by NHSBT and residence in mainland England. Donors were excluded if they had been temporarily suspended from donating (e.g. if they had recently had a tattoo) and if they had recently taken part in a routine survey or research study.

A total of 25 187 donors responded to the survey (25·2%). The donors who responded to the survey were somewhat different to the overall target population (Table 2), e.g. the proportion of donors over 60 years old was higher for the survey responders than the overall target population (21% vs 15%).

Target population

The overall target population was all whole-blood donors who had successfully given blood at least once in the year prior to March 2016 and who resided in mainland England ($N = 781\,028$) (see Table 2). Although all donors were eligible for a health report after each donation, for the strategies that involved changes to opening times of the blood collection venues, the target population was limited to donors who last gave blood at a venue that was not already open at weekends and evenings. The target population for the strategy to reduce the minimum inter-donation interval was limited to those donors whose last blood donation was at a static donor centre.

Predicting total volume of blood

The responses to the stated preference survey were used to predict the average number of whole-blood donations per year following the alternative changes to the blood service defined by each strategy. A major assumption is that individuals' responses to survey questions will predict their actual behaviour. We investigated whether this assumption was plausible and found that, on average, there was a small discrepancy between the donation frequency predicted from the survey responses and the actual donation frequency observed in the PULSE donor register (De Corte *et al.,* 2016; Grieve *et al.,* 2017, in press).

The data from the response to the survey were analysed to estimate the effect of potential service changes on the annual frequency of whole-blood donation. As the response data were categorical and naturally ordered, an ordered logit model was

chosen and included attributes from the stated preference survey as independent (exposure) variables (Greene, 2017). To allow for differences in observed characteristics between the survey responders and the overall target population, the model also included each of the characteristics listed in Table 2 as independent variables.

Adjusting for deferred donations

If a donor's haemoglobin (Hb) levels are below 135 g L^{-1} for males or 125 g L^{-1} for females, blood collection NHSBT policy is that donation will be temporarily suspended, or deferred, for at least 6 months (or longer if Hb is particularly low). Donations can also be deferred due to other reasons, e.g. related to travel, medication, lifestyle or infection/illness. The INTERVAL trial reported that deferrals due to low Hb were higher for the patients randomised to reduced minimum interval (Di Angelantonio *et al.,* 2017). We used estimates from applying a logistic regression model to the trial data, which estimated the effect of changing the minimum interval on deferral rates and allowed for patient characteristics, to predict deferral rates per attendance according to the levels of those characteristics in the target population.

Difference in volume of blood collected between strategies

The incremental effect of each strategy was calculated as the difference between the predicted mean volumes of blood before and after the proposed service change. The number of annual blood donation visits was calculated for each donor in the target population according to the donor's personal characteristics and the service-level attributes that defined each donor's most recent experience of giving blood. We predicted the number of blood donation visits by combining the estimated coefficients from the ordered logit model applied to the survey response data with the characteristics of each donor in the target population. The predicted annual frequency of donation allowed for the estimated probability of deferral. The predicted annual mean number of units of blood donated per donor was then multiplied by the number of donors in the target population to calculate the annual total volume of blood collected across the service. Finally, the predictions were repeated after changing the attribute level associated with each proposed service change (see Table 1).

Costs

Cost measurement was from the NHS and personal social services perspective recommended by NICE (NICE methods guide, 2013). The costs included were those anticipated to differ between strategies, including additional collection and staff costs but not processing, marketing or fixed costs. Costs beyond 1 year were not considered. Three types of cost were included: the variable cost of collecting blood associated with each strategy (staff costs including unsocial hours premium, invitations, consumables), the costs of providing a health report, and the cost of deferrals.

Variable cost of blood collection

The variable costs covered the cost of inviting donors, staff time and disposables. We assumed that processing costs were constant across strategies and that the service was scalable to any volume of blood collected. The cost measurement recognised differences in unit costs between mobile sessions and static donor centres and that, on average, mobile sessions were close to capacity (95%), whereas static centres were not (75%). The base case analysis therefore assumed that strategies which required more blood to be collected would require additional staff at mobile sessions but not in static centres, where additional collection within current opening times would be undertaken by existing staff. In both settings, the costs of staff employed at weekends and during evenings were calculated at appropriate additional rates (The NHS Staff Council, 2016).

Costs of providing a health report

The health report costs assumed that the cholesterol test would be undertaken alongside others routinely undertaken at small additional cost (Czoski-Murray *et al.* 2012; Department of Health 2008). We assumed that to measure blood pressure required an additional 1·5 min per donor. We assumed that 2 % of tests would require a letter to advise clinical follow up.

Cost of deferrals

The cost of deferrals included the time taken for donor carers to undertake a health screen and, where deferral was due to low Hb, a copper sulphate and HemoCue® test (HemoCue®, Radiometer Medical ApS, Denmark). We assumed based on the INTERVAL trial data that 7% of these donors would be referred to their Primary Care Physician (when Hb is less than 125 g L^{-1} for men and 115 g L^{-1} for women) and then that healthcare costs would be incurred. These costs were assumed to include a GP appointment, a full blood count test and Serum ferritin test, iron supplements (50% of donors) and an outpatient appointment (10% donors). The accompanying unit costs were taken from published sources. (Curtis and Burns, 2016; Department of Health, 2016; Health-Care Medical Equipment Group 2017; Joint Formulary Committee 2016; National Institute for Health and Care Excellence, 2015)

Cost-effectiveness analysis

The incremental cost per donor for each strategy compared to the status quo was calculated as an additional (difference in means) cost of collecting the additional (difference in means) volume of blood after the service change. We estimated the incremental cost per additional unit of whole blood collected overall and for subgroups of prime interest. These include five donor characteristics: age (17–30, 31–45, 46–60, 60 or over), high or standard demand blood types, ethnicity (White, Black/mixed Black, Asian/mixed Asian or Other/not stated), 'nursery' donor

status (fewer than four lifetime donations) and the venue (static or mobile).

Interpretation of the threshold

The threshold at which the health service in England is willing to pay to collect an extra unit of blood is unknown. The cost of a unit of blood for the NHS is around £120, half of which arises from the costs of collection, which differ across settings. For example, in England, the collection cost at a mobile session ranged from £23 to £60 per unit of whole blood (2015–2016), and sessions with relatively high cost per unit have since been closed. This implies that, in England, the willingness to pay for a unit of blood is likely to be around £30–£50, which we used to interpret our CEA.

Sensitivity analysis

The cost-effectiveness model was probabilistic; the uncertainty in the estimated incremental costs reflected the uncertainty in the volume of blood collected and associated resource use but not in the unit costs that were assumed fixed. We considered two sources of structural uncertainty: (i) the assumption about current operating capacity and (ii) the statistical model used to predict volume of blood. We recognised that static donor centres could require additional staff time to collect extra units of blood, and this increased the unit cost to £26·49 (£9·41 in the base case). This sensitivity analysis is not relevant for strategies two and three where additional staff costs are already included in the base case as these strategies represent the extension of current opening hours. We also considered alternative predictive models using a two-part model and gamma model, rather than the ordered logit model used in the base case analysis.

RESULTS

The effect of each change to the blood service on the average number of whole-blood donations per donor per year are reported in Table 3 for each target population. The results show that donors would be willing to donate whole blood more frequently following each of the service changes. The largest predicted increase in average annual donation frequency was following strategies to reduce the minimum inter-donation interval and to introduce weekend opening at static centres (annual increases of 0·71 and 0·49 donations per donor, respectively). Introducing a health report and providing mobile sessions in the evenings led to small increases in predicted donation frequency (0·1 and 0·03 per donor per year, respectively).

For each strategy compared to current practice, we report the incremental (difference in means) volume of blood collected, incremental costs and incremental cost per additional unit of blood for the relevant target population (Table 4). Although each service change was predicted to lead to additional donations of whole blood, this also led to additional costs, with the incremental cost per donor per year ranging from £3·16 to £18·12. These additional costs were for the variable cost of collecting the additional blood yield per donor. Aside from the introduction of the health report, these higher average costs were almost exclusively for the costs of collection *per se*.

Table 4 ranks the strategies in order of their cost-effectiveness. The strategy to reduce the minimum donation interval was predicted to provide additional units of whole blood at the lowest additional cost per unit, followed by the strategies of extending opening times for blood collection at static centres. The strategy to substitute mobile weekday sessions with sessions held at weekends had the lowest additional cost (£3·16) but the smallest predicted increase in blood donation, and was unlikely to be cost-effective. At a cost of £136 per additional unit of blood, the introduction of the health report was very unlikely to be cost-effective.

The main subgroup analysis was for donors with 'high-demand' blood types and is reported in Table 5. The results were broadly similar in that the strategies with relatively low costs per additional unit of blood donated were the reduction of the minimum inter-donation interval or weekend or evening opening for collection in static centres. The results of the other subgroup analyses revealed some differences in relative preferences for alternative service changes according to donors' characteristics; in particular, donors of Black, mixed Black, Asian and mixed Asian ethnicities were predicted to donate more frequently than donors of other ethnicities when offered the health report. However, the additional costs of the health report were such that the cost per additional unit of blood donated remained relatively high for this strategy (on average, £69 for Black/mixed Black donors and £102 for Asian/mixed Asian donors, compared to £136 for all donors). The cost-effectiveness results of other strategies were very similar across all the subgroups considered.

In the scenario where staff costs were included in the variable cost per unit of blood for strategies one and six, the cost per additional unit of blood for these strategies increased to £27 (reduced interval) and £139 (health report). In this scenario, evening opening hours at donor centres was ranked the most cost-effective strategy at £23 per additional unit of blood collected. When other analytical models were used for the analysis of the survey data, the ranking of strategies did not change compared to the base case.

DISCUSSION

This analysis found that strategies that improve donation opportunities at static donor centres offered better value for money than the introduction of the health report or moving mobile sessions to weekends or evenings. The cost of opening static centres on weekday evenings or at weekends fell below £30 per additional unit of blood collected. These results were robust to the choice of model used to predict donation frequencies from the survey data and were similar across donor subgroups, including the subgroup of prime policy interest, those donors with

Table 3. Predicted deferral rates and adjusted annual donation frequency

Strategy		Average annual visits predicted per donor	Average annual number of low Hb deferrals per donor	Average annual number of other deferrals per donor	Deferral-adjusted number donations per donor
Health report	Status quo[1]	2·595	0·092	0·151	2·362
	With health report	2·704	0·096	0·157	2·462
	Difference	0·109	0·004	0·006	0·100
Weekend opening of static centres	Status quo	2·604	0·092	0·150	2·374
	With weekend opening	3·142	0·112	0·181	2·864
	Difference	0·538	0·019	0·031	0·489
Evening opening of static centres	Status quo	2·779	0·099	0·160	2·534
	With evening opening	3·229	0·115	0·185	2·942
	Difference	0·45	0·016	0·026	0·408
Weekend opening of mobile sessions	Status quo	2·564	0·091	0·149	2·333
	With weekend opening	2·599	0·092	0·151	2·363
	Difference	0·035	0·001	0·002	0·03
Evening opening of mobile sessions	Status quo	2·518	0·089	0·146	2·291
	With evening opening	2·744	0·097	0·160	2·49
	Difference	0·226	0·008	0·013	0·199
Reduce minimum inter-donation interval at static centres	Status quo	2·804	0·100	0·161	2·557
	Shorter inter-donation interval	3·586	0·128	0·206	3·271
	Difference	0·782	0·028	0·045	0·714

[1]Status quo refers to current blood service provision. The average annual visits predicted differs for the status quo comparator across the strategies because the relevant target population is not the same, as detailed in Table 1.

Table 4. Incremental cost-effectiveness of each strategy compared to the current blood service provision (mean values across 10 000 simulations)

Strategy	Number of donors affected	Incremental blood yield, units all blood types (nearest thousand)	Incremental volume of blood per donor per year, units of blood	Incremental cost, £ GBP	Incremental cost per additional unit of blood, £ GBP
Reduce minimum donation interval	107 811	73 000	0·678	6·71	10
Evening opening of static donor centres	99 312	45 000	0·455	10·46	23
Weekend opening of static donor centres	60 640	31 000	0·519	15·21	29
Evening opening of mobile sessions	582 910	282 000	0·484	18·12	37
Weekend opening of mobile sessions	646 898	45 000	0·07	3·16	45
Health report	781 028	88 000	0·113	15·33	136

'high-demand' blood types. These findings directly relate to the blood service in England and other public-funded blood services required to increase the volume of particular types of blood and add to the limited literature on the cost-effectiveness of alternative changes to a blood collection service (Van Der Pol & Cairns, 1998; Van Der Pol *et al.,* 2000; Varney & Guest, 2003; Dixon *et al.,* 2005; Pereira, 2006; Rautonen, 2007; Katsaliaki, 2008; Lowalekar & Ravichandran, 2010; Abraham & Sunday, 2012; Beliën & Forcé, 2012; Williamson & Devine, 2013).

Reducing the minimum interval between donations at static donor centre was the most cost-effective strategy at £10 per additional unit of blood collected, but concerns remain about 'rolling out' a strategy of reducing the minimum interval for all donors. The INTERVAL trial reported lower levels of Hb for some donors over the 2-year follow-up period (Di Angelantonio *et al.,* 2017). Although our analysis did include the short-term costs related to Hb deferral, the longer-term impact of more Hb-related deferrals on donor retention, and hence the long-term cost-effectiveness of this strategy, is unknown. The next most cost-effective strategies, the opening of donor centres at weekends and evenings, may therefore make more efficient use of scare blood service resources, particularly if there is little capacity within the system to collect additional units of blood.

Not all strategies are scalable to the same degree. Strategies to improve opportunities to give blood for donors at static centres could yield between 60 000 and 100 000 units. To support the collection of additional blood in this quantity, staff

Table 5. Base case results for donors with 'high-demand' blood types

Strategy		Annual cost per donor (£GBP)	Total annual cost (all donors), 000 s (£GBP)	Total units (all) blood collected, 000 s	Incremental cost per additional unit blood (£GBP)
Health report	Status quo	21·57	2414	264	NA
	With health report	36·83	4123	276	NA
	Difference	15·27	1709	11	152
Weekend opening of static centres	Status quo	23·34	186	19	NA
	With weekend opening	37·63	300	23	NA
	Difference	14·29	114	4	29
Evening opening of static centres	Status quo	24·91	321	33	NA
	With evening opening	34·25	441	38	NA
	Difference	9·34	120	5	23
Weekend opening of mobile sessions	Status quo	21·02	1981	220	NA
	With weekend opening	22·37	2108	223	NA
	Difference	1·35	127	3	45
Evening opening of mobile sessions	Status quo	20·64	1756	195	NA
	With evening opening	28·1	2390	212	NA
	Difference	7·46	635	17	37
Reduce minimum inter-donation interval at static centres	Status quo	25·13	349	35	NA
	Shorter inter-donation interval	32·16	446	45	NA
	Difference	7·02	98	10	10

NA, not applicable.

would need to be redeployed from other sessions. Alternatively, the strategies could be implemented so that collection of high-demand blood types is substituted for other blood types. If the extra collection of blood was limited to donors with high-demand blood types, this would imply around 10 000 additional units of whole blood collected – which is much feasible within current staffing constraints. The results from our survey suggest that donors' preferences would be to donate these additional units of blood at more convenient times, namely, during the evenings and at weekends, which would also be relatively cost-effective.

This analysis suffered from three main limitations. Firstly, despite the relatively high response rate for an online survey of the public, it is unclear whether the preferences of our survey responders are representative of the preferences of all recent donors. Although the ordered logit model did adjust for differences in measured characteristics between the sample and the target population, there may be differences in unobservable characteristics between the settings. However, there is no reason to suspect this would bias the CEA in favour of a particular strategy. Secondly, we did not consider the alternative strategies to recruit new donors, nor the effect beyond 1 year on the retention of existing donors. Thirdly, we did not include direct costs to donors, such as travel expenses. These costs may differ by strategy, but taking a wider societal perspective would also require that the increased utility for donors from the act of blood donation itself be included in the analysis.

The findings from the HEMO study are relevant to publicly funded blood supply agencies worldwide as they can be interpreted according to whether the objective is to increase or maintain the supply of particular blood types or for whole blood overall. Although costs and donor preferences are likely to differ between settings, this paper shows how large-scale surveys of donors' preferences can generate the required information about alternative changes to a blood service to guide future policy.

Methods to define and analyse the impact of possible changes to blood collection from a health economic perspective are likely to become increasingly relevant to blood services faced with growing pressures. They offer a way forward in the attempt to balance the sometimes conflicting but insistent demands of economic efficiency, flexibility to accommodate short- and medium-term fluctuations in demand and the need to reach different sections of the community.

CONCLUSION

We found that moving mobile sessions to the weekend or providing health reports did not provide sufficient increases in the predicted donation frequency to justify the additional costs. Reducing the minimum inter-donation interval increased volumes of blood donation at low costs in the short term, but the observed increase in Hb-related deferrals over 2 years, may imply that this strategy is not cost-effective in the longer term. Extending the opening hours of static donor centres is in line with donor preferences and provides a relatively cost-effective way of providing additional units of blood, particularly blood types that are in high demand.

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CONFLICTS OF INTEREST

G. C., D. R., G. M. are all employees of NHS Blood and Transplant.

There are no other conflicts of interest to declare.

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Thesis Title	An approach to stated preference surveys for reducing hypothetical bias and predicting the effects of alternative policy changes: the case of blood donation		
Primary Supervisor	Professor Richard Grieve		

If the Research Paper has previously been published please complete Section B, if not please move to Section C.

SECTION B – Paper already published

Where was the work published?	Plos One		
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If the work was published prior to registration for your research degree, give a brief rationale for its inclusion			
Have you retained the copyright for the work?*	**Yes**	Was the work subject to academic peer review?	**Yes**

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SECTION C – Prepared for publication, but not yet published

Where is the work intended to be published?	
Please list the paper's authors in the intended authorship order:	

Stage of publication	Choose an item.

SECTION D – Multi-authored work

For multi-authored work, give full details of your role in the research included in the paper and in the preparation of the paper. (Attach a further sheet if necessary)	I contributed to the overall design of the study, the preference data collection, preference prediction analysis and interpretation of the results but Zia Sadique was the lead analyst as the expert working with the INTERVAL trial population especially regarding the quality of life and cost data. I contributed to the writing and review of the manuscript.

SECTION E

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Date	22 October 2022

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Date	23 October 2022

PLOS ONE

RESEARCH ARTICLE

Cost-effectiveness of alternative minimum recall intervals between whole blood donations

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Abstract

Background

The INTERVAL trial showed shorter inter-donation intervals could safely increase the frequency of whole-blood donation. We extended the INTERVAL trial to consider the relative cost-effectiveness of reduced inter-donation intervals.

Methods

Our within-trial cost-effectiveness analysis (CEA) used data from 44,863 whole-blood donors randomly assigned to 12, 10 or 8 week (males), and 16, 14 or 12 week inter-donation intervals (females). The CEA analysed the number of whole-blood donations, deferrals including low- haemoglobin deferrals, and donors' health-related quality of life (QoL) to report costs and cost-effectiveness over two years.

Findings

The mean number of blood donation visits over two years was higher for the reduced interval strategies, for males (7.76, 6.60 and 5.68 average donations in the 8-, 10- and 12- week arms) and for females (5.10, 4.60 and 4.01 donations in the 12-, 14- and 16- week arms). For males, the average rate of deferral for low haemoglobin per session attended, was 5.71% (8- week arm), 3.73% (10- week), and 2.55% (12- week), and for females the rates were: 7.92% (12-week), 6.63% (14- week), and 5.05% (16- week). Donors' QoL was similar across strategies, although self-reported symptoms were increased with shorter donation intervals. The shorter interval strategies increased average cost, with incremental cost-effectiveness ratios of £9.51 (95% CI 9.33 to 9.69) per additional whole-blood donation for

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the 8- versus 12- week interval for males, and £10.17 (95% CI 9.80 to 10.54) for the 12- versus 16- week interval arm for females.

Conclusions

Over two years, reducing the minimum donation interval could provide additional units of whole-blood at a small additional cost, including for those donor subgroups whose blood type is in relatively high demand. However, the significance of self-reported symptoms needs to be investigated further before these policies are expanded.

Introduction

The safe and adequate supply of blood is an integral part of any health system. All health systems share a global vision for a self-sufficient supply of whole-blood by 2020, as set out by the World Health Organization (WHO) and the International Federation of Red Cross and Red Crescent Societies (IFRC) [1]. This framework for global action focuses on the importance of voluntary blood donors for blood safety and availability and called for blood supply agencies to encourage more frequent donation from current whole-blood donors. In recent years the demand for whole-blood has declined overall in many high-income countries, but the demand for universal blood type and some rare subtypes has been growing. In England, there is increased demand for the universal blood type O negative (O-),A negative (A-), B negative (B-) and rare blood subtypes (Ro subtypes) more common in black, Asian and minority ethnic (BAME) donors and supply of these blood types is particularly vulnerable to shortfalls. Further threats to the sustainability of voluntary whole-blood services in England are the gender gap in recruiting new donors and difficulty in retaining younger blood donors [2–4].

NHSBT's blood collection service has been severely affected by the ongoing COVID-19 pandemic. In March 2020 the level of donation was 15% lower than expected [5]. The fall in supply has been mitigated by the cancellation of elective procedures, but raises an important challenge for ensuring that the supply of whole-blood is sufficient in the post-COVID-19 recovery period when demand for blood will be high. A key policy objective of NHSBT is to collect more blood in particular for blood types that are relatively in high demand. So evidence to inform changes to the blood service that increase donation frequency for subgroups of donors whose whole-blood type is in high demand, at low additional cost is timely and potentially of strategic importance. However, rigorous evidence about the effects of changes to the blood collection service on the frequency and costs of whole-blood donation is lacking, with most existing economic evaluations based on non-randomised evidence [6–10].

INTERVAL is the first ever randomised controlled trial (RCT) that investigated the efficiency and safety of alternative blood donation services. The INTERVAL RCT assessed whether reducing inter-donation intervals in static donor centres of NHSBT in England would increase donation frequency without compromising donor safety [11]. The trial reported that for both genders, donors randomised to the shorter minimum donation interval (8 weeks for men, 10 weeks for women) successfully donated more whole-blood over two years compared to those randomised to the current minimum donation intervals (12 weeks for men, 16 weeks for women). However, even after the prescribed inter-donation intervals, some donors may fail to regain their previous haemoglobin concentration and fail to pass the haemoglobin threshold mandated for donation (135 g/L for men and 125g/L for women). More frequent donations (ie, shorter inter-donation intervals) were associated with higher rates of deferral

for low haemoglobin over two years follow-up period in the trial. The subsequent extension to the INTERVAL trial that followed donors up for four years, and offered routine rather than intensive reminders, also found that shorter inter-donation intervals continued to increase donation frequency but increased deferral rates [12].

Neither of these reports of the INTERVAL trial considered the relative costs of reduced inter-donation intervals which could be higher given the additional deferrals, nor did they evaluate the effects for policy-relevant subgroups, such as those donors whose blood is in 'high demand' (for example, O negative (O-), A negative (A-), B negative (B-) and blood subtypes more common in black, Asian and minority ethnic (BAME) donors or those donor subgroups who are less likely to continue donating (younger donors, or those who have made relatively few previous donations).

The Health Economics Modelling of alternative blood donation strategies (HEMO) study set out to assess the cost-effectiveness of strategies to maintain the blood supply in England [13]. This paper reports findings from the cost-effectiveness analysis (CEA) of the alternative minimum inter-donation intervals considered over two-years within the INTERVAL trial. This paper extends the CEA published in the NIHR report, in providing a comprehensive assessment of the relative cost-effectiveness of alternative inter donation intervals according to pre-specified policy relevant subgroups for both genders. The subgroups of interest are blood type, age, ethnicity, donor recruitment source and whether the donor was giving blood for the first time or a regular donor.

Methods

Ethics

The INTERVAL trial protocol was approved by the National Research Ethics Service (11/EE/0538). The trial was registered with the International Standard Randomised Controlled Trial Number (ISRCTN) Registry (ISRCTN24760606).

Setting, selection and baseline measures

The INTERVAL was an open, parallel-group pragmatic RCT that recruited whole blood donors aged 18 years or older from 25 static donor centres of NHSBT across England [11,12,14,15]. The initial findings from the INTERVAL trial and the study protocol, are reported elsewhere [11,12,14,15]. In brief, new and existing donors were eligible for inclusion in the trial if they were: aged 18 years or older, met the routine criteria for whole blood donation, were willing to be randomised, had an email address and access to the internet to respond to web-based questionnaires, and were willing to be randomly assigned to any of the trial's intervention groups at one of the 25 static donor centres of NHSBT. Existing donors were defined as donors who had given blood within the last five years. Written consent was obtained from eligible donors, who were asked to complete and sign two copies of the consent form. Completed consent forms were checked for completion of all relevant sections and for the donor's signature. The 'study copy' of the consent form, affirmed by signature by a staff member of the study that he/she had witnessed its completion was retained while the 'donor copy' was provided to the participant. For donors who subsequently were ineligible or unwilling to take part in the trial, consent forms were crossed through and then destroyed. Male participants were randomly assigned to 12- versus 10- versus 8-week inter-donation intervals and female participants were randomly assigned to 16- versus 14- versus 12-week inter-donation intervals. Those donors who were eligible and consented, were randomised to the three gender-specific intervention groups in a 1:1:1 ratio.

This study excluded those donors who withdrew consent, who died during or after the trial follow-up period until December 2016 when linked PULSE (the NHSBT national blood supply database) data were extracted, or who did not have requisite PULSE data available. This led to an overall sample of 44,863 trial participants for the cost-effectiveness analysis. The follow-up period of the study was two years.

Information for baseline characteristics (gender, age, ethnicity and blood type) and donation history (new donor or not, recruitment source, and the number of donations and deferrals for low haemoglobin (Hb) for the two years prior to randomisation) of trial participants was extracted from PULSE database. At the baseline donation visit after trial recruitment, a full blood count was performed which provided the levels of Hb used to define the proportion of low Hb deferrals who would require additional consultations and tests. Trial participants were asked to complete a baseline questionnaire online, which included the SF-36 (Short Form 36) questionnaire [16].

Resource use and costs

The cost analysis took a NHS and personal social services perspective as recommended by the National Institute for Health and Care Excellence (NICE) [17]. The study included cost items that were anticipated to differ over the trial follow-up period and according to intervention groups and included the additional costs of blood collection excluding processing, marketing or fixed costs, cost of deferrals and subsequent health care costs. The relevant additional staff costs, costs of invitation and consumables costs associated with blood collection were included in the study.

The number of successful whole blood donations, deferrals and fainting episodes at a blood donation session were extracted from the PULSE database over the two-year follow-up period. The volume of blood donated was measured in units of whole blood (each unit is 470ml). Donations could be deferred for a number of reasons, such as recent travel, medication, lifestyle restrictions or infection/illness. as described in the donor selection guidelines (https://www.transfusionguidelines.org/dsg). Donors could also be deferred due to low Hb, which was anticipated to differ by randomised arm. The trial used the same deferral policy that is used in routine practice as per the Blood Safety Quality Regulations, for example, donors with Hb levels that were 'low', that is less than 135g/L for males and 125g/L for females, were deferred for three months. All deferrals were associated with resource use consequences in terms of staff time, Hb screening test and downstream healthcare costs (GP appointment, full blood count test, ferritin test, iron supplement, and hospital outpatient appointment) in the case of Hb-related deferrals.

Web-based follow-up questionnaires collected information on health care events occurring between donation sessions (doctor or hospital visits required for falls, transport accidents, angina, heart failure, transient ischaemic attack, stroke, myocardial infarction). While the numbers of these events were reported, they were not anticipated to differ between the randomised arms, and were not included in the cost analysis. Fainting event at donation sessions were anticipated to differ between randomised groups and was included in the cost analysis.

Unit costs were taken from NHSBT financial records, expert opinion, and INTERVAL trial data (see Appendix Table 1 in S1 Appendix). The unit cost of donation appointment reminders was calculated, according to the three-stage reminder process (first appointment, interim appointment and last appointment reminders) specified by the INTERVAL trial protocols. Time required for sending the reminders recorded in the trial were costed according to NHS Band 4 costs [18]. The opportunity cost of staff time lost following a donor deferral whether due to low haemoglobin or other reasons was based on expert opinion. The major opportunity

cost of an additional deferral is the reduced efficiency of collection, that is the number of units of blood collected by a team during a donation session. The opportunity cost therefore includes the time taken for donor carers (NHS Band 4) to undertake a health screen and, where deferral was due to low Hb, a copper sulphate [19] and HemoCue® test (HemoCue®, Radiometer Medical ApS, Denmark) [20]. Informed by INTERVAL trial data we assumed that 7% of donors with low Hb would be referred to their Primary Care Physician (when Hb is less than 125 g/L for men and 115 g/L for women) which would incur healthcare costs. The healthcare costs associated with low Hb were assumed to include a GP appointment, a full blood count test and Serum ferritin test, iron supplements (in 50% of cases) and an outpatient appointment (in 10% cases).

The accompanying unit costs were taken from published sources [18,21–25]. The unit cost of a fainting episode was calculated according to the additional staff (NHS Band 4) time required at a donor centre to manage a typical fainting episode. The unit costs related to blood collection were taken from NHSBT financial records [19]. Resource use data were combined with unit costs to report the total costs for each randomised donor over the trial's two-year follow-up period.

Health outcomes

The main health outcomes for the cost-effectiveness analysis were successful whole blood donations, overall donation deferrals, donation deferrals due to low Hb, and quality of life (QoL). Whole blood donations, donation deferrals due to low Hb and donation deferrals due to other causes were recorded in the trial database. Participants were sent a request by email to complete an online questionnaire, which included the SF-12 (Short Form 12), at six, 12- and 18-months follow-up, and the SF-36 at the final two year follow-up timepoint. The responses to the required SF-12 & SF-36 questions were combined with the published valuation algorithm [26] to report SF-6D (Short-Form Six-Dimension) utility score at each timepoint, anchored on the scale 0 (death) and 1 (perfect health).

Cost-effectiveness analysis

The cost-effectiveness analysis followed the intention-to-treat principle [27]. The time horizon was two years, as per the follow-up period of the INTERVAL trial. The analysis applied logistic regression models for estimating deferral rates, Generalised Estimating Equation (GEE) models for estimating SF-6D score, and seemingly-unrelated regression (SUR) for joint modelling of whole blood donations and cost [28]. Rates of deferral was estimated using the data on number of deferrals and attendances, and applied logistic regression models for grouped data. SF-6D score at each time point of measurement (baseline, six month, 12-month, 18-month and 24-month) was estimated using GEE model. Costs and whole blood donations were estimated jointly by applying a SUR model that accounted for the correlation between whole blood donation and costs.

The cost-effectiveness analysis adjusted for age, 'standard' (donors with blood types O+, A+, B+, AB+ and AB) versus 'high' (donors with blood types O-, A- and B-) demand blood types, ethnicity (white, Asian/Asian mixed, Black/Black mixed, other ethnicity or not stated), new donor or not, and recruitment source (static donor centre vs. mobile session vs. other). Subgroup effects were estimated by including interaction terms for randomised arm by subgroup. Age was defined as a continuous variable in the analysis model, but predictions were provided according to the requisite policy-relevant categories (17–30, 31–45, 46–60, 60+).

QoL data was missing for those individuals who did not complete the items required to calculate the SF-6D utility score; the number and percentage of the analysis sample with

responses sufficient to calculate the SF-6D utility score are reported for each timepoint (baseline, six, 12, 18 and 24 months) (see Appendix Table 2 in S1 Appendix). These missing data were handled by a GEE model that included SF-6D utility score as the dependent variable, with randomised group, timepoint, and the above subgroup variables as the fixed effects of interest, together with fixed interaction terms of timepoint and randomised group. The model included random intercepts for donor centre and individual, to allow for the correlations of measurements within each donor and donor centre. The model reported mean QoL scores at each timepoint within the two-year follow-up of the trial, and the differences in the mean utility scores across the randomised arms. The GEE model assumed that missing QoL data were 'missing at random', conditional on the variables included in the model [29].

We reported incremental (difference in means) costs and number of whole blood donations, and the incremental cost-effectiveness ratio (ICER), as the incremental cost per additional unit of blood donated by those allocated to the reduced inter-donation intervals compared to those giving blood at the standard interval for men and women respectively. The confidence intervals around the ICER were constructed by applying Delta method (Taylor series expansion on the incremental estimates of cost and volume of blood donated) [30]. The accompanying uncertainty around the incremental estimates of cost and the volume of blood donated was represented on the cost-effectiveness plane. We report results overall (by gender), and according to the other pre-specified subgroups.

The base case analyses assumed unit costs for reminders to donate and deferrals from expert opinion; zero costs for non-attendances; downstream health care costs following a deferral due to low Hb; and costs attributable to fainting episodes. We also assumed that static donor centres had staff capacity to collect more bloods. The statistical models for blood volume, QoL and cost assumed that the residuals follow a Normal distribution. The robustness of the results to these assumptions was assessed in the subsequent sensitivity analyses.

Results

Patient characteristics

The baseline characteristics (Table 1) were similar between the randomised groups for both genders. The number of blood donations, deferral for low Hb and for reasons other than low Hb in the two years preceding the trial and baseline QoL were also similar across randomised groups for both genders.

Resource use and costs

The resource use results reported in Table 2 shows that mean number of blood donation visits was relatively higher in reduced minimum donation interval arms for both genders. For males, the mean number of blood donation visits was 7.76 in the 8-week arm, compared to 6.60 and 5.68 in the 10- and 12- week arms. For females the corresponding mean number of blood donation visits was 5.10 in the 12-week arm, compared to 4.60 and 4.01 in the 14- and 16-week arms. The average rate of deferral for low Hb, per session attended, was higher in reduced minimum donation intervals arms for both genders (see Table 2, Appendix Table 3A & 3B in S1 Appendix). For males, Hb-related deferral rate was 5.71% in the 8- week arm, which was relatively higher compared to 3.73% in the 10-, and 2.55% in the 12- week arm. For females, this deferral rate was 5.05% in the 16- week arm compared to 6.63% in the 14-, and 7.92% in the 12-week arm. In accordance with the rate of deferrals the mean number of Hb-related deferrals per donor over two years were also higher in the randomised arms with reduced inter-donation intervals. While the rates and mean number of Hb-related deferrals were higher for randomised groups with reduced inter-donation intervals, the proportion of

Table 1. Baseline characteristics, by randomised arm and gender.

		Randomised arm (male)			Randomised arm (female)		
		8-week (n = 7,417)	10-week (n = 7,413)	12-week (n = 7,411)	12-week (n = 7,549)	14-week (n = 7,545)	16-week (n = 7,528)
Mean (SD) age (years)		44.7 (14.1)	44.7 (14.2)	44.7 (14.2)	40.77 (14.0)	40.89 (13.9)	40.94 (14.0)
Blood type n (%)	High demand	996 (13.43)	933 (12.59)	965 (13.02)	1,130 (14.97)	1,062 (14.08)	1,002 (13.31)
	Standard demand	6,421 (86.57)	6,480 (87.41)	6,446 (86.98)	6,419 (85.03)	6,483 (85.92)	6,526 (86.69)
Ethnicity n (%)	White	6,751 (91.02)	6,752 (91.08)	6,745 (91.01)	6,984 (92.52)	6,992 (92.67)	6,949 (92.31)
	Black/mixed black	101 (1.36)	96 (1.30)	100 (1.35)	103 (1.36)	93 (1.23)	134 (1.78)
	Asian/mixed Asian	255 (3.44)	271 (3.66)	258 (3.48)	171 (2.27)	177 (2.35)	154 (2.05)
	Other or not stated	310 (4.18)	294 (3.97)	308 (4.16)	291 (3.85)	283 (3.75)	291 (3.87)
New donor n (%)	No	6,817 (91.91)	6,818 (91.97)	6,818 (92.00)	6,742 (89.31)	6,744 (89.38)	6,727 (89.36)
	Yes	600 (8.09)	595 (8.03)	593 (8.00)	807 (10.69)	801 (10.62)	801 (10.64)
Recruitment source n (%)	Centre	4,907 (66.16)	4,840 (65.29)	4,855 (65.51)	4,851 (64.26)	4,921 (65.22)	4,901 (65.10)
	Mobile	1,437 (19.37)	1,510 (20.37)	1,512 (20.40)	1,545 (20.47)	1,482 (19.64)	1,486 (19.74)
	No invite	1,073 (14.47)	1,063 (14.34)	1,044 (14.09)	1,153 (15.27)	1,142 (15.14)	1,141 (15.16)
Mean (SD) deferrals for low Hb in previous 2 years		0.04 (0.24)	0.04 (0.23)	0.04 (0.24)	0.12 (0.39)	0.12 (0.38)	0.12 (0.39)
Mean (SD) deferrals for other reasons in previous 2 years		0.32 (0.69)	0.32 (0.68)	0.32 (0.69)	0.36 (0.68)	0.34 (0.68)	0.34 (0.68)
Mean (SD) number of blood donation visits in previous 2 years		4.19 (2.40)	4.22 (2.42)	4.18 (2.40)	3.46 (1.91)	3.45 (1.89)	3.44 (1.93)
Mean (SD) SF-6D score at baseline		0.86 (0.08)	0.86 (0.08)	0.86 (0.09)	0.85 (0.09)	0.85 (0.09)	0.85 (0.09)

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deferrals due to other reasons, mean fainting episodes, and other donor-reported health care events (Table 2 & Appendix Table 4 in S1 Appendix), were similar across the randomised groups for both genders.

The total mean costs per male donor at two-years were relatively lower for reduced minimum donation interval arm for both genders. The corresponding mean costs for males were £61, £52 and £45 in the 8-, 10- and 12- week arms. The mean costs for females were £41, £37 and £33 in the 12-, 14- and 16- week arms (Table 3).

Health outcomes

The estimated effects of randomised group on the mean SF-6D scores at each timepoint are reported in Appendix Table 5A & 5B in S1 Appendix. There was no difference in QoL (SF-6D score) between the randomised groups, at the two-year follow-up (Table 3), and at each of the

Table 2. Resource use over two-year follow-up period, by randomised arm and gender.

	Randomised arm (male)			Randomised arm (female)		
	8-week (n = 7,417)	10-week (n = 7,413)	12-week (n = 7,411)	12-week (n = 7,549)	14-week (n = 7,545)	16-week (n = 7,528)
Mean blood donations visits	7.76	6.60	5.68	5.10	4.60	4.01
Deferrals for low Hb per attendance (%)	5.71	3.73	2.55	7.92	6.63	5.05
Deferrals for other reasons per attendance (%)	4.36	4.58	4.79	6.57	6.95	7.28
Mean deferrals for low Hb per donor	0.44	0.25	0.15	0.40	0.30	0.20
Mean deferrals for other reasons per donor	0.33	0.30	0.27	0.34	0.32	0.29
Mean faints per donor	0.02	0.02	0.02	0.04	0.03	0.03

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Table 3. SF-6D score (at two years), whole blood donations, costs and incremental cost per additional unit of whole blood donated, over two-year follow-up (by gender).

	Male					Female				
	Randomised arm			Mean (95% CI) difference		Randomised arm			Mean (95% CI) difference	
	8-week (n = 7,417)	10-week (n = 7,413)	12-week (n = 7,411)	8-week vs. 12-week	10-week vs. 12-week	12-week (n = 7,549)	14-week (n = 7,545)	16-week (n = 7,528)	12-week vs. 16-week	14-week vs. 16-week
Mean SF-6D score	0.84	0.84	0.84	0.002 (-0.002 to 0.006)	-0.001 (-0.004 to 0.003)	0.82	0.82	0.82	0.001 (-0.003 to 0.005)	0.003 (-0.001 to 0.007)
Mean whole blood donations[±]	6.89	5.98	5.19	1.71 (1.60 to 1.80)	0.79 (0.70 to 0.88)	4.29	3.91	3.45	0.85 (0.78 to 0.92)	0.46 (0.40 to 0.53)
Mean costs (£)[±]	61	52	45	16 (15 to 17)	7 (6 to 8)	41	37	33	9 (8 to 9)	5 (4 to 5)
Incremental cost-effectiveness ratio[±]				9.51 (9.33 to 9.69)	9.00 (8.66 to 9.34)				10.17 (9.80 to 10.54)	9.98 (9.32 to 10.64)

[±] The results for whole blood donations are rounded to two decimal places and costs are rounded to no decimal place. The incremental cost-effectiveness ratio results are rounded to two decimal places.

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intervening time-points (Appendix Table 6 in S1 Appendix) between people who gave blood most and least frequently.

Cost-effectiveness

The cost-effectiveness results are summarised in Table 3 and the regression coefficients from the joint estimation of costs and number of whole blood donations are reported Appendix Table 7 in S1 Appendix. For both genders, the average QoL score were similar between the randomised groups. The differences in mean QoL between randomised groups were small but the 95% CI included zero. Reduced inter-donation interval strategies were associated with higher number of donations. For males, compared to 12-week randomised group (who gave blood least frequently) the average number of whole blood donations over the two years follow-up period increased by 1.71 (95% 1.60 to 1.80) for the 8- week arm, and by 0.79 (95% CI from 0.70 to 0.88) for the 10- week arm. For females the corresponding increase in the average number of donations over the two years follow-up period was 0.85 (95% CI from 0.78 to 0.92) for 12- versus 16 weeks, and 0.46 (95% CI 0.40 to 0.53) for 14- versus 16- weeks. The reduced inter-donation interval strategies were also associated with higher costs. The corresponding ICERs were £9.51 (95% CI 9.33 to 9.69) for the 8-versus 12-week interval arm for males, and £10.17 (95% CI 9.80 to 10.54) for the 12-versus 16-week interval arm for females. The distributions of the mean costs and mean number of donations plotted on the cost-effectiveness plane shows that the joint distribution of costs and number of donations are centred tightly around the means (see Appendix Figure 1 in S1 Appendix).

The subgroup results show that including interaction effects for subgroups by randomised group improved model fit and the interaction term was statistically significant (for males the likelihood test results reported $chi^2 = 79.28$, p = 0.0002; for females, $chi^2 = 46.55$, p = 0.0153). However, the subgroup results (Figs 1–3) show that the incremental cost-effectiveness results were generally similar across almost all subgroups, albeit with considerable uncertainty surrounding the results. The level of uncertainty is higher for the ethnicity subgroup, especially for Asian/mixed Asian and black/mixed black ethnicity where mean incremental costs, whole blood donations, and ICERs have wide confidence intervals for both genders. For the comparison of 14- versus 16-week minimum donation interval strategies for women whose ethnicity

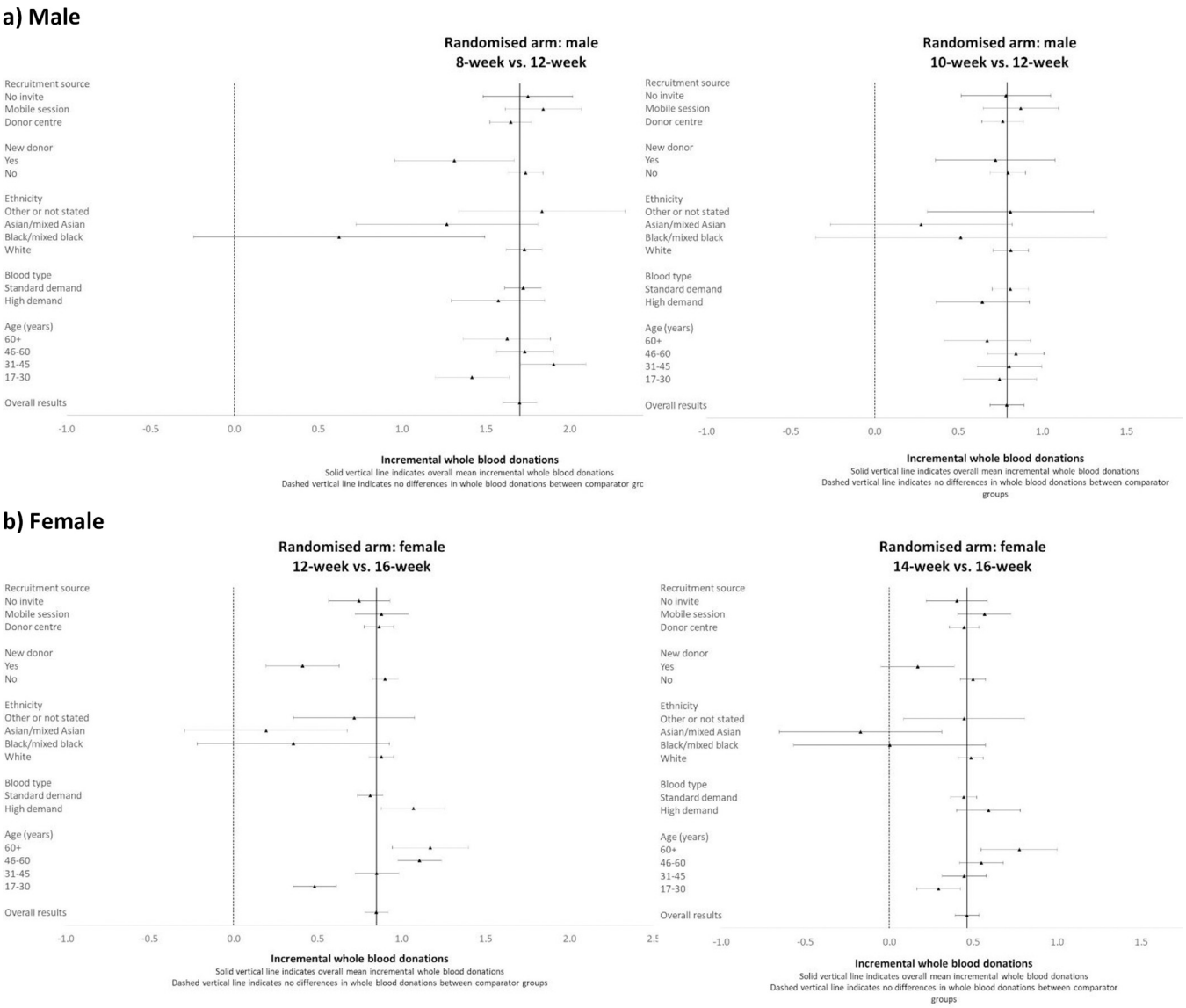

Fig 1. Mean (95% CI) incremental blood donations over two-year follow-up period by subgroup. a) Male b) Female.

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was defined as black/mixed black, the incremental effect of the reduced interval on the number of whole blood donations was small, and so the accompanying mean ICER was large (£258). However, the sample size for this subgroup is low (n = 330 across all 3 arms), and the estimated ICERs are somewhat uncertain.

For females, whose blood type is in 'high demand', and for older women, the strategies of reduced inter-donation intervals led to a greater average increase in donation frequency than for donors whose blood type was in 'standard demand' and younger women. Hence the estimated ICERs were somewhat lower than for women whose blood type is in 'high demand' and older age groups.

The subgroup results for new versus experienced donors reported similar ICERs. The sensitivity analyses show that the base case cost-effectiveness results were generally not sensitive to alternative assumptions considered in the cost-effectiveness analysis (Fig 4). The base case

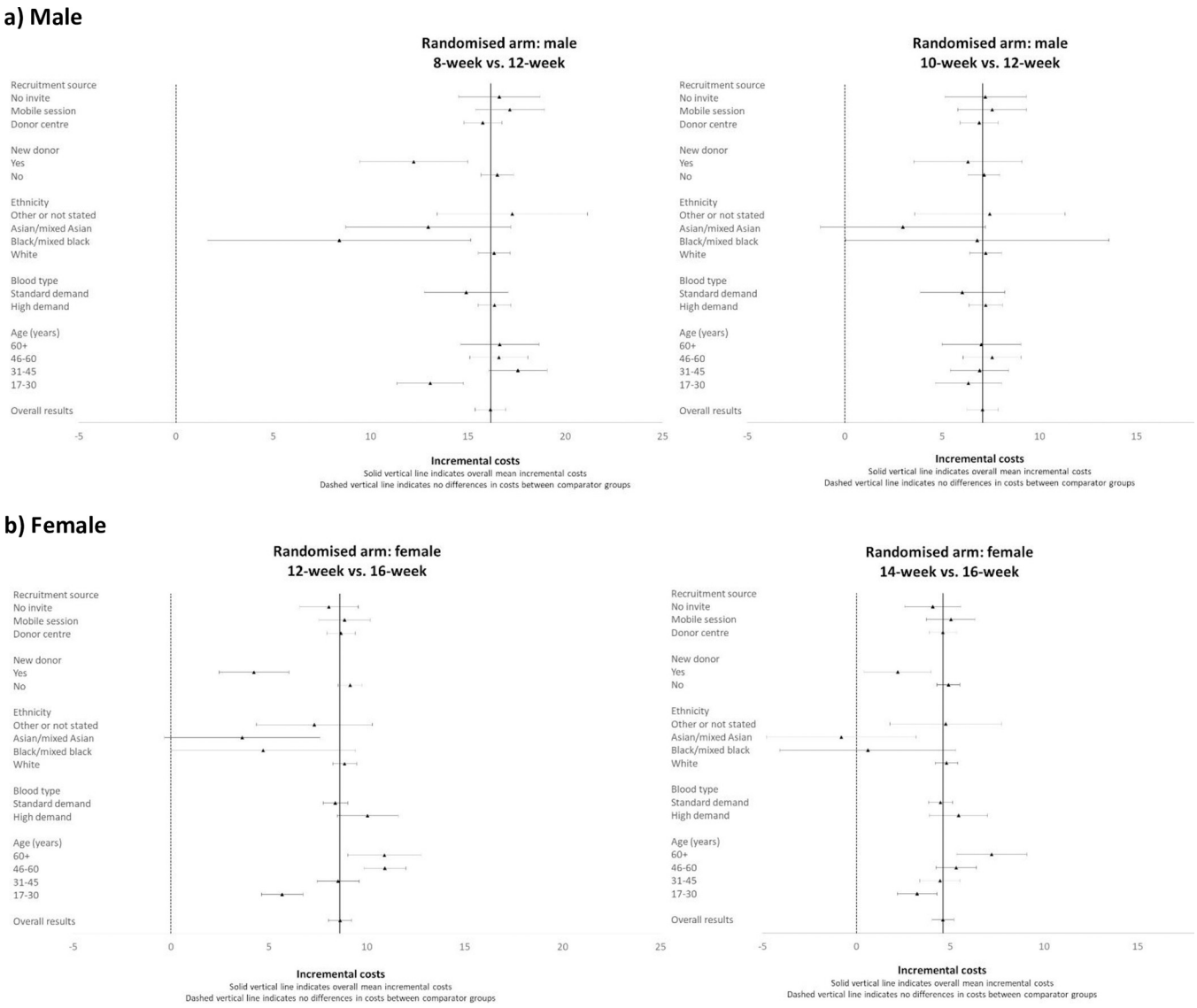

Fig 2. Mean (95% CI) incremental costs over two-year follow-up period by subgroup. a) Male b) Female.

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results for both males and females were most sensitive to the inclusion of the additional staff costs required to collect extra blood followed by additional cost of non-attendance and excluding healthcare costs due to Hb deferral and alternative distributional assumption for costs. The base case results were not sensitive to the exclusion of invitation and fainting costs.

Discussion

Our study is the first ever cost-effectiveness analysis of different inter-donation interval strategies and uses data from a large trial in real life setting. We find that reduced minimum donation interval strategies increase the average number of donations, at a small additional average cost over two years. The study finds that frequent blood donation is more cost-effective for those females whose blood group is in 'high demand' and for older female donors. For all other subgroups the cost-effectiveness results are similar. The study also finds that the rate of

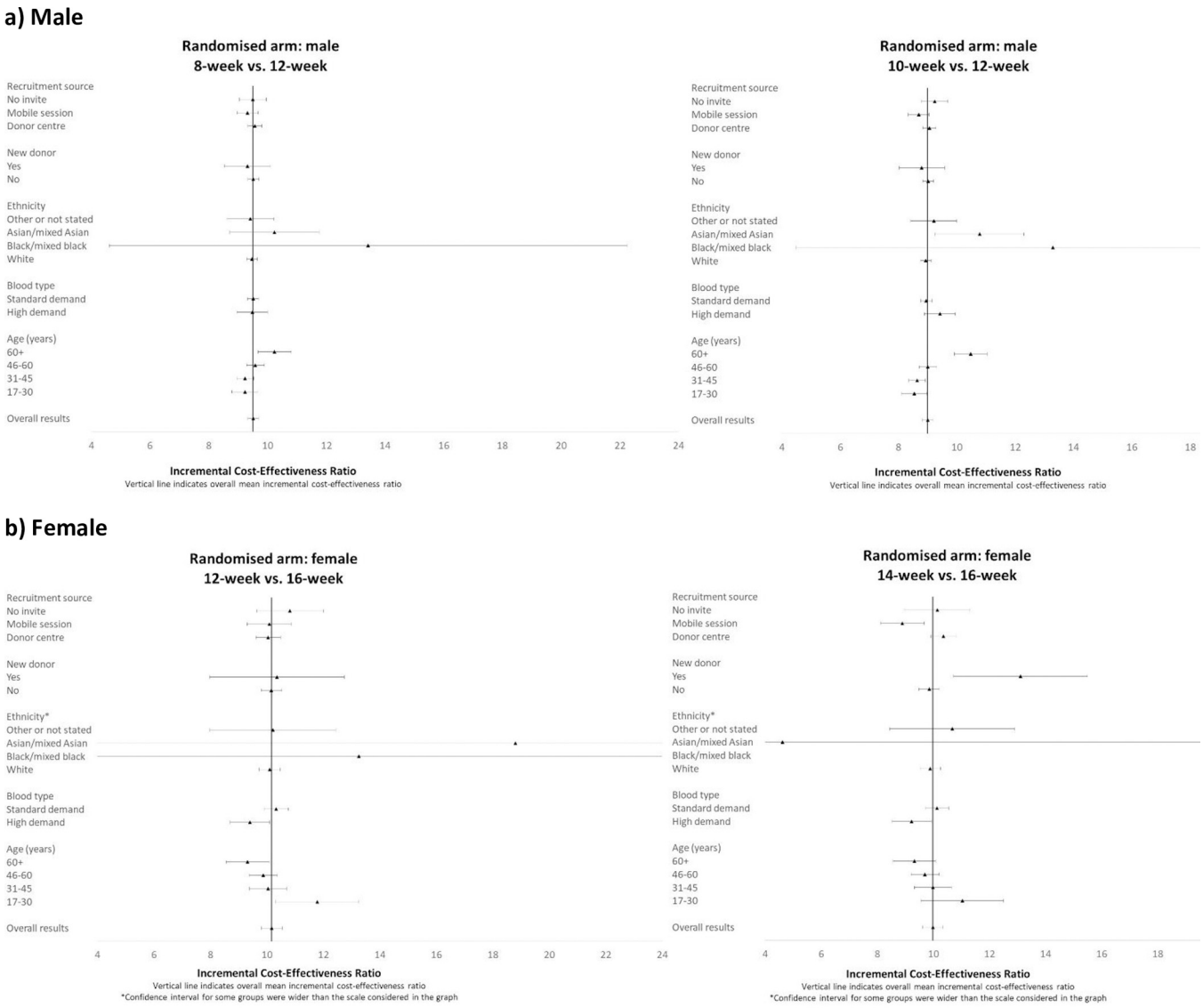

Fig 3. Mean (95% CI) incremental cost-effectiveness ratios over two-year follow-up period by subgroup. a) Male b) Female.

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deferral due to low Hb and the average number of deferrals per donor was higher for the reduced minimum interval strategies, but there was no evidence that donating blood more often led to measurable reductions in QoL, compared to donating every 12 weeks (for men) or every 16 weeks (for women). There were no differences in the self-reported fainting episodes, adverse events, or health care resource use across the randomised arms.

The results show that frequent donation of blood leads to Hb and non-Hb related deferrals, but the depletion of Hb and other self-reported symptoms does not have any detectable effect on QoL up to 2 years follow-up period in the INTERVAL trial. This finding is observed in even longer follow-up period of 4 years in the INTERVAL-extension study [12]. Our study adds that it is not only safe to collect blood more frequently than the current standard, but also a cost-effective strategy. Our study adds to the limited literature on the cost-effectiveness of alternative donation interval strategies for blood collection [3,31–40], and reported cost-

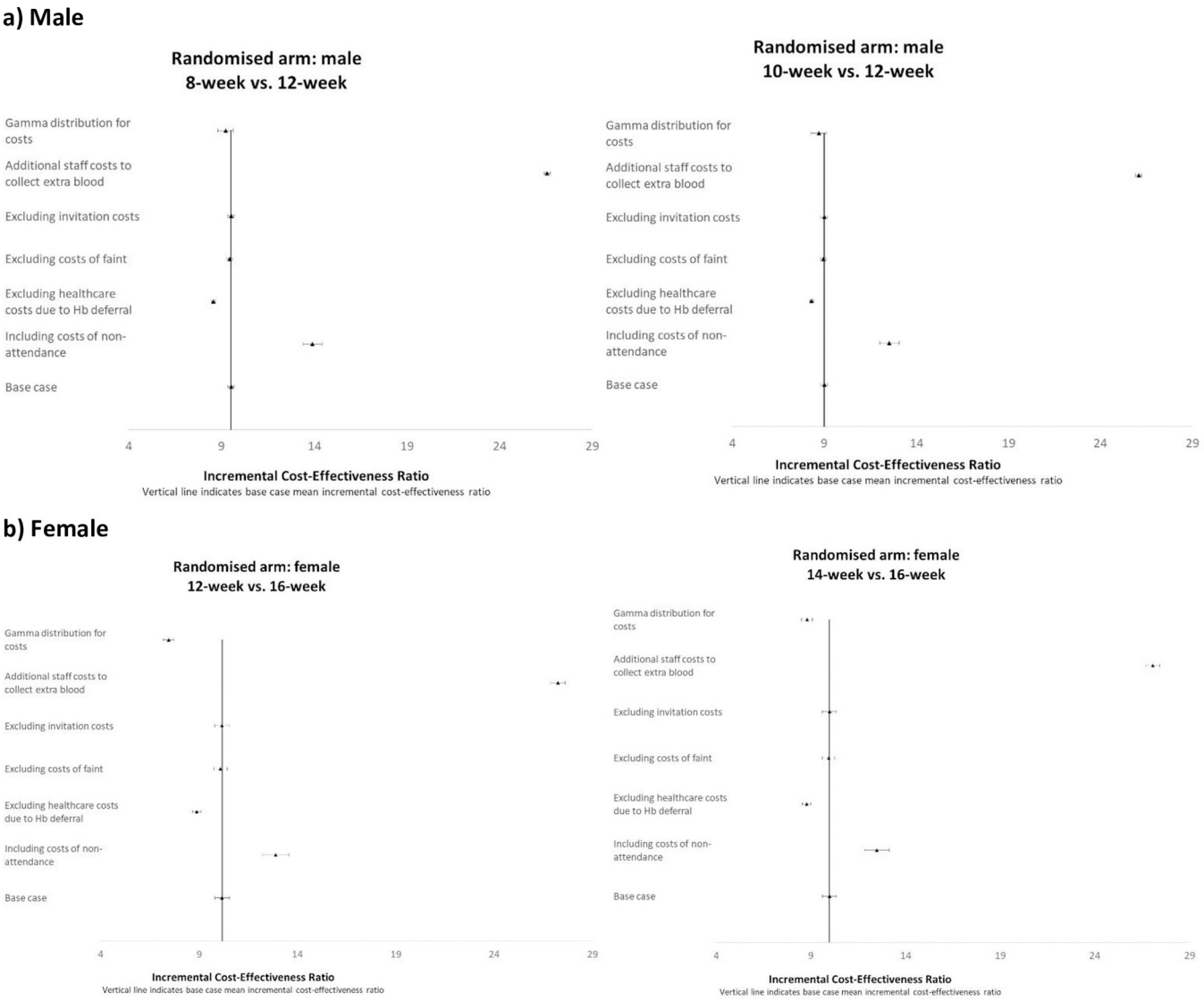

Fig 4. Sensitivity analysis that reports the mean (95% CI) incremental cost-effectiveness ratios over two-year follow-up period according to alternative assumptions compared to the base case. a) Male b) Female.

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effectiveness results across subgroups of prime policy interest related to the blood service in England and other public-funded blood services.

Previous reports from the INTERVAL trial also showed that there was no difference in serious adverse events, cognitive function or levels of physical activity between people who gave blood most and least frequently [11]. However, a higher proportion of donors allocated to shorter donation intervals showed more self-reported symptoms including feeling more tired than usual, dizziness, feeling faint or more breathless, experiencing palpitation and symptoms compatible with restless legs syndrome in men and feeling more tired than usual, dizziness, feeling faint or more breathless in women [11]. On average, compared to people who gave blood less frequently, people who gave blood most frequently had lower iron and haemoglobin levels after two years.

A key strength of this CEA is that it was performed using donor-level data from a large, well-conducted RCT, with complete follow-up data for the main endpoints of interest, and included as a control arm, the current minimum donation interval in England. The large sample size allowed reporting both the overall effect of alternative minimum donation intervals on costs and outcomes and, also the effect according to subgroups of key policy relevance including donors whose blood is in high demand. By reporting cost-effectiveness results for these subgroups of key policy relevance, we extend a previous publication of the CEA that used the INTERVAL trial data for a more restriction range of donor subgroups, pre-specified for the original INTERVAL trial analysis [13].

The study has a few limitations. First, while the INTERVAL trial followed donors for up to four years, the higher Hb-related deferral rates in the reduced inter-donation interval arms could lead to a higher rate of donors leaving the blood donation registry in the long-run if the levels of Hb that were on average lower in the reduced interval arms after four years continue to fall and diverge subsequently. A similar concern is that we were not able to assess whether the increase in self-reported symptoms in the reduced interval arms led to more donors leaving the register over time [11]. Second, the RCT was undertaken at 25 static donor centres and therefore the cost-effectiveness results may not be generalisable to mobile sessions. Third, the CEA did not include the full range of costs that may differ across intervention groups. In particular, costs of non-attendance were excluded as data were not available on the number of non-attendances for each individual. In the sensitivity analysis, when these costs were approximated, the results show that the ICERs of the reduced interval strategies increased somewhat, but generally remained below an additional variable cost of £30 for an additional unit of blood donated. The results were most sensitive to the assumption that the static donor centres have sufficient capacity to collect the additional units of blood donated. This alternative assumption may not be realistic if reduced interval strategies are rolled-out to all donors attending static centres. However, if the reduced interval strategies are only applied to those groups whose blood type is in high demand, then current capacity (on average, 75%) may be sufficient to collect the additional units of blood at an incremental costs of no greater than £10 (the base case ICER). Fourth, we were unable to consider the additional costs that may be associated with the observed increase in self-reported symptoms in those giving blood more frequently, although there was no measurable reduction in QoL, physical activity or neurocognitive function in the those allocated to shorter intervals.

The study raises important questions for further research. First, the INTERVAL trial showed that on average, compared to people who gave blood less frequently, people who gave blood most frequently had lower iron and haemoglobin levels after four years and were more likely to have iron and haemoglobin levels below the minimum threshold required to donate blood. Evidence suggests that donors deferred for low Hb are much less likely to return for future donations than donors who are able to donate blood successfully [41]. Evidences from large national studies suggest that female and younger donors often have low level of ferritin store and their risk of ferritin depletion is relatively higher with reduced inter-donation interval [42,43]. Further research is warranted to customise donation intervals recognising that some donors, including those who self-report symptoms, could be at high risk of Hb and ferritin depletion and thereby more likely to stop donation. Further research on Hb and ferritin depletion and their consequent effect on costs and health outcome would be useful for informing sustainable donation strategies. Second, further studies could consider a wider set of interventions, including educational interventions for blood donation and investigate the relative impact of the wider set of interventions versus reducing inter-donation intervals, on the relative donation frequency and costs. Third, reducing the minimum donation interval is more cost-effective for older females, and those females whose blood groups is in high demand.

Finding effective ways to retain these donors is crucial. Blood collection agencies such as NHSBT should consider developing new retention strategies tailored to blood donors, taking into account the specific profiles of female/male donors including age, blood type, donation history, and ethnicity.

In summary, reducing the minimum donation interval yields additional units of whole-blood at a small additional cost over two years. The incremental costs per donation are relatively low for having inter-donation intervals that are shorter than current standard practice in the UK.

Supporting information

S1 Appendix.
(DOCX)

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