Leeds Institute for Rheumatic and Musculoskeletal Medicine

Research Protocol

Version 3.0; Date 04 Aug 2021

Study Short Title: Development of a Virtual Knee School

Study Full Title: Development of a pre-operative education and prehabilitation digital intervention for patients awaiting total knee replacement: a Virtual Knee School

Sponsor Name: University of Leeds

Sponsor Number: Not applicable

Protocol status: Approved by Sponsor

Details of previous amendments: Not applicable

Key contacts

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INVESTIGATOR DECLARATION AND SIGNATURE(S)

VKS, Version 3.0, Date 04 Aug 2021

DECLARATION OF PROTOCOL ACCEPTANCE

I confirm that I am fully informed and aware of the requirements of the protocol and agree to conduct the study as set out in this protocol.

	4th August 2021
Chief Investigator	Date
Anna Anderson	

ABBREVIATIONS

Abbreviation	**Term**
AE	Adverse Event
BCTTv1	Behaviour Change Technique Taxonomy version 1
BCW	Behaviour Change Wheel
CAH	Chapel Allerton Hospital
CI	Chief Investigator
CRF	Case Report Form
DRMD	Division of Rheumatic And Musculoskeletal Disease
GCP	Good Clinical Practice
HRA	Health Research Authority
ICH	International Conference On Harmonisation
MRC	Medical Research Council
NIHR	National Institute for Health Research
PAS	Publicly Available Specification

Abbreviation	Term
PI	Principal Investigator
PIS	Participant Information Sheet
RCT	Randomised Controlled Trial
REC	Research Ethics Committee
RUSAE	Related and Unexpected Serious Adverse Event
SAE	Serious Adverse Event
TKR	Total Knee Replacement
VKS	Virtual Knee School

PROTOCOL SYNOPSIS

GENERAL INFORMATION	
Short Title	Development of a Virtual Knee School
Full Title	Development of a pre-operative education and prehabilitation digital intervention for patients awaiting total knee replacement: a Virtual Knee School
Sponsor	University of Leeds
Sponsor ID	Not applicable
MREC No.	IRAS 262809
Chief Investigator	Anna Anderson
Co-ordinating Centre	Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds
National / International	National
STUDY INFORMATION	
Indication	Primary total knee replacement (TKR) surgery
Design	Mixed methods with the following four phases: 1. Rapid review and Delphi study (covered by a separate protocol) 2. Focus groups/semi-structured interviews 3. Theoretical modelling 4. Intervention development and refinement through think aloud interviews
Number of sites	1
Study Objective	To develop a pre-operative TKR education and prehabilitation digital intervention, the 'Virtual Knee School' (VKS).
Study Endpoint	Not applicable
STUDY TIMELINES	
Start date	30th April 2020
Subject enrolment phase	Phase 1: December 2019 – January 2020 (covered by a separate protocol) Phase 2: May 2020 – June 2020 Phase 3: Not applicable (theoretical modelling with no participants) Phase 4: September 2021 – March 2022 (The Phase 4 dates are approximate and may change)
Follow-up duration	Not applicable

End of study definition	Completion of Phase 4 data collection
Expected completion date	31st May 2022
STUDY SUBJECT INFORMATION	
Number of study subjects	The overall total number of participants involved in the research covered by this protocol will be ~ 21 (maximum 39), as detailed below: Phase 1: 24 – 70 (covered by a separate protocol) Phase 2: ~ 6 – 18 (maximum 24) Phase 3: Not applicable (theoretical modelling with no participants) Phase 4: ~ 8 – 10 (maximum 15)
Age group of study subjects	Adult (aged 18 years old or over)
Inclusion criteria	• Adult (aged 18 years old or over) • Able to communicate in English • Listed for primary TKR surgery and/or have undergone primary TKR surgery within the past two years • Able to use and have access to the Internet and email (Phase 2 only) • Able to use and have access to the Internet and email and/or be willing and able to be interviewed in person (Phase 4 only)
Exclusion criteria	• Unable to provide informed consent

SCHEMATIC DIAGRAM

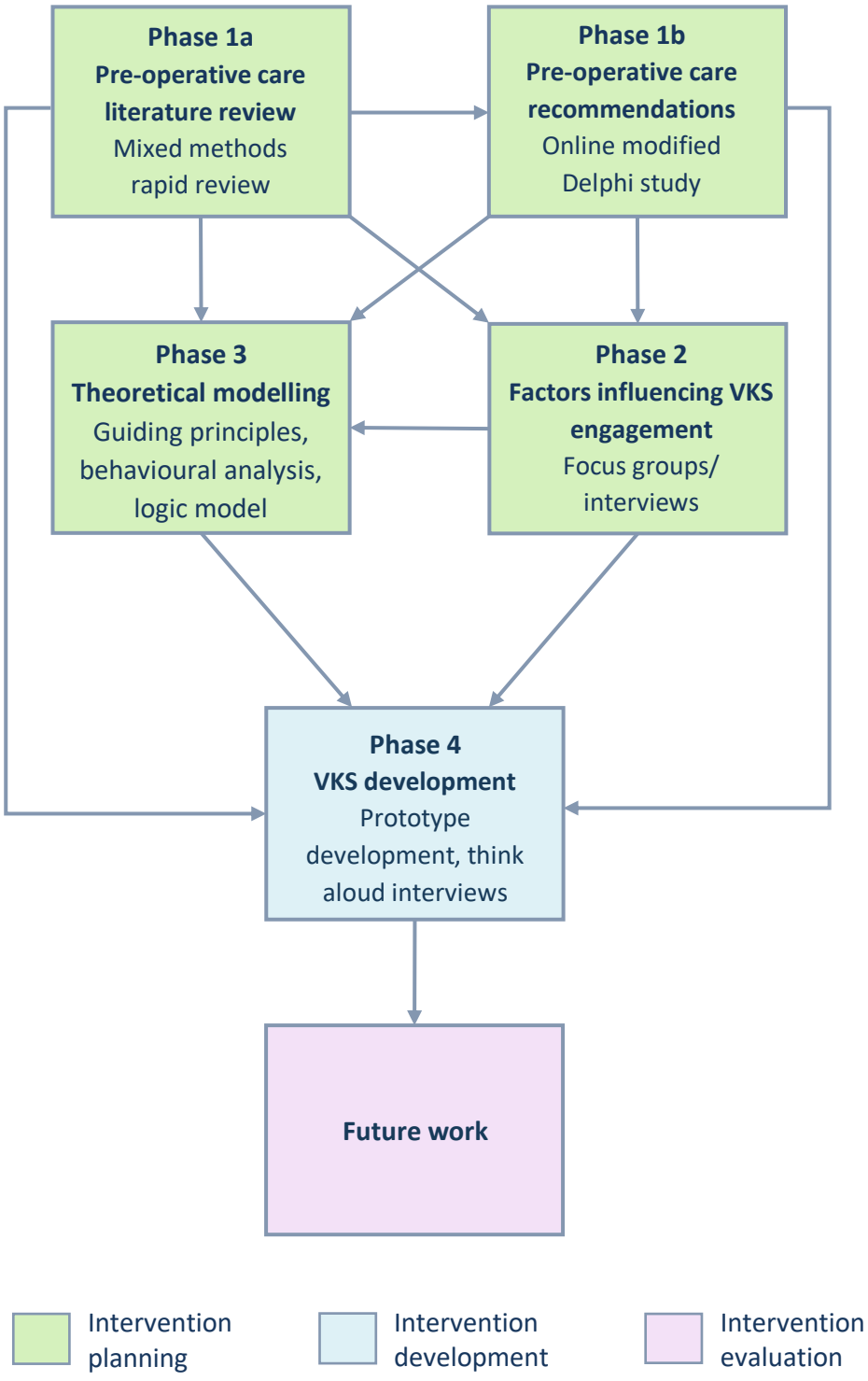

Figure 1a: Project flow chart

VKS – Virtual Knee School

'Pre-operative care' refers to pre-operative education and prehabilitation for patients listed for primary total knee replacement surgery

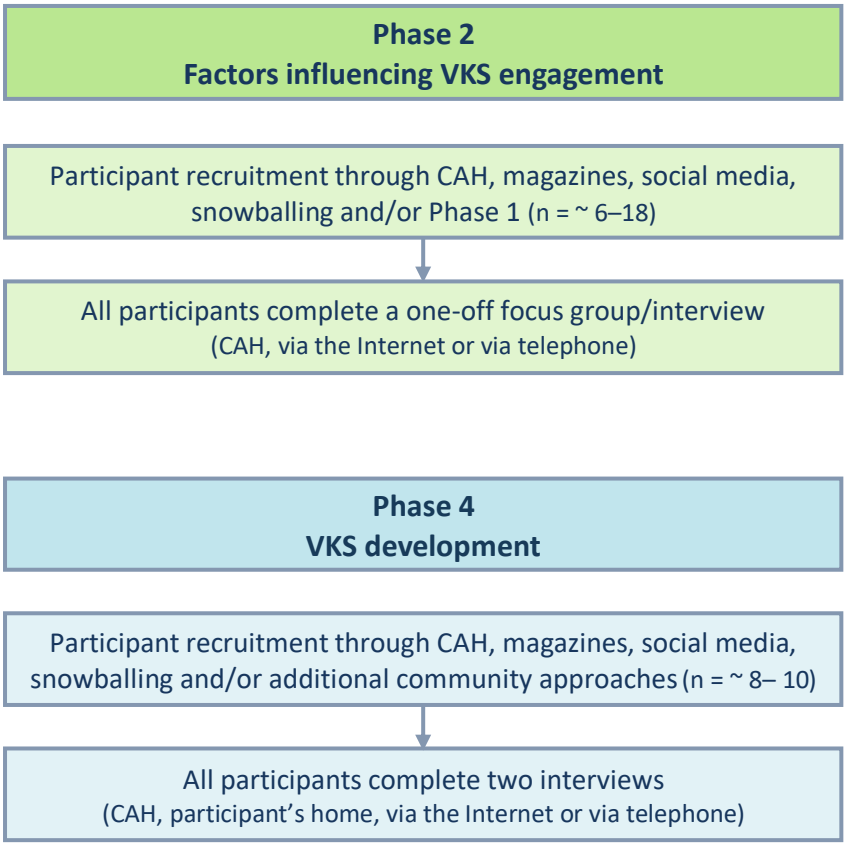

Figure 1b: Participant flow chart

CAH – Chapel Allerton Hospital, VKS – Virtual Knee School

Phase 1 is covered by a separate protocol. Phase 3 consists of theoretical modelling only and will not involve any participants.

1. INTRODUCTION

1.1. Background

This study seeks to address the inadequacies and inefficiencies of current pre-operative total knee replacement (TKR) care provision. The scale of these problems is vast and their impact is profound. Almost 100,000 TKR procedures are performed annually in the UK (1, 2). Furthermore, the demand for TKRs is expected to continue rising due to the ageing population and high obesity levels (3). The majority of TKRs are undertaken amongst older adults due to osteoarthritis (1). Patients awaiting TKR experience significant pain, poor function and low quality of life (4, 5). These problems may deteriorate further whilst patients await surgery (4, 5). Even after TKR, around one in five patients continue to

experience long-term pain (6, 7). Additionally, around one in six patients who undergo TKR are not satisfied with their post-operative outcome (8, 9).

Care provided in the pre-operative phase has a significant influence on patients' overall experiences of TKR (10). Moreover, worse pre-operative pain/function is one of the strongest predictors of poor patient-reported outcomes post-TKR (3). Optimising pre-operative TKR care is therefore a key strategy for improving patient satisfaction and post-operative outcomes (10, 11). Pre-operative TKR education is particularly vital to facilitate patients' preparations for surgery and help ensure they have realistic expectations of the outcomes (12, 13). Furthermore, evidence suggests pre-operative TKR education reduces pre-operative anxiety, shortens length of stay and lowers costs (12, 14). TKR 'prehabilitation' has also been shown to improve pre- and post-operative outcomes (15-17). Prehabilitation involves provision of pre-operative interventions designed to enhance patients' functional capacity prior to surgery (18-20). This is believed to enable patients to better withstand the stresses of surgery and hence improve their post-operative recovery (18-20).

Prehabilitation programmes may include multiple elements, such as exercise, nutritional optimisation and psychological support (19, 20). Exercise is unequivocally recommended for improving pain and function amongst people with knee osteoarthritis (21). Additionally, pre-operative quadriceps strength may predict functional recovery after TKR (22). Exercise is therefore considered a particularly important component of TKR prehabilitation (22, 23). In line with this, systematic reviews and meta-analyses have reported pre-operative exercise reduces length of stay amongst patients undergoing TKR (15, 17, 24). Prehabilitation programmes also present an ideal opportunity for health promotion (20, 25). This is based on the idea that the pre-operative period provides a 'teachable moment', whereby patients' health problems may result in them being more motivated to make healthy lifestyle changes (20, 25).

Despite the many potential benefits of pre-operative TKR interventions, there are significant inconsistencies and limitations in the evidence-base supporting them (14, 15, 17, 24, 26). For example, a Cochrane review investigating pre-operative education for patients undergoing TKR and total hip replacement graded the overall quality of the included evidence as low (14). The intervention reporting of many studies investigating pre-operative TKR education and prehabilitation is also poor (15). This presents a significant barrier to implementing the interventions investigated within clinical practice. In addition, the UK lacks guidelines on pre-operative TKR care. Correspondingly, current pre-operative TKR care provision varies widely across the UK (27).

The importance of standardising TKR care is widely recognised due to the benefits associated with TKR Enhanced Recovery After Surgery (ERAS) programmes (11). These programmes aim to improve patient outcomes and reduce length of stay through delivering a standardised set of interventions at all phases of the care pathway (11, 28). An ERAS Partnership Programme was introduced in the NHS in 2009 (29). However, the uptake of TKR ERAS programmes in the UK has not been universal (30, 31). In addition, there are considerable disparities in existing TKR ERAS programmes (27, 30). For example, pre-operative education is an established TKR ERAS component, but pre-operative TKR education content and delivery varies considerably between hospitals (27). Current delivery formats include booklets, DVDs and/or face-to-face classes called 'knee schools' (27). All these formats have significant limitations. For example, NHS TKR information booklets are frequently outdated and fail to adhere to ERAS principles (32). Patients often struggle to absorb, retain and implement the advice provided at knee schools (33). Additionally, the staff, facilities and materials required by current pre-operative care approaches present substantial costs to the NHS.

The issues discussed above highlight a need for innovative pre-operative TKR education and prehabilitation approaches which are patient-centred, low cost and widely accessible. Digital interventions present an ideal solution to this and offer many potential benefits. These include: improving care quality and efficiency, generating large datasets and facilitating health behaviour change (34, 35). The latter is particularly relevant given the high prevalence of multimorbidity, obesity and sedentary behaviour among patients undergoing TKR (36, 37). Providing TKR care via digital interventions also corresponds with the growing internet use amongst older adults in the UK (38). Recent studies have demonstrated the potential value of using digital interventions within TKR care (39-43). For example, a recent observational study reported incorporating patient and health professional websites within TKR care reduced length of stay, improved patient experience and was cost-effective (39). The validity of these findings is however limited by the study's design and delivery of the websites alongside co-interventions. Furthermore, the websites required health professionals' input and were integrated with the hospital computer systems, limiting their applicability to other settings (39).

Two recent American studies also reported providing digital interventions to patients undergoing TKR may improve outcomes, but did not specify how the digital interventions were developed (40, 41). Conversely, international expert consensus suggests using a 'user-centered' or 'person-based' approach is vital to developing effective digital behaviour change interventions (35). The person-based approach involves using iterative mixed methods research, including in-depth qualitative studies, to gain a thorough understanding of the perspectives and contexts of target users (44, 45). This understanding is used to help ensure the intervention developed is accessible, relevant and engaging for users (44, 45).

The person-based approach has proven particularly successful. For example, it has recently been highlighted as a key intervention development framework by Public Health England (46). Drawing on appropriate theory is also key to intervention development (35, 47). Evidence suggests greater use of theory improves the effectiveness of digital behaviour change interventions (48).

Various published and ongoing studies describe additional relevant digital interventions (42, 43, 49, 50). However, the interventions all present notable limitations, such as being available in mobile application ('app') format only (43, 49, 50). Members of the NIHR Leeds Biomedical Research Centre (BRC) Patient and Public Involvement (PPI) group highlighted this would be a significant drawback due to limiting the intervention's accessibility. There is therefore a need for a new TKR digital intervention to address the limitations of existing interventions.

1.2. Rationale for the proposed study

As discussed above, current pre-operative TKR care provision is variable and limited. Members of the NIHR Leeds BRC PPI group have also raised concerns about disparities in pre-operative TKR care provision and highlighted currently available pre-operative TKR services often fail to meet patients' needs. Furthermore, identifying the most effective education support was ranked amongst the top 10 priorities at a hip and knee replacement James Lind Alliance Priority Setting Partnership (51).

Providing pre-operative care via a digital intervention presents an ideal solution to the above issues. However, currently available digital interventions present numerous limitations (39-43). This study seeks to overcome these limitations through developing a novel pre-operative TKR education and prehabilitation digital intervention – the 'Virtual Knee School' (VKS). The VKS will be developed and optimised using a rigorous evidence-, theory- and person-based approach.

The VKS will have the potential to improve the quality and accessibility of pre-operative TKR care and reduce unwarranted variations in service provision. This could result in multiple benefits for patients awaiting TKR, such as reduced pain and improved function. Pre-operative pain/function influences post-operative outcomes (2). Therefore, the VKS could also improve patient outcomes post-operatively. The VKS could result in significant NHS cost-savings through mechanisms such as improving service efficiencies, decreasing length of stay and minimising patients' post-operative care needs.

Identification of all the clinical and economic benefits of the VKS will not be achieved until a randomised controlled trial (RCT) investigating its effectiveness is undertaken. This is outside the scope of this study. However, this study will provide the preparatory work required prior to developing a feasibility study and subsequent RCT investigating the clinical and cost-effectiveness of the VKS.

2. STUDY AIM AND OBJECTIVES

2.1. Study aim

To develop a pre-operative TKR education and prehabilitation digital intervention, the 'Virtual Knee School' (VKS).

2.2. Study objectives

1. To develop evidence- and consensus-based recommendations on pre-operative TKR education and prehabilitation (addressed in a separate protocol).
2. To explore patients' perspectives of potential barriers and facilitators to engagement with the VKS.
3. To use theoretical modelling to guide the design, description and evaluation of the VKS.
4. To develop a prototype version of the VKS and iteratively refine it based on how patients use it and their perspectives of it.

3. STUDY ENDPOINTS

3.1. Study endpoint

Not applicable.

4. STUDY VARIABLES

4.1. Standard variables

Phases 2 and 4 will involve qualitative research only. Phase 3 will consist of theoretical modelling. Therefore, no standard assessment variables have been defined.

4.2. Efficacy variables

Not applicable as the study involves qualitative research and theoretical modelling only.

4.3. Safety variables

Not applicable as the study involves qualitative research and theoretical modelling only.

4.4. Routine laboratory assessments

Not applicable as the study involves qualitative research and theoretical modelling only.

5. STUDY DESIGN

5.1. Study description

This study will involve developing and optimising the VKS using an evidence-, theory- and person-based approach. In line with this, a mixed methods approach will be used (45, 52). This will involve the following four phases (Figure 1a):

1. Mixed methods rapid review of pre-operative TKR intervention components and delivery approaches (Phase 1a) and online modified Delphi study to develop pre-operative TKR education and prehabilitation recommendations (Phase 1b).
2. Focus groups/semi-structured interviews with patients who are listed for TKR or have undergone TKR within the past two years to explore patients' perspectives of potential barriers and facilitators to engagement with the VKS.

3. Theoretical modelling to guide the design, description and evaluation of the VKS. This will include developing guiding principles, conducting a behavioural analysis and developing a logic model.
4. Development and iterative refinement of the VKS based on the findings of Phases 1 – 3 and think aloud interviews with patients who are listed for TKR or have undergone TKR within the past two years.

Phases 1-3 will involve three complementary approaches to intervention planning that draw on evidence-, theory- and person-based elements (Objectives 1-3). The findings of Phases 1 – 3 will be used during the development of the VKS in Phase 4 (Objective 4). The VKS will be developed by a web design and development company called 'Frank' (53). Frank is a well-established company that has extensive experience of developing digital tools for NHS and other Health and Care Organisations.

Phase 1 is covered by a separate protocol (IRAS 259807). Phase 1 is therefore not described in this protocol. Phase 3 will involve theoretical modelling only and will not involve any participants. A description of Phase 3 is provided in Planned analyses. Phases 2 and 4 both involve primary research with adults who are listed for TKR or who have undergone TKR within the past two years. The subsequent sections of this protocol therefore focus on these two phases.

5.2. Study duration

This study commenced on the 1st June 2019 and is expected to end on the 31st May 2022. It is anticipated Phase 2 will commence around April 2020. The total duration of the phases described in this protocol is therefore approximately 2 years and 2 months.

5.3. Rationale for study design

Using a rigorous process to develop and optimise an intervention maximises the chances of the intervention proving successful during future feasibility and effectiveness testing (45, 47). This study will therefore focus on rigorously developing and optimising the VKS. Correspondingly, the design of this study has been informed by the Medical Research Council (MRC) guidance on developing and evaluating complex interventions (54) and more recent guidance which specifically addresses the development phase of complex interventions (47). Both these sets of guidance highlight the importance of incorporating

evidence, theory and user input within intervention development. Therefore, an evidence-, theory- and person-based approach will be used to develop and optimise the VKS.

6. SELECTION AND WITHDRAWAL OF SUBJECTS

6.1. Target population

Phases 2 and 4: Adults who are listed for primary TKR or have undergone primary TKR within the past two years.

6.2. Estimated number of eligible participants

A combination of recruitment approaches will be used for this study. These may include recruitment through Chapel Allerton Hospital (CAH), magazines, social media, snowballing, sending invitations to the patient panellists from the Phase 1b Delphi study (Phase 2 only) and additional community approaches (Phase 4 only). It is therefore not possible to accurately estimate the number of eligible participants overall. However, estimates for CAH and sending invitations to the patient panellists from the Phase 1b Delphi study are provided below.

Over 440 knee procedures were recorded on the National Joint Registry for CAH in 2019 (55). It is estimated approximately 400 of these were TKR procedures. The average age of patients undergoing TKR in the UK is approximately 69 (1). Data from the Office for National Statistics suggests Internet use amongst people in the 65 to 74 years age group is 83% (56). Patients who are currently listed for TKR or who have undergone TKR within the past two years will be eligible to participate. Participants in Phase 2 must be able to use and have access to the Internet and email. Participants in Phase 4 must be able to use and have access to the Internet and email and/or be willing and able to be interviewed in person. It is therefore estimated that approximately 1,000 and 1,100 patients at CAH will be eligible for Phase 2 and 4 per year. However, the current COVID-19 pandemic means it may not be possible to recruit participants through CAH. In addition, the figures from 2019 used in the estimates are not reflective of the number of TKR procedures performed in 2020 and 2021, but have been used for illustrative purposes as TKR surgery postponements will have reduced the number of patients who have undergone TKR surgery, but increased the number of patients who are listed for TKR surgery.

For Phase 2, patient panellists from the Phase 1b Delphi study will be invited to participate. Twenty six patient panellists completed the Phase 1b Delphi study. The Delphi study eligibility criteria are almost identical to the Phase 2 eligibility criteria. However, some patient panellists who met the criterion of having undergone TKR within the past two years may no longer meet that criterion due to the length of time that has elapsed since their TKR. Therefore, it is anticipated that approximately twenty two patient panellists from the Delphi study will be eligible for Phase 2.

6.3. Eligibility criteria

6.3.1. Inclusion criteria

(a) Adult (aged 18 years old or older)

(b) Able to communicate in English

(c) Listed for primary TKR at a hospital in the United Kingdom (UK) and/or have undergone primary TKR at a hospital in the UK within the past two years

(d) Able to use and have access to the Internet and email (Phase 2 only)

(e) Able to use and have access to the Internet and email and/or be willing and able to be interviewed in person[a] (Phase 4 only)

[a] Potential participants will be considered able to be interviewed in person if they live in West Yorkshire and meeting in person is permitted by the most up-to-date COVID-19 guidance from the government and the University of Leeds.

6.3.2. Exclusion criteria

(a) Unable to provide informed consent

Unless otherwise stated, all criteria apply to Phases 2 and 4.

6.3.3. Exclusions for general safety

No exclusions for general safety are required.

6.3.4. Sampling

For Phases 2 and 4, participants will be purposively selected based on age, gender, varying confidence in using the Internet and varying experience of TKR (listed for TKR surgery versus undergone TKR surgery). In line with a previous relevant study, confidence in using the Internet will be rated by potential participants on a four-point scale (unconfident, neither confident nor unconfident, confident, very confident) (57). For Phase 4, ethnicity and highest level of educational qualification completed will be included as additional purposive selection criteria. Due to the current COVID-19 pandemic, it is anticipated that it may be difficult to fulfil all these purposive selection criteria. Therefore, some of these purposive selection criteria may be omitted if necessary.

6.4. Withdrawal criteria

Due to the low risk nature of this study, there will be no withdrawal criteria. However, all participants will be free to withdraw at any time, should they wish to.

6.5. Recruitment and consent processes

6.5.1. Recruitment

6.5.1.1.1. Overview

A combination of recruitment approaches will be used for Phases 2 and 4. These may include recruitment through CAH, magazines, social media and, for Phase 2 only, sending invitations to the patient panellists from the Phase 1b Delphi study. In addition, participants may be encouraged to share the study information with other people they know to facilitate recruitment through snowballing. For Phase 4 only, additional community recruitment approaches may be used to help ensure that a diverse range of participants are recruited.

Recruitment will be conducted using a phased approach and will be stopped once sufficient participants have been recruited. Correspondingly, the recruitment approaches described below may not all be used.

All potential participants will be given as long as they require to decide whether to participate in the study. Any approach made to a patient about the study may be documented in the patient's medical notes or electronic health record, if required by the recruiting site and in line with the site and University of Leeds's guidance on remote working.

6.5.1.1.2. Recruitment through CAH (Phases 2 and 4)

If recruitment through CAH is undertaken, potential participants will be identified at CAH by members of their direct care teams. This will include the CI, who has an Honorary Contract with Leeds Teaching Hospitals NHS Trust and is considered a member of the direct orthopaedic care team. Identification of potential participants will be based on the following two criteria:

- Adult (aged 18 years old or older)
- Listed for primary TKR at a hospital in the UK and/or has undergone primary TKR at a hospital in the UK within the past two years

Information about these criteria will be obtained from patient records and/or clinic/operation lists. These will only be accessed by members of patients' direct care teams.

The initial approach to potential participants will be made by members of their direct care teams via their clinic appointment or via an Invitation Letter.

1. Clinic appointment

Patients approached at their clinic appointment will be given a verbal explanation of the study and screened to determine whether they meet the eligibility/purposive selection criteria. Eligible patients will be given the Phase 2 or 4 Participant Information Sheet (PIS) and Contact Form, as appropriate. Patients will also be offered an opportunity to ask any questions they may have about the study.

Patients will be informed that, if they are happy to be contacted about the possibility of participating in the study, they must confirm this using one of the following options:

- Completing the Contact Form and returning it to the CI at their clinic appointment.

- Completing the Contact Form and returning it to the CI by post. Patients who indicate they would prefer this option will be provided with a prepaid/stamped addressed envelope addressed to the CI.
- Emailing their contact details to the CI.

2. Invitation letter

Patients approached via an Invitation Letter will be posted the Phase 2 or 4 Invitation Letter, PIS and Contact Form, as appropriate. These documents will be posted by the CI along with a prepaid/stamped addressed envelope addressed to the CI. The Invitation Letters indicate patients interested in participating must confirm this using one of the following options:

- Completing the Contact Form and returning it to the CI by post.
- Emailing their contact details to the CI.

On receipt of a posted Contact Form or email from a patient interested in participating, the CI will contact the patient by email and/or telephone. If the CI contacts the patient by email, the CI will arrange an appropriate time to discuss the study with the patient via telephone. During the telephone conversation with the patient, the CI will explain the study further, screen the patient to determine whether they meet the eligibility/purposive selection criteria and offer the patient an opportunity to ask any questions they may have about the study.

6.5.1.1.3. Recruitment through magazines (Phases 2 and 4)

If recruitment through magazines is undertaken, editorial team members of the North Leeds Life and NorthernLife magazines will be approached and asked whether they would be happy to include the Phase 2 or 4 Magazine Advert in their magazine, as appropriate.

The Magazine Adverts indicate individuals interested in participating should contact the CI via email. On receipt of an email from an individual interested in participating, the CI will reply to the individual's email to provide the Phase 2 or 4 PIS as appropriate and arrange a suitable time to discuss the study with the individual via telephone. During the telephone discussion, the CI will explain the study further, screen the individual to determine whether they meet the eligibility/purposive selection criteria and offer the individual an opportunity to ask any questions they may have about the study. If the individual has not already provided all the contact details specified in the Phase 2 or 4 Contact Form then, with the

individual's consent, the CI will obtain the remaining contact details from the individual during the telephone conversation.

6.5.1.1.4. Recruitment through social media (Phases 2 and 4)

If recruitment through social media is undertaken, recruitment adverts may be shared on Twitter and/or Facebook as described below.

The Phase 2 and 4 Twitter Adverts will be posted on Twitter by members of the study team and accompanied by any of the Phase 2 or 4 tweets respectively.

Phase 2 tweets:

> Do you have experience of knee replacement surgery? Would you like to take part in a research study to help develop a new website – the Virtual Knee School?
> Email anna.anderson6@nhs.net if you think you could help

> We are looking for patients with experience of knee replacement surgery to help with our research study. Taking part would involve sharing your views of preparing for knee replacement surgery.
> Email anna.anderson6@nhs.net if you think you could help

> We are still looking for patients with experience of knee replacement surgery to take part in our research study to help develop a new website – the Virtual Knee School.
> Email anna.anderson6@nhs.net if you think you could help

Phase 4 tweets:

> We're looking for patients with experience of knee replacement to help with our research study. Taking part would involve sharing your views of a new website – the Virtual Knee School.
> Email anna.anderson6@nhs.net if you think you could help

> Exciting opportunity for patients with experience of knee replacement to take part in a research study. Taking part would involve reviewing a new website – the Virtual Knee School.
> Email anna.anderson6@nhs.net if you think you could help

> We're still looking for patients with experience of total knee replacement to help with our research study. Taking part would involve sharing your views of a new website – the Virtual Knee School.
> Email anna.anderson6@nhs.net if you think you could help
>
> We're looking for volunteers who <<details of eligibility and/or purposive selection criteria>> to help with our research study.
> Email anna.anderson6@nhs.net if you think you could help

Retweets of the above tweets may be made to attract interest. Additional comments may also be added to attract interest and/or for clarification purposes. Tweets may include relevant twitter handles and hashtags e.g. @NIHRcommunity, #kneereplacement etc.

The Phase 4 Twitter Advert and fourth tweet listed above will be amended as required to include text about specific eligibility and/or purposive selection criteria to facilitate recruitment of a diverse range of participants. An example of the potential amended text for the Twitter Advert text is as follows:

> We're looking for volunteers who are **waiting for a total knee replacement** or who've **had a total knee replacement** within the past two years.
>
> We want to make sure we hear a wide range of views and **particularly welcome** people from **Black, Asian or other minority ethnic groups.**
>
> The study will involve **reviewing a new website** and **telling us what you think** of it during two telephone or video calls.
>
> The new website is called the **Virtual Knee School**. It provides **information** and an **exercise plan** to help people prepare for having a knee replacement.

Administrators of the following patient Facebook groups will be approached and asked whether they would be happy to share the Phase 2 or 4 Facebook Advert, as appropriate, with their group:

- UK Total Knee Replacement and Recovery UK
- Knee Replacement UK

If an administrator agrees to share the relevant Facebook Advert, the administrator will be asked to post the advert on their Facebook group.

As for the Twitter Advert, the Phase 4 Facebook advert will be amended as required to include text about specific eligibility and/or purposive selection criteria.

The Twitter Adverts and Facebook Adverts indicate individuals interested in participating should contact the CI via email. On receipt of an email from an individual interested in participating, the CI will reply to the individual's email to provide the Phase 2 or 4 PIS as appropriate and arrange a suitable time to discuss the study with the individual via telephone, as described above for Recruitment through magazines.

Social media will not be used to identify and approach specific individuals about participating in the study. Social media will be used purely for the purposes of recruitment and will not be used as a platform for conducting research.

6.5.1.1.5. Recruitment from the Phase 1b Delphi study (Phase 2)

If recruitment from the Phase 1b Delphi study is undertaken, patient panellists who completed the Phase 1b Delphi study will be provided with the following overview of Phase 2 at the end of an email from the CI updating them about the Delphi study.

> Lastly, I just wanted to let you that I am currently in the process of looking for volunteers to take part in the next stage of my PhD project. This stage would involve discussing your views of preparing for knee replacement surgery and how a website could with preparing for surgery. The discussion could take place online, via telephone or possibly in-person, either during a one-to-one interview or during a group discussion called a 'focus group'. I appreciate you have already given a lot of your time to this project and there is absolutely no pressure to take part in the next stage. However, if you would like to receive any further details about the next stage then just let me know.

If an individual indicates they would like to receive further details of Phase 2, the CI will email them the Phase 2 PIS and arrange a suitable time to discuss the study with the individual via telephone, as described above for Recruitment through magazines.

6.5.1.1.6. Recruitment through additional community approaches (Phase 4)

To help ensure a diverse range of participants are recruited for Phase 4, additional community recruitment approaches may be employed. These may include one or more of

the Project Advisory Group PPI representatives sharing the following WhatsApp message with contacts in their communities:

> Opportunity to take part in a research study to improve care for people waiting for a knee replacement
>
> We're looking for volunteers who <<details of eligibility and/or purposive selection criteria>>.
>
> The study will involve reviewing a new website and telling us what you think of it during two telephone or video calls.
>
> The new website is called the Virtual Knee School. It provides information and an exercise plan to help people prepare for having a knee replacement.
>
> To find out more about the study please contact Anna Anderson via <<mobile number>> or anna.anderson6@nhs.net.

In addition, the CI may approach the following Leeds-based community centres/networks and ask them whether they would be happy to share the Phase 4 Twitter Advert, Facebook Advert and/or Community Advert:

- Bangladesh Centre Leeds
- Hamara Healthy Living Centre
- Reginald Centre
- Shantona Women's Centre
- Leeds Black Elders Association
- Forum Central
- Leeds City Council BAME Health and Wellbeing Hub
- Leeds Older People's Forum
- 100% Digital Leeds

As for the Twitter and Facebook Adverts, the Community Advert will be amended as required to include text about specific eligibility and/or purposive selection criteria. The Community Advert may be provided in an electronic and/or paper format.

The WhatsApp message and Community Advert indicate individuals interested in participating should contact the CI via telephone or email. If an individual who is interested in participating contacts the CI via telephone, the CI will explain the study further, screen the individual to determine whether they meet the eligibility/purposive selection criteria and offer the individual an opportunity to ask any questions they may have about the study.

If the individual meets the eligibility/purposive selection criteria and confirms they are still interested in participating, the CI will obtain their name, date of birth, telephone number, email address (if they have one) and postal address (if the individual requests to be interviewed in-person) and send them the Phase 4 PIS via email or post.

If an individual who is interested in participating contacts the CI via email, the CI will reply to the email to provide the Phase 4 PIS and arrange a suitable time to discuss the study with the individual via telephone, as described above for Recruitment through magazines.

6.5.2. Consent

During Phases 2 and 4, potential participants will be asked to provide electronic informed consent by completing the Phase 2 or 4 eConsent Form, as appropriate. Potential participants will be required to fully complete and submit the eConsent Form prior to participating in an interview or focus group.

For Phase 2, the link to the Phase 2 eConsent Form will be sent to the potential participant via email. For Phase 4, the link to the Phase 4 eConsent Form will be sent to the potential participant via email if possible. If the potential participant does not have email access, the CI will provide the potential participant with access to the Phase 4 eConsent Form in person immediately prior to their first interview. The final page of the Phase 2 and 4 eConsent Forms will provide the participant with the option of downloading their responses. If a participant does not have email access, the CI will provide them with a printed copy of their completed eConsent form either on the day of their interview or afterwards via post depending on whether a University of Leeds printer is accessible at their interview location.

The CI will download the participant's completed Phase 2 or 4 eConsent Form from Online surveys. The CI will then add the participant's identification number to the eConsent Form and sign and date it. One copy of the completed and signed eConsent Form will be filed in the study site file. When possible, a paper site file will be stored in a locked filing cabinet in the CI's office at CAH. An electronic site file will be stored within password protected folders on the University of Leeds secure servers. An additional copy of the completed and signed eConsent Form may be filed in the participant's medical notes or uploaded to their electronic health record if required by the recruiting site and in line with the site and University of Leeds's guidance on remote working.

The right of the potential participant to refuse consent without giving reasons will be respected. Further, the participant will remain free to withdraw from the study at any time

without giving reasons and without prejudicing any further treatment. All potential participants recruited will be informed about the nature of the study by both the PIS for the relevant study phase and by supplementary verbal information provided by the CI.

If there are any concerns about whether a potential participant has capacity to decide whether to participate in the study, then the individual will not be asked to participate. Patients who are not able to speak English will not be asked to participate in this study.

6.5.3. Participants who withdraw consent

Participants may withdraw from the study at any time without giving a reason. However, any data collected from a participant before they withdraw consent will be retained. This is clearly stated in each PIS.

6.5.4. Managing/replacing participants who withdraw early

Participants who withdraw from the study early will not be replaced.

6.5.5. Definition for the end of the study

The end of study is defined as completion of the Phase 4 data collection.

7. STUDY TREATMENTS

7.1. General information on the products or interventions to be used

Phase 2 will involve exploratory qualitative research only. Therefore, participants in this phase will not receive an intervention. During Phase 4, participants will work through a prototype version of the VKS. Participants in this phase will therefore be able to access the VKS briefly as detailed in section 7.2 below.

The VKS will be an interactive multimedia website that provides pre-operative TKR education (including guidance on making healthy lifestyle changes) and an exercise

programme. The content of the VKS will be based on the findings of Phases 1 – 3 (Figure 1a). Phase 1 involved a mixed methods rapid review of pre-operative TKR interventions and a UK-wide Delphi study to develop agreed recommendations on pre-operative TKR care. Using the Phase 1 findings during the development VKS will therefore help ensure the VKS exercise programme and additional content are safe and in line with current best practice for pre-operative TKR care.

The VKS will be developed by a web design and development company called 'Frank' (53). Frank is a well-established company that has extensive experience of developing digital tools for NHS and other Health and Care Organisations. They are ISO 27001 and NHS Data and Security Protection Toolkit accredited and use a secure hosting platform with 99.8% uptime and 24/7 backup. Frank will not have access to identifiable data about any participants in the study.

The British Standards Institution Publicly Available Specification (PAS) 277:2015 (58) will be referred to throughout the development of the VKS. The PAS 277:2015 provides a code of practice for health and wellness app developers in the United Kingdom to help ensure the apps they develop are of high quality, safe and appropriate for their intended purposes. The PAS 277:2015 covers all stages of the development, testing and maintenance of health and wellness apps, including web-based apps. This includes guidance on a wide range of aspects such as risk management and governance.

7.2. Use within the trial

In the present study, the VKS will only be used during Phase 4. Participants will access the VKS via their own digital device or, if the interview is conducted in-person, via their own digital device or a digital device provided by the CI. Participants will only be able to access the VKS from a designated URL via a secure login process. Participants will be provided with login details for the VKS so that they do not need to enter any of their personal details into the VKS.

If a participant plans to access the VKS via their own digital device, the CI will email them the VKS URL and login details prior to their interview. The participant will be asked not use the VKS before or after their interview, but may be asked to check that they can log onto the VKS successfully prior to their interview. If a participant plans to access the VKS via a digital device provided by the CI, the CI will provide them with a digital device that has an open

browser at the correct URL and the login details in person immediately prior to their interview.

The routine clinical care of patients will not be affected by their participation in any phases of this study.

7.3. Prior and concomitant illnesses

As specified in Eligibility criteria, patients who are unable to provide informed consent will not be eligible to participate in this study. Therefore, patients with major cognitive impairment will not be eligible to participate. The VKS will include a range of multimedia content. Therefore, it is not anticipated that any other prior or concomitant illnesses will prevent patients being able to use the VKS.

7.4. Prior and concomitant medications and procedures

Given the routine clinical care of patients will not be affected by their participation in this study, all prior and concomitant medications and procedures will be permitted.

Details about whether a participant has previously undergone TKR surgery will be collected for participants in all phases.

7.4.1. Permitted prior medications and procedures

All prior medications and procedures will be permitted.

7.4.2. Prohibited prior medications and procedures

No prior medications and procedures will be prohibited.

7.4.3. Permitted concomitant medications and procedures

All concomitant medications and procedures will be permitted.

7.4.4. Prohibited concomitant medications and procedures

No concomitant medications and procedures will be prohibited.

7.4.5. Surgical procedures

All surgical procedures will be permitted.

7.5. Special warnings and precautions for use

As discussed in General information on the products or interventions to be used, the PAS 277:2015 (58) will be referred to during development of the VKS to help ensure the VKS is safe to use. If it is identified that any special warnings or precautions of use are required for the VKS, these will be clearly highlighted within the intervention content.

7.6. Withdrawal of treatment

7.6.1. Subject compliance

No participants will be withdrawn from the study based on their compliance.

8. METHODS OF ASSESSMENT

8.1. Data collection

8.1.1. All phases

With their consent, the following personal data will be collected directly from potential participants during the screening stage:

- Name
- Date of birth
- Telephone number
- Email address (if the individual has one)

If a potential participant for Phase 4 does not have an email address and/or chooses to be interviewed in their own home, they will be asked to provide their postal address.

Data will only be collected at the screening stage if the data is necessary to decide whether the individual meets the eligibility/purposive selection criteria, to contact the individual about participating in the study or to record the approach made to the patient in their medical notes or electronic health record. In order to document the approach made to the patient in their medical notes or electronic health record, it will be necessary to record the patient's name and date of birth at the screening stage. Details of how identifiable personal data will be stored and retained are provided in Patient confidentiality.

As part of the screening process for Phases 2 and 4, potential participants will be asked to provide their gender and rate their confidence in using the internet on a four-point scale (unconfident, neither confident nor unconfident, confident, very confident) (57). Potential participants for Phase 4 will also be asked to provide their ethnic group and the highest level of educational qualification they have completed during the screening process.

Once a participant has provided consent, additional clinical and sociodemographic details will be obtained via the Phase 2 Questionnaire or Phase 4 Questionnaire as appropriate. These questionnaires will be administered via Online surveys (59) along with the Phase 2 or 4 eConsent Form respectively.

8.1.2. Phase 2

During Phase 2, qualitative data will be collected using semi-structured interviews and/or focus groups. If focus groups are conducted, each focus group will consist of approximately six participants. Participants will be able to choose whether they would like their interview or focus group to take place via the Internet or via telephone. Participants who live in West

Yorkshire may also be offered the opportunity to have their interview or focus group in-person at CAH. Interviews and focus groups conducted via the Internet will be undertaken using a secure videoconferencing tool (Blackboard Collaborate Ultra (60); Microsoft Teams (61); Zoom (62); or Webex (63)).

The interviews and focus groups will explore patients' perspectives of potential barriers and facilitators to engagement with the VKS. The CI will prompt discussions by asking questions and referring to digital trigger materials (examples of potential digital features that could be included in the VKS). All participants will be emailed the digital trigger materials in advance of their interview or focus group. In addition, if the interview or focus group is conducted via the Internet or in-person, the trigger materials may be presented during the interview or focus group.

The CI's prompt questions will be guided by the Phase 2 Topic Guide. This Topic Guide has been developed based on the study objectives and previous relevant research (64, 65). The Phase 2 Topic Guide may be amended if required after completion of each interview or focus group. In addition to the CI, another member of the research team may join the interview or focus group. The interviews and focus groups will be audio-recorded using a digital voice recording device.

8.1.3. Phase 4

During Phase 4, a prototype version of the VKS will be developed based on the findings of Phases 1 – 3 (Figure 1a). Qualitative data about patients' perspectives of the prototype version of the VKS will be collected using think aloud interviews (66). Given the VKS will contain a lot of content, each participant will be invited to participate in two think aloud interviews to help ensure that they able to provide feedback on the majority of the VKS, whilst keeping the length of each interview manageable. All participants will be offered the opportunity to have their interviews via the Internet or via telephone. Participants who live in West Yorkshire may also be offered the opportunity to have their interviews in person at CAH or in their own home, if permitted by most up-to-date COVID-19 guidance from the government and the University of Leeds. Interviews conducted via the Internet will be undertaken using a secure videoconferencing tool (Blackboard Collaborate Ultra (60), Microsoft Teams (61) or Zoom (62)). The decision about how to conduct the interviews will be based on the most up-to-date COVID-19 guidance from the government and the University of Leeds and the participant's preference where possible. For example, if there are no restrictions on meeting in person, the decision will be based solely on the participant's preference. In contrast, if meeting in person is only permitted when essential,

the interviews will be conducted via the Internet or via telephone unless the participant does not have Internet/email access and so would be unable to complete the interviews remotely.

During the interviews, participants will be asked to work through the VKS. The participants may access the VKS on their own digital device or, if the interview is conducted in person, on a digital device provided by the CI. If the interview is conducted via the Internet or via telephone, the participant may be sent a booklet that includes some of the VKS content prior to the interview, to facilitate the interview process. As they work through the VKS, the CI will instruct the participant to say everything they are thinking out loud. In addition, the CI will ask them to answer specific probing questions related to the VKS content and usability. Where possible, the CI will observe how the participant uses and responds to all key parts of the VKS. The CI may ask the participant to access specific information/sections/pages of the VKS if required to facilitate this. After completion of the *'think aloud'* component of the interview, the CI will ask the participant some brief semi-structured interview questions to gain an insight into their perspectives of the VKS as a whole. In addition to the CI, another member of the research team may join the interview.

The questions the CI asks will be guided by the Phase 4 Topic Guide. This Topic Guide has been developed based on the study objectives and suggested questions for using in think aloud interviews (67). The same topic guide will be used for each participant's first and second interview. The interviews will be audio-recorded using an encrypted mobile phone and/or laptop. They may also be recorded using the built-in recording functionality of one of the secure video conferencing tools specified above. The video conferencing tool recordings may include audio, video and on-screen activity, such as screen sharing and chat text. The findings of the interviews will be used to iteratively modify the VKS as decribed in Planned analyses. Once a modification has been made, the subsequent think aloud interviews will be used to determine whether the changes that have been made are appropriate.

8.2. Standard assessment variables

Phases 2 and 4 will involve qualitative research only. Phase 3 will consist of theoretical modelling. Therefore, no standard assessment variables have been defined.

8.3. Efficacy assessment variable(s)

Not applicable as the study involves qualitative research and theoretical modelling only.

8.4. Safety assessment variables

Not applicable as the study involves qualitative research and theoretical modelling only.

8.5. Routine laboratory assessments

Not applicable as the study involves qualitative research and theoretical modelling only.

9. STUDY PROCEDURES BY VISIT

9.1. Summary schedule of study assessments

Phase	Number of visits	Location of visits	Explanation
2	0 or 1	CAH	All participants will be offered the opportunity to have their interview or focus group via the Internet or via telephone. Participants who live in West Yorkshire may also be offered the opportunity to have their interview or focus group in-person at CAH.
4	0, 1 or 2	CAH or participant's home	All participants will be offered the opportunity to have their interviews via the Internet or via telephone. Participants who live in West Yorkshire may also be offered the opportunity to have their interviews in person at CAH or in their own home, if permitted by most up-to-date COVID-19 guidance from the government and the University of Leeds.

Table 1: Visit summary

CAH – Chapel Allerton Hospital

All participants who attend CAH to participate in a focus group or interview will be able to claim reimbursement for travel expenses and, if permitted by the most up-to-date COVID-19 guidance from Leeds Teaching Hospitals NHS Trust and the University of Leeds, they will be

provided with light refreshments. If provision of refreshments is not permitted, participants will be clearly informed beforehand and asked to bring their own refreshments. In addition, all participants will be able to claim reimbursement for childcare, carer or personal assistant costs if required.

A summary of participants' flow through the study is provided in Figure 1b (see SCHEMATIC DIAGRAM).

10. SAFETY ISSUES

10.1. Defining serious adverse events (SAEs)

A **serious adverse event** (SAE) is an adverse event which is defined as serious, i.e. that it:

- Results in death. All deaths occurring during patients' participation in the study will be treated as an SAE and reported as such. All deaths which may be considered as related to the VKS, regardless of the interval, must be treated as a SAE and reported as such.
- Is life-threatening.
- Requires inpatient (overnight) hospitalisation or prolongation of an existing hospitalisation.
- Results in a persistent or significant disability or incapacity.
- Results in a congenital anomaly or birth defect.
- Additionally, important medical events that may not result in death, be life-threatening, or require hospitalisation may be considered SAEs when, based on appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
- Any other significant clinical event, not falling into any of the criteria above, but which in the opinion of the Investigator requires reporting.

10.2. AEs of special interest

Not applicable as the study involves qualitative research and theoretical modelling only.

10.2.1. Pregnancy

Not applicable.

10.3. Defining related and unexpected serious adverse events (RUSAEs)

A serious adverse event suspected to have a reasonable causal relationship to the study treatment or procedure which is unexpected i.e. where the nature or severity is inconsistent with the available information relating to the treatment or procedure, or is not listed in this protocol as an expected occurrence is subject to expedited reporting.

10.4. Exemptions from safety reporting

The following events are expected and will not be reported: None.

10.5. Recording and reporting of (RU)SAEs

10.5.1. Recording and reporting of (RU)SAEs

SAEs will be collected during the following time periods:

- Phases 2 – the time between the participant's commencement of the interview or focus group and the end of their participation in the interview or focus group.
- Phase 4 – the time between the participant's commencement of their first interview and the end of their participation in their first interview and the time between the participant's commencement of their second interview and the end of their participation in their second interview. SAEs will not be collected between the end of their participation in their first interview and their commencement of their second interview.

The study is non-interventional; therefore, the chance of any safety issues occurring during the study is minimal. Monitoring for SAEs during the study will be performed by the CI and any other members of the study team members who are involved in the data collection

During the time periods specified above, the investigator will:

- Record all SAEs.
- Report all RUSAEs to the Sponsor via governance-ethics@leeds.ac.uk within one working day of the research team being made aware of the RUSAE.
- Report all RUSAEs on a 'Serious Adverse Event report form for non-CTIMPs', available from the HRA website. This form should be sent to the main REC for the trial.

The Investigator must follow up on all SAEs until the events have subsided, returned to baseline, or, in case of permanent impairment, until the condition has stabilized. SAEs that are (or develop into) chronic conditions will be followed up until it is established that the condition is chronic at which point no further follow-ups will be made since the condition will unlikely resolve. The Sponsor will maintain detailed records of the SAEs reported by an Investigator in accordance with good clinical practice and applicable local regulations.

10.5.2. RUSAE reporting requirements

All SAEs identified by the local Investigator as both likely to be related to protocol-treatment and unexpected will be reviewed by the CI. The CI, local PI or other qualified and delegated individual may declare an SAE a RUSAE. This may be downgraded in discussion with the CI but if no agreement can be made, or in the absence of the CI, the event should be reported as a RUSAE. All RUSAEs will be reported to the Sponsor via governance-ethics@leeds.ac.uk within one working day of the research team being made aware of the RUSAE. A RUSAE once reported can be downgraded at a later date upon the receipt of new information. All investigators should refer to this protocol when determining whether a SAE is expected.

Identifiable patient data, other than linked anonymised data required by the non-CTIMP SAE form, must not be included when reporting RUSAEs.

The CI will then inform the Research Ethics Committee (REC) that gave the favourable opinion for the study of RUSAEs within the required expedited reporting timescales. RUSAEs must be reported to the REC within 15 calendar days of the CI (or their research team) being informed of the event.

RUSAEs will be reported in accordance with the principles of ICH GCP and the Research Governance Framework 2005. They will all be signed off by the CI or PI or, in their absence, by a delegated individual.

10.6. Urgent safety measures

If the research team becomes aware of information affecting the risk/benefit balance of the study they may take immediate action to ensure patient safety. Urgent safety measures deemed necessary must be reported immediately by telephone to the main REC for the study and must be followed within three days by notice in writing setting out the reasons for the urgent safety measures and the plan for further action. The REC co-ordinator will acknowledge within 30 days.

10.7. Serious breaches of protocol

A **serious breach** is a breach which is likely to effect to a significant degree either:

- The safety or physical or mental integrity of the subjects of the study; or
- The scientific value of the study

Serious breaches of GCP or the study protocol will be reported to the Sponsor via governance-ethics@leeds.ac.uk within 24 hours (same day, except weekends) from the time the research team becomes aware of the incident.

10.8. Laboratory Investigations

Not applicable.

10.9. Other safety measures

During any Phase 4 interviews conducted in person, the participant, CI and additional member of the research team if present, will all be required to follow the most up-to-date guidance on lowering the risks of COVID-19 from the government and the University of

Leeds. If the interview is being conducted at CAH, the COVID-19 guidance from Leeds Teaching Hospitals NHS Trust will also be followed.

During Phases 4, it is possible some participants may be interviewed in their own home by the CI alone. If this occurs, the risk of lone working will be minimised by using a 'buddy system'. This will involve the following steps:

- In advance of each lone visit, the CI will identify another member of the research team who is happy to be her 'buddy' for that visit
- The CI will provide the buddy with the following details: anticipated visit start time, anticipated departure time and the participant's name, address and telephone number
- When the CI arrives at the participant's home, the CI will contact the buddy via text/email/telephone to inform the buddy of her arrival and confirm her anticipated departure time
- When the CI leaves the participant's home, the CI will contact the buddy via text/email/telephone to confirm her safe departure
- If the CI has not made contact with the buddy within half an hour after her planned departure time, the buddy will try contacting the CI and, if that is not possible, the participant and/or the CI's next of kin
- If the buddy has not been able to make contact with the CI within one hour of the CI's planned departure time, the buddy will liaise with senior members of the research team if appropriate, and decide whether the police need to be informed

10.10. Annual reports

An annual report describing the general progress and any relevant safety data related to the study must be submitted to the main REC and the Sponsor on the anniversary of the REC approval being granted. The appropriate form for non-CTIMPs is available from the HRA website.

The CI must review and sign / date the report.

10.11. End of study report

Upon completing the study, as defined in Definition for the end of the study, an end of study report must be submitted to the REC within one year of the end of the study. A copy of this end of study report should also be submitted to the Sponsor's office and supplied to all support departments involved in the study.

The CI must review and sign / date the report.

11. STUDY MANAGEMENT AND ADMINISTRATION

11.1. Good clinical practice (GCP)

This clinical trial will be run in accordance with the Principles of ICH GCP and the Research Governance Framework 2005.

11.2. Adherence to protocol

The Investigator should not deviate from the protocol. In medical emergencies, the Investigator may use his/her judgment and may remove a study participant from immediate hazard before notifying the Sponsor and the REC in writing regarding the type of emergency and the course of action taken.

11.3. Monitoring and audit

The Sponsor reserves the right to audit any site involved in the study and authorisation for this is given via the study contract or agreement. A site may be audited by DRMD or an independent contractor working for DRMD, and the Investigator should allow direct access to study documentation.

11.4. Study management

11.4.1. Definition of source data

Source documents are original records in which raw data are first recorded. These may include, but are not limited to audio/audiovisual recordings, file notes and self-report online questionnaires. All source documents will be stored securely

Further details about data storage are provided in Patient confidentiality.

11.4.2. Source data verification

Source data verification ensures accuracy and credibility of the data obtained. Where appropriate, the Investigator will review the reported data to ensure they are accurate, complete and verifiable from source documents.

11.4.3. Study oversight

Independent oversight of the study will be provided by an established Project Advisory Group. This group consists of the CI, the CI's supervisors based at the University of Leeds, three Patient and Public Involvement representatives, an independent chair from NHS Digital and a key collaborator from the West Yorkshire Association of Acute Trusts. The Project Advisory Group will meet approximately every six months for the duration of the study. The Terms of Reference of the Project Advisory Group are provided in Appendix 2.

Due to the low risk nature of this study, a Data Monitoring Committee will not be established.

11.5. Data handling

11.5.1. CRF completion

Not applicable.

11.5.2. Database entry and reconciliation

During Phases 2 and 4, quantitative data will be collected using Online surveys (59). This is an established and secure system for administering online questionnaires. Once all participants' questionnaire responses have been exported from Online surveys, the data will be deleted from Online surveys.

11.5.3. Screening logs and participant identification lists

Screening logs will be used to record details of all patients screened for each study phase. These screening logs will record each patient's initials, their date of screening and details about whether they met the eligibility and purposive selection criteria. No additional information, such as the patient's name or contact details, will be recorded in the screening logs.

Participant identification lists will be used to record details of all patients who have consented to participate in each study phase. These lists will be used for the unambiguous identification of each participant. The participant identification lists will only be accessible to the CI, the CI's primary academic supervisor and authorised representatives of the Sponsor, regulatory authorities and the NHS Trust. The participant identification lists for all phases will contain the participant's identification number, name, date of birth, telephone number, email address if provided, postal address if provided, screening date and consent date.

If required by the recruiting site and in line with the site and the University of Leeds's guidance on remote working, the participant's consent and enrolment in the study will be recorded in their medical notes or electronic health record. The data recorded will identify the study and relevant study phase, and the date(s) of the patient's participation.

11.6. Archiving and data retention

All essential study documents that contain participants' personal details will be retained for five years following the completion of the study. Arrangements for confidential destruction will then be made. If a patient withdraws consent for their personal data to be stored, it will be confidentially destroyed at the earliest opportunity. Any non-identifiable data collected from the patient will however be retained. This is specified in each PIS. No records/study documentation/data may be destroyed without first obtaining permission from the Sponsor.

All essential study documents that do NOT contain participant's personal details will be retained for ten years following the publication of the study. This length of data retention is in line with guidance on storing research data from the University of Leeds Research and Innovation service (68).

Essential documents include (this list is not exhaustive):

- Completed consent documents for all participants
- Participant ID lists and screening logs
- Record of all communications between the Investigator, the REC and the Sponsor.
- List of sub-investigators and other appropriately qualified persons to whom the Investigator has delegated significant study-related duties, together with their roles in the study and their signatures

All digital files will be archived within password protected folders on the University of Leeds secure servers. All paper files will be archived in a locked filing cabinet in the CI's office or the CI's primary academic supervisor's office, both of which are at CAH. If this is not possible, then permission to make alternative arrangements will be sought from the Sponsor. Details of these arrangements should be documented.

All audio/audiovisual recordings will be kept securely until the end of the study and then confidentially destroyed.

11.7. Study suspension, termination and completion

Suspension or termination of the study may occur at any time for any reason, following discussion between the Investigator and the Sponsor. Upon premature study completion, the Investigator will provide the Sponsor with final reports and summaries as required by regulations, and will be responsible for completing a premature end of study report to the Research Ethics Committee (REC) within 15 days.

11.7.1. Sample storage

Not applicable

12. DATA EVALUATION

12.1. Responsibilities

All data analysis and report writing will be performed by the CI. To help ensure rigour, the CI will have regular supervision throughout this study, including formal supervisory team meetings every month and approximately one to two hours of informal supervision from her University of Leeds supervisors each week. The CI will also discuss the study findings with other members of the study team and with members of the Project Advisory Group.

12.2. Hypotheses

Not applicable.

12.3. General considerations

The majority of data collected during this study will be qualitative. The only quantitative data collected will be the Phase 2 and 4 questionnaire responses and the additional participant sociodemographic and clinical characteristics collected during the Phase 2 and 4 screening processes. The quantitative data will be analysed using appropriate descriptive statistics. This will be undertaken using Microsoft Excel and/or IBM SPSS Statistics software (69).

All the focus groups and interviews conducted in Phases 2 and 4 will be audio recorded using an encrypted mobile phone and/or laptop. Interviews conducted in Phase 4 may also be recorded using a secure video conferencing tool (Blackboard Collaborate Ultra (60); Microsoft Teams (61); Zoom (62)). The video conferencing tool recordings may include audio, video and on-screen activity, such as screen sharing and chat text. All the recordings will be transcribed verbatim (intelligent verbatim or full verbatim) by the secure video conferencing tool and/or 1st Class Secretarial Services (70) as described below in Patient confidentiality~~Patient confidentiality~~. Accuracy of the transcriptions will be verified by the CI. Field notes will be referred to where appropriate to assist the analysis. NVivo software (71) will be used to facilitate the analysis where appropriate.

12.4. Planned analyses

12.4.1. Phase 2

The data collected during the interviews and focus groups in Phase 2 will be analysed using thematic analysis (72). This is a well-established approach for analysing qualitative data which focuses on identifying patterns ('themes') in the data (72). To facilitate the design of the VKS, the findings of the thematic analysis will be entered into a table specifying:

- Key barriers and facilitators to engagement with the VKS
- VKS design features that could address each barrier and facilitator

12.4.2. Phase 3

Phase 3 will involve the following three integrated approaches to theoretical modelling to help guide the design, description and evaluation of the VKS:

1. Development of 'guiding principles', which is a core component of the person-based approach (44, 52). The guiding principles will specify:
    - Key design objectives of the VKS
    - Key features of the VKS that could address each objective
2. Behavioural analysis using the Behaviour Change Wheel (BCW) (73) and the Behaviour Change Technique Taxonomy (v1) (BCTTv1) (74). The BCW is a theoretical framework underpinned by the capability, opportunity, motivation model of behaviour ('COM-B model') (73). The BCTTv1 is a hierarchically organised taxonomy of 93 behaviour change techniques (74).
3. Development of a logic model to provide a visual representation of the proposed causal pathways of the VKS (47, 75). This will include specifying aspects such as the problems the VKS is seeking to address, the VKS components and the intended outcomes of the VKS.

12.4.3. Phase 4

The data collected during the think aloud interviews in Phase 4 will be analysed using an approach specifically designed to enable the efficient analysis of qualitative data during intervention development studies (76). This approach will involve identifying positive and negative comments about the VKS and, for each negative comment, identifying what modification(s) could be made to the VKS to address that particular comment (76). It will also involve deciding whether to implement each potential modification. This will be based on factors such as whether the modification is consistent with the guiding principles specified in Phase 3, how much of a priority the modification is and how likely it is that the modification will affect the desired behaviour change (76).

Data collection, data analysis and modifications to the VKS will be conducted iteratively, until further interviews suggest no significant additional modifications are needed.

12.5. Safety analyses

All SAEs will be listed in the end of study report. The frequency of all SAEs recorded during the study period will be presented. The data will be displayed as number of participants experiencing the SAEs, percentage of participants, and number of SAEs.

12.6. Handling of dropouts and missing data

Phase 2 will involve participants taking part in a one-off focus group or interview and completing a brief online questionnaire. Phase 4 will involve participants taking part in two interviews and completing a brief online questionnaire. The 'Required' question functionality of Online surveys will be used to ensure participants cannot miss required questions in the online questionnaires. Dropouts and missing data are therefore unlikely to occur. If dropouts and missing data do occur, they will be monitored and recorded with reasons where available.

12.7. Planned interim analysis

Not applicable.

12.8. Determination of sample size

Phases 2 and 4 are purely qualitative. Therefore, the sample sizes for these phases will be guided by the aim of achieving data saturation. Based on previous studies, approximate sample sizes have been estimated as specified below (64, 65, 77-79). Maximum sample sizes are provided in brackets to ensure the study can be completed within the allocated time frame:

- Phase 2: ~ 6 – 18 (maximum 24) (64, 77, 79)
- Phase 4: ~ 8 – 10 (maximum 15) (65, 78)

The total number of participants to be included in this study overall will therefore be approximately 14 – 28 (maximum 39).

13. ETHICS AND REGULATORY REQUIREMENTS

13.1. Good Clinical Practice

This study will be conducted in accordance with applicable laws and regulations including, but not limited to, the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice (GCP) and the recommendations guiding ethical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964, amended at the 48th General Assembly, Somerset West Republic of South Africa, October 1996. The Research Ethics Committee (REC) must review and approve the protocol and informed consent documents before any patients are enrolled. Before any protocol-required procedures are performed, the patient must complete the REC-approved (e)Consent Form for the relevant study phase. The right of a patient to refuse participation without giving reasons must be respected. The patient must remain free to withdraw at any time from the study without giving reasons and without prejudicing his/her further treatment. The study will be submitted to and approved by a Research Ethics Committee (REC) prior to entering patients into the study.

13.2. Delegation of Investigator duties

The Investigator should ensure that all persons assisting with the study are adequately qualified and informed about the protocol, any amendments to the protocol, the study treatments, and their study-related duties and functions.

The Investigator should maintain a delegation log of co-investigators and other appropriately qualified persons to whom she has delegated significant study-related duties.

13.3. Patient information and informed consent

As detailed in Recruitment and consent processes, all patients must provide informed consent prior to being enrolled in the study. All patients will receive the PIS for the relevant study phase before being asked to provide consent. In addition, they will receive an explanation of the study and be given the opportunity to ask any questions they may have about the study.

13.4. Patient confidentiality

Details of the identifiable personal data collected during this study are provided in the All phases data collection section.

Medical records of potential participants will not be accessed by anyone outside their direct healthcare team during this study. Relevant sections of participants' medical records and research data may be accessed during this study by individuals from the University of Leeds, regulatory authorities or the NHS Trust, where it is relevant to their participation in the study. This is stated in the (e)Consent Form and Participant Information Sheet for each study phase.

All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (GDPR) and Data Protection Act 2018 regarding the collection, storage, processing and disclosure of personal information and will uphold the GDPR's and Act's core principles. All information collected during the course of the study will be kept strictly confidential, unless there are any legal or safeguarding concerns that require confidentiality to be breached. If any legal or safeguarding concerns do arise, they will be managed in line with the University of Leeds Research Ethics Policy. This will include considering the situation on an individual basis and asking the University Secretary for guidance if required. Given the nature of the study, it is very unlikely that it will be necessary to breach confidentiality. The PIS and (e)Consent Form for each study phase

provide details of the circumstances in which a participants' confidentiality might need to be breached.

Information will be held securely on paper and electronically. This will include all paper files that contain identifiable personal data of participants/potential participants, including completed Contact Forms, being stored in a locked filing cabinet in the CI's office at CAH. It will also include all digital files that contain identifiable personal data of participants/potential participants being stored within password protected folders on the University of Leeds secure servers, in line with the University of Leeds Data Protection Policy (80). The mobile phone and/or laptop used to record focus groups/interviews will be encrypted. Participants will not be required to enter any of their personal details into the VKS and the web development and design company (Frank) will not have access to any identifiable data about participants.

Only participants' identification number will be recorded on documents that contain participants' focus group/interview/questionnaire responses. The CI will maintain a participant identification list for each phase to enable documents to be identified. The participant identification lists will only be accessible to the CI, the CI's primary academic supervisor and authorised representatives of the Sponsor, regulatory authorities and the NHS Trust. The participant identification lists for all phases will contain the participant's identification number, name, date of birth, telephone number, email address if provided, postal address if provided, screening date and consent date.

It is necessary to collect and record the name and date of birth of participants/potential participants during this study to enable details of the approaches made to potential participants and the provision of consent by participants to be documented in the relevant patient's medical notes or electronic health record, as appropriate. Use of the patient's name only is not sufficient for this purpose due to many patients having the same name.

If a participant in Phase 4 chooses to be interviewed in their own home, a 'buddy system' will be used to minimise the risks of lone working (see Other safety measures for further details). This will involve the CI providing another member of the research team (the 'buddy') with the name, telephone number and postal address of the participant. These details will be provided via email in an encrypted Word document. The buddy will only keep the participant's details until the buddy process for that particular participant is complete, and will then confidentially destroy the details.

The PIS and (e)Consent Form for each study phase provide details about how participants' personal data will be processed during the study. This includes specifying that representatives of the Sponsor, regulatory authorities or the NHS Trust may inspect patients' medical and research records.

The (e)Consent Form for each study phase requires participants to consent to their data being stored for the purposes of the study. In addition, the Contact Form for each study phase states:

> I agree to my personal information being stored for the purpose of contacting me about this study.

If a potential participant first contacts the CI via email, the initial email response sent by the CI will include the following statement:

> Please note that by responding to this email, you are agreeing to your personal information being stored for the purpose of contacting you about this study.

If a potential participant first contacts the CI via telephone, the CI will only collect and store their personal information for the purpose of contacting them about the study if the individual verbally consents to that during the telephone conversation.

Social media will be used purely to share the recruitment adverts rather than to collect identifiable personal data. All the online consent documents and questionnaires used in this study will be administered via email using Online surveys (59). This is an established and secure system for administering online surveys. Once all participants' questionnaire responses have been exported from Online surveys, the data will be deleted from Online surveys.

All interviews and focus groups conducted via the Internet will be undertaken using a secure videoconferencing tool (Blackboard Collaborate Ultra (60); Microsoft Teams (61); Zoom (62)). All three of these tools are provided by the University of Leeds and hence meet the University of Leeds data protection standards.

All the focus groups and interviews conducted in Phases 2 and 4 will be audio recorded using an encrypted mobile phone and/or laptop. The Phase 4 interviews (including those conducted via the Internet, via telephone and in person) may also be recorded using the

built-in recording functionality of one of the secure video conferencing tools specified above. The video conferencing tool recordings may include audio, video and on-screen activity, such as screen sharing and chat text. After a recording has been created using an encrypted mobile phone, laptop or secure video conferencing tool, it will transferred to secure University of Leeds servers at the earliest opportunity and then deleted from the initial recording location.

When a video conferencing tool recording is made, a transcript of the recording may be automatically generated, depending on the specific tool and settings used. If a transcript is generated, it will be transferred to secure University of Leeds servers at the earliest opportunity and then deleted from the initial recording location. Any video conferencing tool transcripts generated will be reviewed by the CI for accuracy. If the transcript is largely accurate, the CI will correct any inaccuracies to create an intelligent/full verbatim transcript to be used during the analysis. If there are significant inaccuracies in the transcript, the CI will arrange for the corresponding recording to be transcribed by 1st Class Secretarial Services (70) as described below.

All the recordings created during Phases 2, and any recordings created in Phase 4 that require transcription, will be transmitted to 1st Class Secretarial Services for transcription (70). 1st Class Secretarial Services provides a secure online system for uploading files, which involves an encrypted channel. A data processing agreement will be in place between the University of Leeds and 1st Class Secretarial Services. 1st Class Secretarial Services will not have access to the participant identification lists which link participants' identification numbers to the corresponding participants' personal details. All the audio/audiovisual recordings will be kept on the secure University of Leeds servers until the end of the study and then confidentially destroyed.

Direct quotations from the focus groups and interviews may be included in reports, publications and presentations. However, all quotations will be anonymised and will not identify individual participants.

13.5. Approval of clinical study protocol and amendments

Before the start of the study, the study protocol, all patient documents listed in Appendix 1 and any other appropriate documents will be submitted to the REC and the Sponsor with a cover letter or a form listing the documents submitted, their dates of issue, and the site for which approval is sought.

Before the first patient is enrolled in the study, all ethical and legal requirements must be met, including approval of the study by the NHS, the Sponsor Research and Development department and the REC.

Amendments must be evaluated to determine whether formal approval must be sought and whether the informed consent documents should be revised, thus all protocol amendments and administrative changes must first be discussed with and approved by the Sponsor before being submitted to the REC, in accordance with legal requirements. The Investigator must keep a record of all communication with the REC and the Sponsor.

13.6. Protocol amendments

Requests for any amendments to the study must be sent to the Sponsor by the CI. The Sponsor will determine whether said amendments are substantial or non-substantial prior to their submission to the appropriate bodies for approval. Patients should be re-consented to the study if the amendments affect the information they have received, patient safety, or if the change alters the type or quality of the data collected for the study. Patients should only be re-consented AFTER an amendment has been fully approved.

13.7. Ongoing information for Research Ethics Committee

Unless otherwise instructed by the REC and the Sponsor, the Investigator must submit to the REC and the Sponsor:

- Information on serious adverse events that are unexpected and related to study procedures (RUSAEs) from the Investigator's site, within 15 calendar days of the research team becoming aware of them.
- Expedited safety reports, as soon as possible.
- Annual reports on the progress of the study.
- The HRA Declaration of End of Study form.

14. FINANCE AND INSURANCE

14.1. Indemnity and insurance

The University of Leeds will provide insurance to cover for liabilities and prospective liabilities arising from negligent harm. Clinical negligence indemnification will rest with the participating NHS Trust or Trusts under standard NHS arrangements.

14.2. Financial disclosure

None of the Investigators or members of the research team will receive personal benefits, incentives or payment over and above normal salary.

15. PUBLICATION

All foreground Intellectual Property arising from this study will be owned by the University of Leeds.

It is anticipated that the authorship of the final report and any publications arising from this study will include all members of the research team for the relevant study phase. All authors named on the report and publications will meet the recommendations specified by The International Committee of Medical Journal Editors (81). Any contributors who do not meet the specified criteria will not be named as authors but will be acknowledged. Professional writers will not be involved in writing the final study report.

The dissemination and reporting plans for this study will be finalised with the Project Advisory Group and are anticipated to include:

- Provision of plain English summaries for participants
- Presentation(s) to the NIHR Leeds Biomedical Research Centre Patient and Public Involvement group
- Publication in a peer-reviewed journal(s)
- Presentation at a professional conference(s)
- Sharing with professionals, patients and the public through social media
- Reporting of the study in the CI's PhD thesis

The Patient and Public Involvement representatives who are members of the Project Advisory Group will be involved in a presentation to the NIHR Leeds Biomedical Research

Centre Patient and Public Involvement group and in reviewing the plain English summaries for participants.

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17. Appendices

17.1. Appendix 1 – Patient Documents

- Phase 2 Invitation Letter
- Phase 2 Magazine Advert
- Phase 2 Twitter Advert
- Phase 2 Facebook Advert
- Phase 2 Contact Form
- Phase 2 Participant Information Sheet
- Phase 2 eConsent Form and Questionnaire
- Phase 2 Topic Guide
- Phase 4 Invitation Letter
- Phase 4 Magazine Advert
- Phase 4 Twitter Advert
- Phase 4 Facebook Advert
- Phase 4 Community Advert
- Phase 4 Contact Form
- Phase 4 Participant Information Sheet
- Phase 4 eConsent Form and Questionnaire
- Phase 4 Topic Guide

17.2. Appendix 2 – Project Advisory Group Terms of Reference

Aim

To provide oversight of the research project **Development of a Virtual Knee School** to help make sure:

- The safety and rights of everyone involved/taking part in the research are protected
- The research is valid and credible

Roles

- Offer advice on the research design, management and commitment that is being asked of everyone involved/taking part in the research
- Monitor the progress of the research
- Help identify, and suggest solutions for, any issues or concerns that arise during the research
- Review any relevant new information that arises from other sources during the course of the research
- Define success criteria for the research
- Agree dissemination plans for the research and assist with implementing these where appropriate
- Support Anna Anderson with achieving the aims of her PhD

Meetings

- Meetings will take place approximately every 6 months throughout the 3 year research project (01/06/19 – 31/05/22)
- Meetings will be held at the NIHR Leeds Biomedical Research Centre and/or online and last approximately 1.5 hours

Members

- Independent chair (NHS Digital)
- PhD student
- Three University of Leeds supervisors
- Three Patient and Public Involvement representatives
- Key collaborator (West Yorkshire Association of Acute Trusts)