A Clinical Investigation of an Autonomous Phone Conversational Agent for Cataract Surgery Follow-up

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A clinical investigation of an autonomous phone conversational agent for cataract surgery follow-up

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Sponsor	Imperial College London
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1 STUDY INFORMATION

1.1 Full/Long Title of the Study

A clinical investigation of an autonomous phone conversational agent for cataract surgery follow-up

1.2 Short Study Title

Autonomous telephone follow-up after cataract surgery

1.3 Protocol Version Number(s) and Date(s)

.0	Initial draft	10 November 2020
.1	Pre-IRAS format submission draft	19 January 2021
.2	Updated to reflect feedback from trial team	2 February 2021
.3	Revisions from joint call with trial team	22 February 2021
.4	Minor revisions	23 February 2021
.5	Minor revisions	30 March 2021
.6	Sponsor feedback revisions	27 April 2021
.7	Minor revisions	14 May 2021
1.0	Submission version	17 May 2021

1.4 Research Reference Numbers

IRAS Number:	297548
SPONSORS Number:	21WE6780
NIHR Award Number:	AI_AWARD01852

2 SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's procedures, and other regulatory requirements.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:		
Signature:		Date: ...../...../.....
Name (please print):		
Position:		
Chief Investigator:		
Signature:		Date: ...../...../.....
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3 KEY STUDY CONTACTS

Table 1. Key Study Contacts

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4 ABBREVIATIONS AND KEY TERMS

Table 2. Abbreviations

Abbreviation / Key Term	**Full Phrase / Definition**
AHSN	Academic Health Science Network
AI	Artificial Intelligence
BRC	Biomedical Research Centre
CONSORT	Consolidated Standards of Reporting Trials
DPA 2018	Data Protection Act 2018
EHR	Electronic Health Record
FAQ	Frequently Asked Question
GDPR	General Data Protection Regulation
GIRFT	Getting It Right First Time programme
ICORG	Imperial College Ophthalmology Research Group
Imperial	Imperial College Healthcare NHS Trust
NASSS	Non-adoption, Abandonment, Scale-up, Spread, and Sustainability framework
NHS	National Health Service
NOD	National Ophthalmology Database
NPS	Net Promoter Score
Oxford	Oxford University Hospitals NHS Foundation Trust
PERC	Patient Experience Research Centre
PPI	Patient and Public Involvement
SPIRIT-AI	Standard Protocol Items: Recommendations for Interventional Trials - Artificial Intelligence
SUS	System Usability Scale
TUQ	Telehealth Usability Questionnaire
Ufonia	Ufonia Limited (Company Number: 10692039)

5 STUDY SUMMARY

Table 3. Study Summary

Study Title	A clinical investigation of an autonomous phone conversational agent for cataract surgery follow-up
Short title	Autonomous telephone follow-up after cataract surgery
Study Design	The study will be a multi-centre, mixed-methods clinical investigation to develop evidence regarding the feasibility, acceptability and potential effectiveness of **DORA**.
Study Participants	The study will include adults (aged 18 years or older) who are on the waiting list for either their first or second eye cataract surgery at Oxford or Imperial. To be eligible, the patients must have no history of significant ocular comorbidities and have a routine surgery with no intraoperative complications.
Planned Size of Sample	The planned sample size is 591 patients, split mostly equally between Oxford and Imperial clinical sites (see Table 1 for details on how this estimate was produced).
Follow up duration	Imperial: patients will receive the standard face-to-face appointment within a few days of having the autonomous call (dependent on current Covid-19 restrictions). Oxford: there will be no face-to-face follow-up for patients at the Oxford site as this is the standard of care. At both sites, an additional 3-month follow-up period where unplanned eye-related clinical visits will be recorded and assessed.
Planned Study Period	The total duration of the study will take up to 3 years, including the recruitment of patients, intervention refinement period, main intervention period, and analysis of results.
Research Question/Aim(s)	The aim of the study is to assess the evidence for the safety of using **DORA** to deliver autonomous cataract surgery follow-up assessments. This ability will be evaluated in comparison to an expert human clinician to assess the research question: Can **DORA** identify which patients need clinical follow up after a cataract operation?

5.1 Funding and Support in Kind

Table 4. Funding Information

FUNDER	FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN
National Institute for Health Research (NIHR) Dr Aayesha Hassan	£503,524.00

Programme Management Office Grange House 15 Church Street Twickenham TW1 3NL aayesha.hassan@nihr.ac.uk	

5.2 Role of Study Sponsor and Funder

This study is funded by an NIHR Artificial Intelligence in Health and Care Award granted to Ufonia. Ufonia distributes on behalf of NIHR funding to Imperial College London, the University of Plymouth and the University of Oxford for this study execution. This funding arrangement is governed by a consortium agreement which defines Imperial College London as being responsible for the study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results in collaboration with the academic consortium including the University of Plymouth and the University of Oxford. Whilst Ufonia has contributed and reviewed the study design and will support the trial in providing technology support, the academic collaboration, led by Imperial College London, is solely responsible for the study execution and dissemination of results to assure an independent assessment of Ufonia's technology. The academic consortium maintains a free and independent unrestricted right of publication of the study's findings as to avoid any conflict of interest.

5.3 Roles and Responsibilities of Study Management Committees/Groups and Individuals

A study steering board composed of the Chief Investigator, Principal Investigators, Co-Investigator, a member of the public, Ufonia's CEO, Ufonia's Medical Director and an external researcher (from the study) will meet every two months to review progress against the protocol to provide study governance and oversight. Reports shall be distributed for review by the study team for action.

Ufonia will appoint a Patient and Public Involvement (PPI) committee. With input from the Imperial College Patient Experience Research Centre (PERC), the Oxford University Academic Health Science Network (AHSN) and based on NIHR Involve guidance, a term of reference, confidentiality agreement and a background assessment form to Ufonia to structure the aims of the PPI group. Membership of this Ufonia PPI group is voluntary but requires members to be committed to attend meetings and to respond to emails/correspondence. The initial term of membership is for the duration of the study from early in the preparation phase (March 2021). Further details about PPI are included in the study protocol (see section 9.4).

5.4 Protocol Contributors

The sponsor, **Imperial College London**, controls the final decision regarding any aspect of the study.

Dr Eduardo Normando: Dr Normando defined clinical methods for the study. He will oversee the clinical investigation and lead the clinical delivery of the study at Imperial.

Dr Edward Meinert: Dr Meinert oversaw the drafting of the study protocol and coordinated revisions. He will lead the mixed-methods evaluation and the preparation of study findings for dissemination.

Dr Kanmin Xue: Dr Xue defined clinical methods for the study. He will lead the clinical delivery of the study at Oxford.

Dr Ernest Lim: Dr Lim contributed to drafting and revising the study protocol and facilitated patient review and feedback.

Dr Aisling Higham: Dr Higham contributed to drafting and revising the study protocol.

Ms Madison Milne-Ives: Ms Milne-Ives contributed to drafting and revising the study protocol.

Dr Guy Mole: Dr Mole contributed to drafting and revising the study protocol. Dr Mole is the Medical Director of Ufonia and assures compliance with company clinical protocols.

Dr Nick de Pennington: Dr Pennington conceived of the study topic, contributed to the study design and is the NIHR grant holder on behalf of Ufonia in his role as Chief Executive Officer.

5.5 Keywords

Artificial Intelligence (MeSH), Natural Language Processing (MeSH), Telemedicine (MeSH), Cataract (MeSH), Aftercare (MeSH), Speech Recognition Software (MeSH)

6 STUDY FLOW CHART

Patients receiving usual care for cataract surgery typically progress through four stages. Participants in this study will undergo two additional stages that are specific to the study (stages 4 and 6). There are six stages that participants of the study will potentially go through. These stages, and their approximate timeline, are visualised in the flow diagram below (Figure 1).

1. Stage 1. The patient is referred by a clinician for cataract surgery.
2. Stage 2. The patient's suitability for surgery is determined at a pre-assessment appointment or a one-stop cataract clinic. Patients who meet the eligibility criteria for the study at this stage will be provided with a participant information sheet (see 13.1 Appendix 1) and, if they are willing to participate, informed consent will be collected (see 13.2 Appendix 2).
3. Stage 3. The patient undergoes their scheduled cataract surgery. If the surgery was uncomplicated, a patient may also consent to participate in the study in the recovery lounge.
4. Stage 4. If the patient is consented to participate in the study, they will receive a follow-up call from **DORA** (supervised by a clinician). The call script used by **DORA** will be reviewed by supervising PIs in advance in order to reduce incidence of non-compliance through misunderstanding.
5. Stage 5. If the patient had the surgery at Imperial, regardless of whether or not they are participating in the study, they will have a scheduled follow-up with a clinician.
6. Stage 6. If the patient consented to participate in the study, they may be randomly selected to participate in a semi-structured interview, to provide more in-depth feedback about their experience using **DORA**.

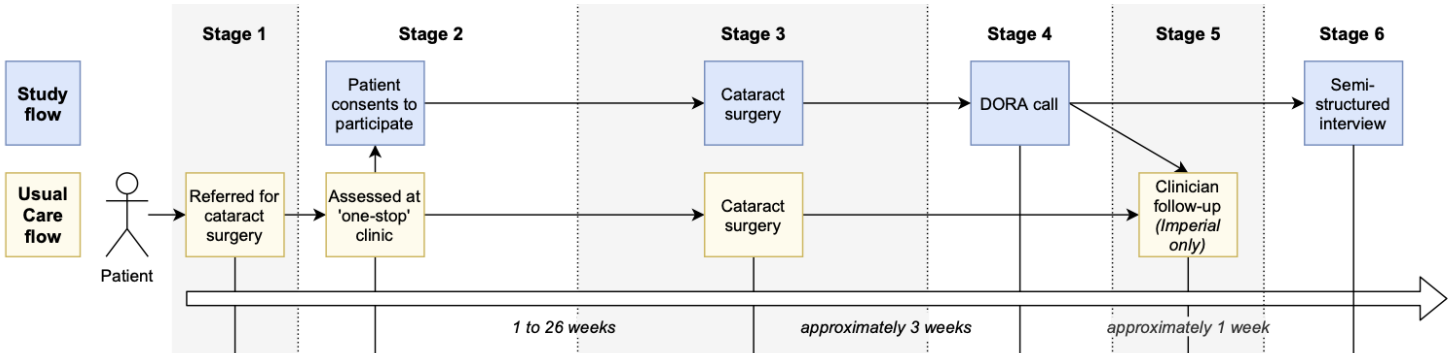

Figure 1. Participant flow diagram

The patient flow described above reflects the delivery stage of the study (see Figure 2). Before delivery begins, the first part of the study will be dedicated to obtaining the necessary ethical approvals, NHS contracts, and technical capabilities to deliver the intervention. These steps are captured in the project management, technical, and evaluation work packages (see WPs 1, 2, and 4 in Figure 2). Participant recruitment will begin approximately one month before data collection, with Imperial starting recruitment and delivery two months before Oxford (see WPs 3a and 3b in Figure 2). Prior to the main intervention period, a 4-week intervention refinement period will be conducted to identify any issues and make adjustments to the intervention execution. The final six months of the study will see the completion of data collection and will focus on conducting the evaluation, and reporting results for publication (see WPs 1, 4, and 5 in Figure 2).

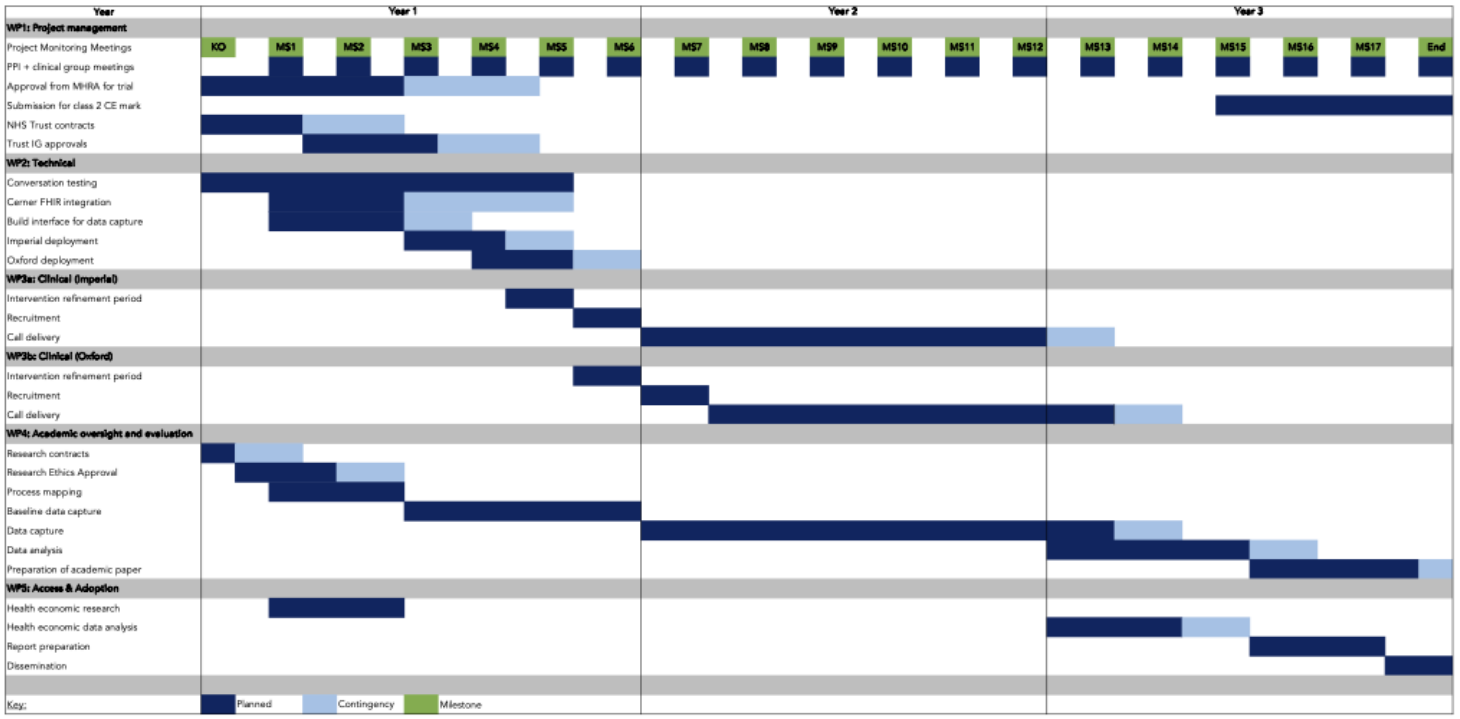

Figure 2. High-level study gantt chart

7 INTRODUCTION

7.1 Background

The UK's ageing population is causing an increased demand for healthcare services that is exceeding clinical capacity [1]. Demand has been further exacerbated by the Covid-19 pandemic, as the widespread cancellation of elective care has created a large backlog of clinical work [2]. However, a large proportion of this clinical work is taken up by highly repetitive and low skill tasks. Therefore, there is a need to improve efficiency in the delivery of care, and to collect data that can be analysed to support routine improvement and optimisation, through the automation of routine clinical interactions.

One area of care where improved efficiency is urgently needed is cataract surgery. Cataract surgery is already the most common operation in the NHS, with approximately 450,000 procedures conducted per year [3]. Covid-19 has caused record delays in receiving planned surgeries [4], and average wait times for cataract surgery were already approximately 2.5 months [5]. The ageing population will also have a significant impact on the number of patients with cataracts, which is expected to double between now and 2050 [6]. The cataract pathway is also an ideal case for optimisation because there is little variability and high levels of patient safety; the most significant postoperative complication (endophthalmitis) occurs in fewer than 1 in 1,000 cases [7]. To address this clinical need, an innovative solution is required.

7.2 Rationale

Like most operations, cataract surgery requires a post-operative check to monitor for complications and assess success. This has historically been performed with a face-to-face visit; prior to the Covid-19 pandemic, this was standard procedure for 72% of NHS Trusts [8]. However, this post-operative system has a high operational demand and is not always necessary; a recent ophthalmology Getting It Right First Time (GIRFT) report stated that a hospital review of cataract surgery patients is not required, if alternative follow-up arrangements are in place [8]. In the current context of the Covid-19 pandemic, face-to-face visits also pose a high risk for virus transmission due to the proximity of patient and clinician. This is reflected in the latest guidance from GIRFT and the Royal College of Ophthalmologists on restarting cataract surgery during the pandemic which recommends that patients should not be followed up in hospital after routine uncomplicated cataract surgery and should instead receive a telephone consultation or review with their local optometrist [9].

The solution developed to improve clinical efficiency for cataract surgery follow-up is a natural language, voice telemedicine conversation delivered to patients via telephone call (**DORA**, Ufonia). Since Ufonia's conception in 2016, several grants and partnerships have supported **DORA's** development and pilot testing at Buckinghamshire Healthcare NHS Trust (BHT), Department of Ophthalmology. For the patient, this is intended to be no different than a regular telemedicine consultation with a doctor or nurse; it does not require the download of an app, the provision of a device, or any training. This is important because the populations that consume the majority of healthcare services (elderly and socio-economically disadvantaged) tend to be relatively more digitally disenfranchised [10].

The solution potentially has several benefits for patients and healthcare staff, which will be evaluated in the study [11]. For patients, **DORA** will provide a reliable, consistent safety-net after surgery. Patients will be able to ask questions about their recovery from the convenience of home. Reducing the number of in-person follow-ups will also benefit clinicians by enabling them to spend their time on higher-value clinical activities, making patients more likely to receive timely care for their initial

cataract surgery or for other conditions. In addition, telephone follow-up reduces the risk of Covid-19 transmission and frees up hospital space to help meet the increasing patient demand. Whilst this study focuses on cataract surgery follow-up, the underlying platform will be applicable to a wide range of routine clinical tasks. The need for an effective automated tool is especially great as a 'new normal' of widespread remote clinical care is established in the wake of Covid-19.

7.3 Theoretical Frameworks

Two complementary frameworks were used to support the conception and development of the study plan by ensuring that a holistic set of variables were included in the evaluation [12,13]. Several quantitative analyses will be conducted to achieve the study's objectives; including comparing the agreement of **DORA's** and the supervising clinician's decisions and using validated questionnaires to evaluate **DORA's** usability [14,15]. Qualitative analysis will be completed by semi-structured interviews with a subset of users structured according to the Theoretical Framework of Acceptability [16]. The use of both quantitative and qualitative methods to evaluate usability will enable the data to be triangulated.

These three frameworks and two scales will form the theoretical basis for the evaluation of **DORA**:

1. Assessment of Health Information Technology Interventions in Evidence-Based Medicine Evaluation Framework [12]. This framework was chosen to help structure the study evaluation because it includes a holistic set of outcomes, including safety, privacy, appropriateness, and cost-effectiveness.
2. Long-term adoption and suitability to further trials will be evaluated using the Non-Adoption, Abandonment and Challenges to the Scale-up, Spread and Suitability (NASSS) framework [13]. This framework is important to include because interventions can only add value if they are successfully adopted and used. This framework emphasises the consideration of the multiple levels - individuals and systems - that influence adoption and non-adoption.
3. The Theoretical Framework of Acceptability (TFA) will be used to structure the semi-structured interview guide [16]. This framework was chosen because it was developed specifically for health interventions, captures a multi-faceted view of acceptability (with seven components), and emphasises the importance of considering different time points when evaluating acceptability [16].
4. The System Usability Scale (SUS) [14]. The SUS is one of the most widely-adopted measures of usability and is still recommended for use after several decades of use [17].
5. The Telehealth Usability Questionnaire (TUQ) [15]. In addition to the SUS, the TUQ will be used in the study because it was developed recently and focuses specifically on modern telehealth interactions. It has been demonstrated to be a reliable measure of the quality of telehealth technologies.

7.4 Research Question

DORA was developed to provide an alternative for conducting post-cataract surgery follow up assessments to save nurses' and other clinicians' time. The key outcome of this study is evaluating **DORA's** ability to accurately identify which patients have postoperative complications which would justify specialist care, and assessing **DORA's** accuracy compared to an expert clinician. To assess this critical capability, the research question that this study will investigate is: Can **DORA** identify which patients need clinical follow up after a cataract operation?

7.5 Aims and Objectives

The purpose of this clinical investigation is to evaluate the safety, usability, acceptability, efficacy, and cost-effectiveness of Ufonia's autonomous cataract follow-up call system (**DORA**) at detecting patients that require further assessment. The aim is to establish preliminary safety evidence by examining the level of agreement between **DORA** and the supervising clinician on symptom and overall management plan decisions. Therefore, the focus will be on patients undergoing routine surgery. In order to achieve these aims, there are several objectives (see Figure 3):

1. To evaluate the level of agreement between **DORA** and an expert human clinician and identify any factors that affect that level of agreement;
2. To establish baseline rates of sensitivity and specificity for **DORA's** detection of patients that have postoperative complications;
3. To evaluate **DORA's** feasibility; i.e. whether **DORA** can engage with patients enough to produce sufficient data to perform an accurate assessment;
4. To evaluate the usability of an autonomous call, in comparison with existing standards of care, explore patient perceptions about whether **DORA** is acceptable, appropriate, satisfactory and evaluate cost-effectiveness of autonomous calls in comparison with existing standards of care.

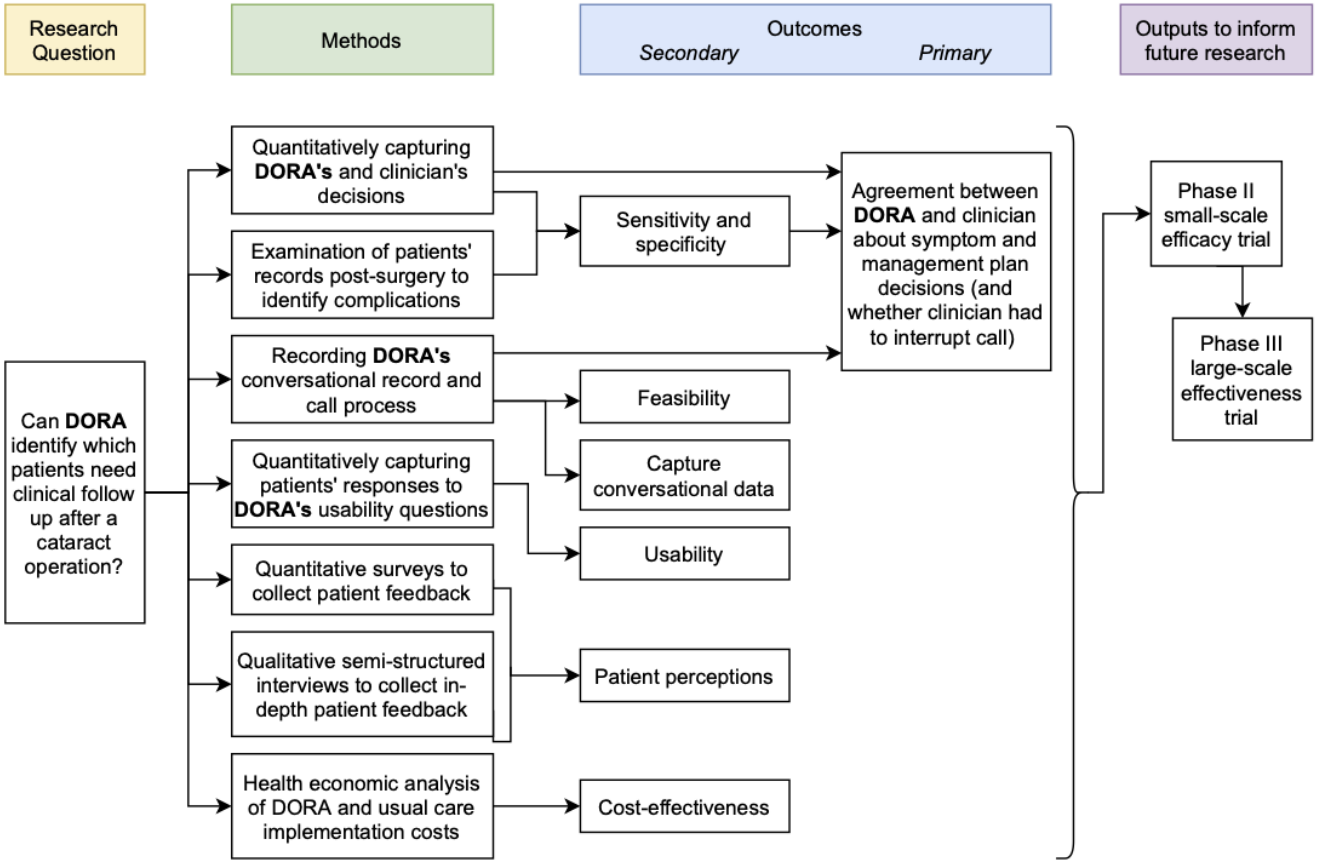

Figure 3. Logic diagram of the study

8 METHODS

8.1 Trial Design

Using an implementation science construct, the study will use mixed methods. Quantitative methods will be examining the inter-rater reliability between **DORA** and the supervising clinician for assessments of symptoms and management plan decisions. Usability will also be assessed using validated, quantitative questionnaires. Qualitative methods using semi-structured interviewing will also assess **DORA's** usability, acceptability, satisfactoriness, and appropriateness to collect more in-depth feedback and explore **DORA's** strengths and weaknesses. The development of the protocol incorporated the guidelines from the SPIRIT-AI checklists (see 13.3 Appendix 3) [18]. Public Health England's guidance summaries for evaluation in health and well-being were also consulted when developing the protocol [19].

The study will last up to three years: the first year will be focused on evaluation and intervention refinement, including a 4-week trial of the intervention execution to identify any adjustments needed; this will be followed by the study implementation and follow-up; and the last several months will be dedicated to post-evaluation analysis and write-up.

8.1.1 Timeline

The study may last up to three years with **DORA** calls taking place over a six- to twelve-month period at both clinical sites to enable sufficient flexibility to meet the recruitment targets. Recruitment will begin approximately one month before the start of call delivery at both sites, but the start dates for the two sites may be staggered. Call delivery will last for approximately a year after recruitment. For both sites, recruitment will stop approximately 6 weeks prior to the end of the call delivery period. This timeline assumes return to elective surgery; any changes due to COVID-19 will require amendment. The overall study timeline is summarised in Figure 4.

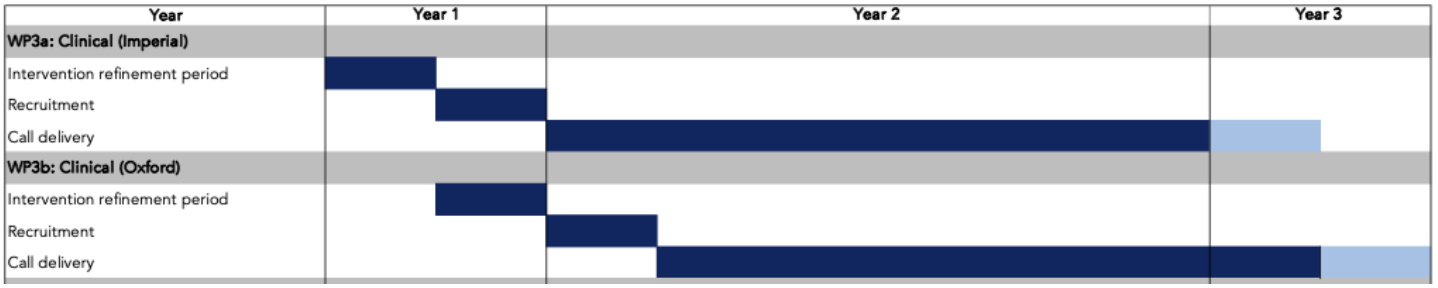

Figure 4. Overall call delivery timeline

8.2 Study Context

8.2.1 Participants

Patients who are listed for routine cataract surgery at either Imperial or Oxford NHS Trusts are eligible for this study.

8.2.2 Setting

This is a multi-centre study incorporating two NHS academic teaching hospitals - Imperial College Healthcare NHS Trust and Oxford University Hospitals NHS trust.

The management of the intervention (**DORA**) is accessible through any web-browser and investigators will be provided with secure log in.

8.2.3 Intervention(s)

DORA uses a variety of AI technologies to deliver the patient follow-up call, including: speech transcription, natural language understanding, a machine-learning conversation model to enable contextual conversations, and speech generation. Together, these technologies cover the input, processing and analysis, and output needed to maintain a natural conversation. **DORA** is configured to deliver calls through a telephone connection as a real-time, stand-alone system: the operator inputs individual patient details to initiate the call and completes a summary in the electronic health record (EHR) afterwards. The call that patients will receive from **DORA** will include several conversational elements:

- Greeting and introduction
- Identification of patient
- Cataract follow-up questions
- Patient's queries
- (Decision)
- Questions about acceptability
- Closure of call

The entire conversation will be supervised by a clinician. This clinician will be able to interrupt the call at any point if the system fails, the patient struggles to interact with it, or **DORA** does not collect sufficient information from the patient. The call will proceed in the following stages (visualised in Figure 5):

1. Stage 1. Call initiation: the supervising clinician will confirm the suitability of the patient, input their details, and initiate the call.
2. Stage 2. Symptom assessment: Once the call has begun, **DORA** will verify the identity of the patient and proceed through the cataract follow-up questions. As the patient answers the questions, both **DORA** and the supervising clinician will record their independent assessment about the clinical significance of the symptoms elicited.
3. Stage 3. Management plan decision: Once all of the follow-up questions have been asked, **DORA** and the supervising clinician will independently make and record their decisions about the management plan for the patient. **DORA** will then inform the patient of the clinician's decision about their management plan (i.e. whether specialist review is required or not).
    - Stage 3a: Optionally, if required, the supervising clinician can ask additional clarifying questions.

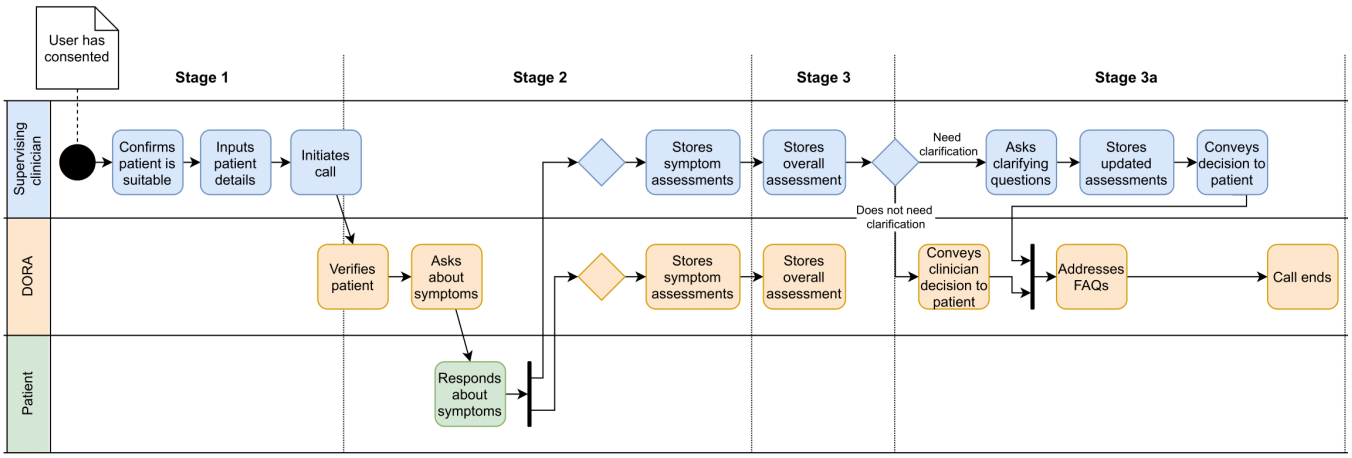

Figure 5. Flow Diagram of **DORA's** call with patient

8.2.4 Comparator(s)

Imperial sees all of their post-operative cataract patients at a face-to-face out-patient appointment with an ophthalmologist or specialist nurse. This is conducted between three to four weeks following the procedure. Therefore, patients at Imperial will receive their call from **DORA** within 3 days before their scheduled appointment (day 25-27 post-surgery). This will enable the results of the **DORA** call to be compared with the face-to-face appointment at Imperial to assess whether any complications were correctly identified and if the management plan remains the same.

For patients at both clinical sites, health records will be examined 90 days after the call to determine if the patient presented to an eye clinic with any complications from surgery. This comparison of the follow-up with actual complication rate will enable an assessment of **DORA's** safety (see Table 6).

8.2.5 Outcomes

8.2.5.1 Primary Outcomes

Agreement

The primary outcome of the study is to establish preliminary safety evidence by evaluating the level of agreement between **DORA** and the expert human clinician on symptom and overall management plan decisions.

To evaluate agreement, **DORA's** ability to classify five key symptoms from the conversation will be compared with a supervising clinician's classification of the same five symptoms: redness, pain, reduced vision, flashing lights, and floaters (see Table 5). For this study, the supervising clinician's decision - made based on the information from the call with **DORA's** decision masked - is considered the gold-standard for evaluation. Both **DORA** and the supervising clinician (masked to each other) will independently indicate for each symptom, whether the symptom is:

1. Absent (e.g. no pain)
2. Present but not clinically significant (e.g. mild gritty sensation)
3. Present and clinically significant (e.g. deep and persistent pain)
4. Insufficient information for classification

The agreement between **DORA** and the clinician on the patient's management plan will be evaluated in the same way as the symptoms. **DORA** and the clinician will independently select one of the following options for the patient's management plan:

1. Passes check (patient continues to next step of their care as planned, e.g., Discharge from hospital care, add to waiting list for second eye surgery, or continue routine follow-up in clinic for another ophthalmic condition)
2. Needs clinical assessment relating to the cataract surgery

Ability to gather sufficient information

To evaluate **DORA's** ability to gather enough information for a clinician to decide a patient's management plan and the necessity for the clinician to ask clarifying questions will be assessed. If clarifying points are necessary for the clinician to make a decision, the clinician will ask the necessary questions, and then document updated assessments for symptoms and overall management (see Figure 5). Either 12 or 18 data points will be collected from each call depending on if clarifying questions are asked.

- Every Conversation

    - 5 symptom decisions from **DORA** + 1 clinical decision from **DORA**
    - 5 symptom decisions from Clinician + 1 management plan from Clinician
- If clarifying questions asked
    - Post-clarification 5 symptom decisions from Clinician + 1 management plan from Clinician

This will allow us to test the hypothesis that clarifying questions affect the clinical management plans (see Table 5).

Table 5. Primary Outcome Measurement

Primary Outcome	Outcome Measure
Agreement	● Whether or not the clinician had to interrupt the call to ask clarifying questions ● Inter-rater reliability: the degree of agreement between **DORA** and the clinician on their assessments of the individual symptoms and the management plan

8.2.5.2 Secondary Outcomes

There will be several secondary outcome measures to assess the clinical safety, feasibility, usability, and acceptability of the system (see Table 6).

Clinical safety

To examine safety, two outcomes will be captured. Firstly, patients at both sites will have a retrospective case review of both general and ophthalmic electronic health records at 90 days after their initial operation. Complications will be identified from patient's medical records related to any unplanned eye-related clinical episode.

Secondly, all cataract surgery patients at Imperial were historically followed up face-to-face between 3-4 weeks post-surgery in a dedicated post-op clinic. Any complications requiring a change in patient management at slit lamp review or from attending eye casualty services (as the Oxford site does not normally perform face-to-face follow-ups) will be compared with the decisions made by **DORA** and the clinician. If Imperial changes their method of follow-up due to the COVID-19, assessment for complications will be done by checking hospital medical records as is done at the Oxford site.

Feasibility

Feasibility will be assessed by examining the proportion of autonomous calls that were completed without needing any intervention from the supervising clinician. All interruptions or clarifying questions of the supervised call will be logged; the supervising clinician will be asked to log the reason for asking clarifying questions. If clarifying questions were asked because the clinician felt that there was insufficient information for either individual symptoms or to make a management plan, the clinician's management plan before and after clarifying questions will be captured to see if clarifying questions changed the management plan.

Usability

Usability will be assessed using questions presented to patients following calls delivered by online and paper surveys distributed to participants. These questions will be drawn from the System

Usability Scale (SUS) and Telehealth Usability Questionnaire (TUQ; see 13.4 Appendix 4 for a sample survey) [14,15].

Acceptability, satisfaction, and appropriateness

DORA's acceptability, satisfactoriness, and appropriateness will be assessed during qualitative interviews with a subset of the patients. These semi-structured interviews will provide an opportunity for patients to provide more in-depth feedback about what they liked about **DORA** and any barriers to use that they experienced during the call (see 13.5 Appendix 5 for a sample topic guide). The supervising clinician will also be asked to provide feedback about their level of satisfaction with the system and any safety concerns they might have.

Patients' willingness to recommend **DORA** to others will also be assessed at the end of the call [20]. **DORA** will calculate a net promoter score (NPS) by asking patients "on a scale of 1 to 10, how likely would you be to recommend this automated service to a friend or colleague." **DORA** will follow up by asking patients to "tell me why you gave that score."

Cost-effectiveness

Cost-effectiveness will be examined by collecting and analysing health economic data before and during the study. The costs of implementing **DORA** will be compared with historical data about the costs of the usual standard of care.

Table 6. Secondary Outcome Measurement

Secondary Outcome	Outcome Measure
Clinical Safety	Complications identified from patients' electronic health records up to 90 days following cataract surgery
	Congruence between complications identified and management planned in **DORA** call and face-to-face follow up (Imperial) Comparison to data from patients attending eye casualty (Oxford)
Feasibility	Proportion of autonomous calls that were completed without needing any intervention from the supervising clinician
	Clinician-reported reasons for asking clarifying questions
Usability	System Usability Scale (SUS) [14,17]
	Telehealth Usability Questionnaire (TUQ) [15]
	Qualitative feedback from semi-structured interviews
Acceptability	Qualitative feedback from semi-structured interviews
Satisfaction	Qualitative feedback from semi-structured interviews, Net Promoter Score (NPS)
Appropriateness	Qualitative feedback from semi-structured interviews
Cost-effectiveness	Comparison of the costs of implementing **DORA** and the costs of the usual standard of care
Identify improvements	Synthesis of all of the outcome measures previously described

8.3 Sample and Recruitment

8.3.1 Eligibility Criteria

8.3.1.1 Inclusion Criteria

- Willing and able to provide informed consent;
- Aged 18 years or older;
- On the waiting list for routine cataract surgery. Cataract surgery as part of a combined procedure with other ocular surgery will not be included;
- No history or presence of significant ocular comorbidities that would be expected to alter the risks of cataract surgery or normal post-operative follow-up schedule. Note that significant ocular comorbidities do not include stable, chronic, or inactive ocular conditions such as amblyopia, drop-controlled stable glaucoma or ocular hypertension, previous squint surgery, inactive macular pathology, previous refractive surgery, or previous vitreoretinal surgery with stable retina.

8.3.1.2 Exclusion Criteria

- Individuals with any condition that could preclude the ability to comply with the study or follow-up procedures;
- Presence of ocular or systemic uncontrolled disease (unless deemed not clinically significant by the Investigator and Sponsor);
- Involved in current research related to this technology or been involved in related research to this technology prior to recruitment;
- Cognitive difficulties, hearing impairment or non-English speakers;
- History of current or severe, unstable or uncontrolled systemic disease (unless deemed not clinically significant by the Investigator and Sponsor).

8.3.1.3 Withdrawing

- Participants will be withdrawn from the study if complications were encountered during their cataract surgery and documented in their medical records. Complications of cataract surgery may include, but are not limited to, capsular tear/rupture, anterior vitrectomy, zonular dehiscence, sulcus intraocular lens implant, dropped lens fragments, other concurrent vitreoretinal procedure;
- Patients who have undergone unplanned clinical review (e.g. eye casualty attendance or any planned appointment as a result of deviation from normal intraoperative course, e.g. suture) or additional ocular procedure prior to the follow-up call will be withdrawn from the study.

8.3.2 Sampling

8.3.2.1 Sample Size

An audit of historical data was conducted for both Imperial and Oxford sites to provide evidence for an estimate of the study's sample size (see Appendices 7 and 8, respectively). All types of pre-assessment appointments throughout October 2020 were audited. October 2020 was used to project capacity in May-July 2021 on the assumption that recovery from this wave of the Covid-19 pandemic would follow a similar trajectory to recovery from the first wave. At Imperial, three consultant-led one-stop clinics are expected to be in place in July to mitigate surgery backlog.

Sample size calculations were based on estimates deriving from this audit. As outlined in Table 7, Imperial currently sees about 7 patients per week in their one-stop clinic and pre-assesses about another 64 per week, almost 90% of whom are listed for surgery. If 80% of the total patients seen are estimated to be eligible for the trial, approximately 230 patients could be recruited from this clinic over the course of the study period. At Oxford, about 60 new patients are seen for pre-assessment per week, with approximately another 20 phone assessments for second eye are also done, with 90% being listed for surgery. With an estimated 70% of patients consenting to participate, and an attrition rate of 15%, 591 patients are expected to be recruited over the course of 26 weeks. An *a priori* power calculation was conducted to determine the minimum sample size necessary to achieve a power greater than 0.8 for a 0.05 level of significance [21]. On the basis of a total population of 1014, a 95% confidence level, and a 3% margin of error, a sample size of 520 is required for statistical significance.

Table 7. Indicative recruitment targets with assumptions of dropout at each stage. Screening capacity is set at 2 days due to staffing constraints.

	Imperial	**Imperial**		**Oxford**	**Oxford**
	One-stop (Projected 3 clinics per week from 1/2021)	Pre-assessment (excluding one-stop)		Pre-assessment	Phone pre-assessment (2nd eye)
Current Numbers Assessed					
Mean Patients assessed per clinic	10	8		12	4
Clinics per week	3	8		5	5
Mean Patients Assessed per week	30	64		60	20
Eligibility Assumptions					
% proceeding to surgery	80%	90%		90%	90%
% routine cases	80%	80%		80%	80%
% eligible for trial	80%	80%		90%	90%
% ineligible due to complicated surgery	5%	5%		5%	5%
Screening					
Compound daily eligibility rate	49%	55%		62%	62%

Number of days screening	2	2		2	2
Patients screened per week	10	9		15	5
Estimated recruitment					
% consenting to trial	70%	70%		70%	70%
Estimated average recruited per week	7	6		10	3
Duration of trial (weeks)	26	26		26	26
Estimated % of patients dropping out	15%	15%		15%	15%
Estimated recruitment over trial	150	135		229	76
Site Total	286			305	
Total	591				

8.3.2.2 Sampling Technique

All patients who are willing and eligible will be included in the sample receiving the **DORA** call. Of this sample, a subset will be selected to participate in a semi-structured interview to collect qualitative data about patients' perceptions of **DORA** (see 13.5 Appendix 5).

To select this subset, a stratified random sampling technique will be used. Patients will be divided based on demographic characteristics (gender, age, socio-economic status, and ethnicity) and clinical location (Oxford or Imperial). From these subgroups, patients will be randomly selected so that the sample interviewed is representative of the UK population. For example, we will randomly select to ensure the subset of patients being interviewed is split equally by gender and clinical location.

8.3.3 Recruitment

8.3.3.1 Participant Identification

Recruitment will take place in the pre-assessment sites and post-operative discharge lounges at the Imperial College Healthcare and Oxford University Hospitals NHS Trusts that conduct cataract surgeries. Participants will be made aware of the study via leaflets and discussion with healthcare providers during their pre-assessment and, if they are eligible, will be invited to participate. Patients

in the discharge lounges who have undergone uncomplicated cataract surgery will also be invited to participate in the study. Screening will continue at both sites until the target enrolment is achieved.

8.3.3.2 Consent

Study information will be shared with cataract surgery patients at their initial visit (and via post or telephone call for patients who are delayed by Covid-19 or cannot visit in person). Informed consent will be obtained in written form or verbally at the time of pre-assessment, surgical listing (in-person or virtually depending on the current Covid-19 guidelines), or in the discharge lounge following surgery (see 13.2 Appendix 2). Patients who have consented to participate will be given further information while they are in the discharge lounge to remind them about the call from **DORA**. This work will be performed by a dedicated research nurse at each site.

8.3.4 Adherence

The **DORA** calls will be recorded and the study team will monitor the use of the technology and assure the system is being used within designed parameters during the study.

8.4 Data Collection

8.4.1 Randomisation

8.4.1.1 Sequence Generation

Demographic data will be collected from all patients in the surveys that will be distributed to assess **DORA's** usability after patients have completed the call (see 13.4 Appendix 4). A computer random number generator will then be used to randomly select patients for semi-structured interviews from within each demographic subset collected at post-call surveys.

8.4.1.2 Allocation Concealment Mechanism

A masked computer algorithm will be used to generate the subset of patients for interview and deliver the outcome to researchers at the time that they are assigning patients to be invited to interview.

8.4.1.3 Implementation

A computer will generate the random allocation sequence and assign participants to interventions. Healthcare professionals at the pre-assessment clinics will enrol participants in the study.

8.4.2 Blinding

No blinding of participants will be done in the study, as all eligible patients will receive the same intervention. The clinicians listening to the call will be blinded to **DORA's** decisions when they are making their own assessments.

8.4.3 Methods of Data Collection

8.4.3.1 Quantitative data collection

The key data to be collected are **DORA** and the clinician's decisions. This will include data on symptoms as well as an overall assessment. Both **DORA** and the clinician will separately record their decisions about symptoms, clinical assessment, and management plan. **DORA** will record the decisions in the **DORA** database, which will be accessed by the study team during the evaluation to compare against the clinician decisions. Usability of the system will be assessed using the SUS and

TUQ questionnaires (see 13.4 Appendix 4). These will be delivered to all participants shortly after they have had the call with **DORA** via an online or paper survey (see Figure 6).

8.4.3.2 Qualitative data collection

A subset of participants will also be invited to an interview, so that more in-depth, qualitative feedback can be collected about the user experience with **DORA** (see Figure 6). For the interviews, a semi-structured interview approach will be followed (see 13.5 Appendix 5 for a sample topic guide). If patients consent, the interviews will be audio recorded and professionally transcribed. If not, the interviewer will take notes, and provide the notes to the patient at the end of the interview for verification.

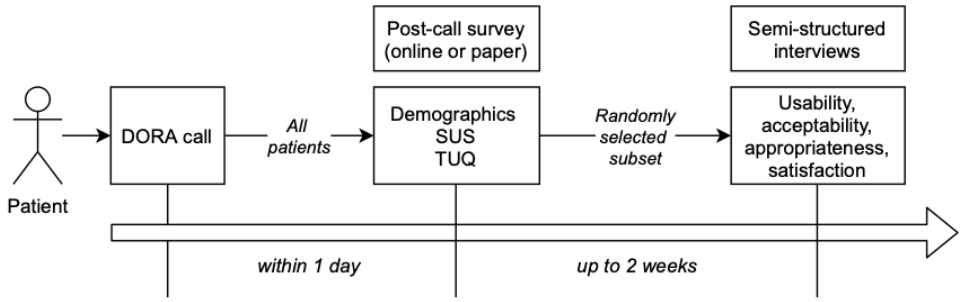

Figure 6. Patient data collection flow diagram

8.5 Data Analysis

8.5.1 Statistical Methods for Primary Outcome

The primary analysis will be the calculation of a kappa statistic of inter-observer (**DORA** & clinician) reliability of the decision made. Additionally, the outcome of the assessment will be compared with the 'real' complication rate determined by hospital medical records. This will be established by identification of any hospital presentation within 90-days after the last call. Given the specialist nature of ophthalmology services it can be assumed that patients will present through the eye casualty or clinic services offered by each site. Patients who present to the hospital eye service will be analysed on a case-by-case basis to ensure that complications that were missed by **DORA's** original assessment and complications that developed later can be differentiated. This analysis will provide baseline sensitivity and specificity data for use in preparing subsequent evaluations of efficacy.

8.5.2 Other Data Analyses

The usability and acceptability questions delivered to patients via online or paper surveys after the completion of the call will be analysed quantitatively based on the scales' scoring criteria - for instance, a score above 80 on the System Usability Scale is generally considered to indicate an above average user experience [17]. The semi-structured interview recordings will be transcribed and assessed using thematic analysis.

8.6 Limitations

There are a couple limitations with the protocol. First, the number of issues identified during routine follow-up at the two sites cannot be directly compared. Unlike Imperial, Oxford does not proactively review patients following uncomplicated cataract surgery, instead relying on patients to self-present to the eye casualty service. This introduces a potential risk for missed complications if **DORA** decides

that a clinical review is not needed. However, this risk is minimised by the safety net established by the expert clinician oversight of the call and is a part of the current standard of care at the Oxford NHS Trust. The limitation is also mitigated by the examination of patient records after 90 days to identify any complications that might have been missed.

The second limitation is related to generalisability. The evaluation will only include patients who had uncomplicated cataract surgeries. This focus on routine care is important for establishing the feasibility of **DORA**, but means that **DORA**'s effectiveness for dealing with post-operative follow-up of complex patient groups cannot be assessed in this study. The National Ophthalmology Database (NOD) audit report however shows that the most common complication of posterior capsule rupture occurs in only 1-2% of patients [3].

Technical limitations of the system also affect generalisability. At present, patients with cognitive difficulties, hearing impairment or non-English speakers are not able to use **DORA** and will not be included in the study. However, this reflects the same limitations as human telemedicine services.

Finally, potential bias is introduced to the results by the use of qualitative interviews because of the influence of the interviewer on how participants respond (e.g. social desirability bias). This potential bias will be assessed by examining the balance of positive and negative feedback and by comparing the qualitative and quantitative data about **DORA's** usability.

8.7 Generalisability

Limitations to the generalisability of the study results were noted in the previous section. However, it is expected that the results will be generalisable to the majority of cataract surgery patients. The vast majority of cataract surgeries are uncomplicated; only approximately 2.5% of cataract surgeries have intraoperative complications (which would have resulted in exclusion from this study) [3]. Therefore, if the results of this study are positive, they will demonstrate **DORA's** potential to manage almost all cataract surgery follow-up assessments.

9 ETHICAL AND REGULATORY CONSIDERATIONS

9.1 Assessment and Management of Risk

Risks will be monitored on a weekly basis via the project management process and mitigated by Risks/Actions/Issues/Decisions log.

The Covid-19 pandemic has raised potential issues for recruitment for the study. To address this risk, an ethics submission will enable remote informed consent if restrictions prohibit face-to-face contact.

Risks regarding the system include it failing to detect patients who require urgent clinical review - this will be mitigated by having a clinician supervise the call in real-time, able to intervene if needed. The risk of lack of trust in the system has been mitigated by an extensive co-creation process for **DORA** that focused on user-centred design.

The interviews are scheduled to take place for between 20 to 30 minutes in order to mitigate time risk to participants. The nature of interview questions avoid areas of cultural or psychological sensitivity and are purely focused on impact of the intervention. Since Brexit, the General Data Protection Regulation (GDPR) no longer applies to the UK; however, it has been incorporated in UK domestic law [22]. To control any potential perceived issues in this area, participant confidentiality will be protected using data protection procedures that are compliant with the Data Protection Act 2018 (DPA 2018) [23]. For more details about data protection and patient confidentiality plans for this study, see section 9.7.

9.2 Research Ethics Approval

Ethical approval is being sought from the Health Research Authority and the relevant Research Ethics Committee with this submission [24]. As the IRAS system brings together these assessments, only one application is needed [24]. The protocol will therefore receive medical device review from the associated REC.

HRA approval is the ethical approval route used for studies with NHS patients at both Imperial College London and the University of Oxford [25,26]; additional independent ethical approval will be sought from the University of Plymouth. At the University of Plymouth, an application for ethical approval will be submitted through the Plymouth Ethics Online System (PEOS) to the Health Faculty Research Ethics and Integrity Committees (FREIC) [27].

Imperial College London, as the study sponsor, will ensure that the study has received ethics approval from a research ethics committee (REC) and has received Health Research Authority (HRA) approval.

9.3 Peer Review

The study will undergo peer review at Imperial College London, where the Peer Review Office (PRO) commissions proportionate, independent peer reviews and confirms that the reviews have been done correctly [28]. The University of Oxford does not require a separate review outside what is completed by the HRA approval process [29]. An independent peer review will be conducted by the University of Plymouth.

9.4 Patient and Public Involvement

The Oxford University AHSN and Imperial College London have robust PPI support infrastructures to ensure we are able to have the necessary support in place to establish our PPI framework for the research study. Partnerships with both of these institutions will ensure we align our PPI practices as we move through the research cycle.

At Oxford, PPI will be coordinated by Dr. Sian Rees who is the director of Patient and Public Involvement at the Oxford AHSN to better understand how to incorporate best-practices into our co-production processes.

At Imperial, the Imperial College Ophthalmology Research Group (ICORG) has close ties to the NIHR Biomedical Research Centre (BRC) Patient Experience Research Centre (PERC). Serge Miodragovic, the clinical research manager at ICORG will advise on the use of Imperial's PPI framework and the PERC will be used to structure the public engagement strategy. Furthermore, the Western Eye Hospital already has an established PPI reference group to advise and feedback on the clinical aspects of the service, these are a group of expert patients who have an interest in ophthalmic conditions and a source of potential representatives to join the study monitoring and PPI groups.

9.4.1 Involving a lay representative on the study monitoring group

A lay representative will be appointed to the study monitoring group, additional the patient representative will be invited to key strategic and public meetings. The lay representative will be involved in all aspects of the study, specifically, these include, but are not restricted to review of each milestone and acceptance of deliverables - seeking their views around acceptability of patient-facing materials, study procedures. and plans for translation to clinical practice.

9.4.2 Involving a dedicated PPI group

The broad aims of the PPI group are to support the governance of patient and public involvement and engagement approaches and activities within this study and ensure the public voice is present through all stages of the research cycle. Membership of the PPI group will be open to those both with a direct interest in telemedicine or eye health, but also any lay member with an interest in our broader aims. We will include patients and lay members both with and without previous experience of PPI to make sure we have a variation of skills and expertise.

With input from the Imperial College PERC, we have drafted, based on NIHR Involve guidance, a term of reference, confidentiality agreement and a background assessment form to allow us to realise the broad aims of our PPI group. Membership of this Ufonia PPI group is voluntary but requires members to be committed to attend meetings and to respond to emails/correspondence. The initial term of membership is for the duration of the study from early in the preparation phase (October 2020). We aim to have a minimum of four formal members at the inception of the panel and each subsequent meeting with representation from both London and Oxfordshire. We will seek to make participation as diverse as possible by selecting members based on 1) demographics 2) levels of PPI experience and 3) connection to telemedicine or eye health based on the results of our basic background form. In particular, we are aware that we have to ensure Ufonia's product is as accessible to as wide a range of possible demographics as possible, and the first phases of setting up our PPI group will involve a wide search using networks from both Oxford and Imperial AHSN but also through INVOLVE's "People in Research" platforms. Given that this is a cohort who are elderly with potential forms of disability, we are aware that additional resources may be required to cover the costs of translators or communication support, or equipment and training to enable participation in telecommunication.

The panel will aim to convene every four months for a 90 minute formal group discussion, given the evolving COVID situation, we anticipate at least some of these group discussions to be conducted via video-conferencing, with more informal discussions happening via email or phone-calls. As the study spans two sites, we envision using teleconferencing to help enable maximal participation of our participants and to lower the barriers to involvement. At both sites, a dedicated location for teleconferencing will be designated to ensure we are not excluding participants less comfortable with or less willing to use technology.

We anticipate that we will be having an ongoing dialogue with study participants both formally in the afore-described evaluation phase, and informally via ongoing feedback. As such, we anticipate that new members may be recruited to the PPI group if there are gaps in experience. The panel may choose to invite other patients/members of the public involved; other university members and/or representatives of voluntary or community organisations such as the Royal National Society of the Blind (RNIB) on a one/off or long term basis. Observers, guests and presenters may also be invited on a one/off basis.

The meetings will be co-chaired by a lay chairperson who is nominated by all attendees of the meeting, and a professional chairperson will be a senior Ufonia team member who has received formal experience in chairing PPI meetings. We have drafted a “role” specification with Imperial PERC of a chairperson which may be a different individual between meetings depending on topics of discussion.

Payments will be made in recognition of members’ time based on NIHR Involve guidance on payment of fees and expenses for our members actively involved [30]. Travel expenses will be reimbursed in accordance with this policy together with other expenses and travel costs. We have budgeted based on suggested reimbursement schedules and have produced our estimates following use of the Involvement Cost Calculator.

9.5 Protocol Compliance

Bi-monthly study governance meetings will be held, alternating between monitoring and clinical reference group sessions. Monitoring meetings will include all study partners and NIHR/NHS representatives, and patient representatives. They will review progress against the study plan and budget, sign-off study deliverables and update the project’s risk register. Clinical reference group meetings will include senior representatives from both clinical sites who will provide oversight of progress, approval for go-live and ongoing monitoring of delivery. A group of external academics will be appointed as a trial monitoring committee who will also perform audits to ensure compliance to procedures.

Planned deviations or waivers to the protocol are not allowed under the UK regulations on Clinical Trials and will not be used. Any accidental protocol deviations will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately should they happen. Immediate action will be taken towards any deviations to avoid serious breach. The Sponsor will be notified immediately should there be a serious breach of the safety or physical or mental integrity of the participants of the trial or the scientific value of the trial. The Sponsor will notify the licensing authority in writing of any serious breach.

9.6 Consent

BERA guidelines have been followed for voluntary informed consent, use of methods, and university policies in the event there are issues in delivery [31]. Prior to completing informed consent, participants will be given information that fully describes the process of the study (including the possibility of being randomly selected to be invited to participate in a semi-structured interview),

including why their participation is necessary, how their data will be used, and who the results will be reported to. As many patients are understandably concerned about how their data will be used, data management will be explained in detail as part of the consent process. It will also make clear their right to withdraw from the study at any time and have their data destroyed. Patients will also be asked to separately consent for their data to be used to further train the conversational systems. Declining to share this conversation data will not affect patients' participation in the study or their clinical care.

9.7 Data Protection and Patient Confidentiality

The Ufonia system stores patient identifiable data as part of the clinical record. Explicit consent is obtained from patients to use that data in ongoing development. The solution is in compliance with the UK Data Protection Act 2018 (DPA 2018) [23], as well as being built to meet specific NHS regulations. All data movement shall be via encrypted data transfer and will not be stored outside the EEA. The organisations involved in this study (including each Trusts' Data Protection Officer and Caldicott Guardian) will undertake a Data Protection Impact Assessment and, where needed, create Information Sharing Agreements to ensure compliance with relevant data protection regulation. All collaborators (Imperial, Oxford, Plymouth, Ufonia) and correlating hospitals (Oxford University Hospitals, Imperial College Healthcare) will be joint controllers.

During the study implementation, each participant will be given a unique identifier. The primary key between unique ID and participant will be securely held and given to the participant as a reference ID. Data will be analysed using the unique IDs; the primary key is only maintained to enable participants to withdraw their data from the study. If such a request is made before data aggregation or publication, all of their corresponding data and files shall be destroyed.

Follow-up interview sessions shall be audio recorded by the Academic PI and his Research Associate. The interview will be transcribed by a transcription service with only reference to the unique identifier provided in the audio file for transcription (the audio file will be reviewed by the PI to ensure no identifying information is in the audio recording; if any is provided it will be edited out); the risk of identification of the interview sessions shall be very low due to this measure being taken. The original audio recording will be destroyed following transcription.

Only the Academic PI, his Research Associate and clinical staff will have access to research data. The transcription service will have access only to interview audio transcripts, following the controls previously mentioned. Records of consent will be kept for three years after the publication of final study results. Audio recordings will be immediately following transcription.

9.8 Stopping Guidelines

The study monitoring group will review the interim data for consideration of stopping the study early. Given that the estimated sample size is close to the minimum required for adequate power, the study will not be stopped early on the basis of efficacy or benefit. If the monitoring committee identifies any risks that have not been foreseen and mitigated against, the study will be paused while those risks are assessed.

9.9 Indemnity

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study. The Imperial College Healthcare NHS Trust and the Oxford University Hospitals

NHS Foundation Trust hold standard NHS Hospital Indemnity and insurance cover with NHS Resolution for NHS Trusts in England, which apply to this study.

9.10 Access to DORA's code

At the time of the close of the intervention refinement period, the **DORA** code base will be stored in a source code repository and version number recorded. Changes to the platform required to maintain safety, security or 3rd party software dependencies will be approved by the trial steering committee and ratified by an external trial monitoring committee. Changes will be validated before and after the trial by an independent software engineer on Ufonia's source code repository.

9.11 Access to Final Study Data

Audio recordings, transcriptions, and meta-data about the calls will be securely stored in UK data-centres with strict role-based access control. The transcription service will only have reference to the unique IDs and the audio recording will be reviewed by the PI to remove any identifying information before being shared. Patient identifiable data will not be sold to any other party and will not be shared with any organisation unless they are a partner in the study and have an appropriate information sharing agreement in place. Records of consent will be kept for three years after the publication of final study results, but no other personally identifiable information will be stored beyond the end of the study.

10 DISSEMINATION POLICY

10.1 Dissemination Strategy

The project's two clinical sites are leading medical centres with strong reputations for high quality patient care. They have large teams of clinicians, with extensive professional networks and training programmes that involve junior staff from across the globe. These factors mean that their participation in this project will ensure its outputs are communicated to a wide audience.

The project's academic partners are world renowned institutions with a track record of delivery and publication of high-quality research. Senior clinical academics will ensure the project is conducted robustly and even at this early stage the outputs are presented and published in high impact journals.

Alongside its clinical and academic partners, the project will leverage relationships with several organisation to support dissemination:

- NHS Clinical Entrepreneur Programme - three of the Ufonia team are members of this programme. They will work with Tony Young and the programmes networks to ensure visibility of the project to members of the central NHS leadership team. The network of other entrepreneurs will also provide a potential source of employees to support wider deployment.
- Oxford Foundry - Ufonia is a current member of the competitively selected LEV8 Accelerator programme. Through this initiative they are given access to senior mentors and advisors (including technical directors and product managers from firms like Google and venture capital investors) who can support the delivery and growth of the company to meet a pull for wider adoption.
- Oxford University Innovation - as the University of Oxford's technology transfer office they hold an investment stake in Ufonia and support its business development, as well as applying specific expertise to contracting and intellectual property protection and exploitation.
- DigitalHealth.London - Ufonia have engaged with the team and held discussions with their navigators in order to ensure the Imperial work can be supported by their extensive network.

10.2 Authorship Eligibility Guidelines and Use of Professional Writers

The International Committee of Medical Journal Editors (ICMJE) guidelines will be used to determine the study authors [32]. The ICMJE stipulates four criteria that people involved in the study must meet to be considered authors for this paper:

1. Having made a substantial contribution to the design or execution of the study;
2. Having drafted or significantly contributed to the revision of the paper;
3. Having final approval over submission for publication;
4. Agreeing to be accountable for the published work.

No professional writers will be employed.

11 DECLARATIONS

11.1 Funding

Ufonia has been supported by grant funding from Innovate UK and the Science and Technology Facilities Council. The company has received business support from Oxford University Innovation and the Oxford Foundry. The Department of Ophthalmology at Buckinghamshire Healthcare NHS Trust has collaborated in the development of Ufonia's system.

This study is supported by the NIHR AI in Health and Care Award (AI_AWARD01852).

11.2 Protocol Registration

The protocol will be registered through this IRAS submission 297548 and additionally on the database clinicaltrials.gov (reference number TBD) [33].

11.3 Competing Interests

NdP and GM are all employees of Ufonia, a voice artificial intelligence company. Although these authors were involved in the drafting and revision of the protocol, the final decision on the evaluation design lies with the academic consortium led by Imperial College London.

NdP is employed part-time by Oxford University Hospitals NHS Trust and responsible for the development of innovation activities at the Trust. His work for Ufonia has been approved by his line manager (Chief Digital and Partnerships Officer) and declared in the Trust's register of interests. None of the resources NdP is responsible for within the Trust are used to support the project.

GM is employed part-time by Oxford University Hospitals NHS Trust. This employment is as a clinician so he has not been a decision maker regarding any resources from the Trust that relate to this study. His work for Ufonia has been approved by his line manager at the Oxford University Hospitals NHS Trust and declared in the Trust's register of interests.

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13 APPENDICES

13.1 Appendix 1. Participant Information Sheet

Dr Eduardo Normando, Chief Investigator (Imperial)
e.normando@imperial.ac.uk

Dr Kanmin Xue, Principal Investigator (Oxford)
kanmin.xue@ouh.nhs.uk

Dr Edward Meinert, Co-Investigator (Evaluation Lead)
edward.meinert@plymouth.ac.uk

Autonomous telephone follow-up after cataract surgery
PARTICIPANT INFORMATION SHEET

Integrated Research Application System (IRAS) Reference: 297548
Health Research Authority (HRA) Approval Reference: #insert
Research Ethics Committee (REC) Approval Reference: #insert
University of Plymouth Faculty Research Ethics and Integrity Committee: #insert

We would like to invite you to take part in this research project. You should only take part if you want to; choosing not to take part will not disadvantage you in any way. Before you decide if you wish to take part, you need to understand why the research is being done and what taking part will involve.

Please take time to read the following information carefully and talk it through with others if you wish. Please contact us at the above email if there is anything that is not clear or if you would like more information.

1. **Why is this research being conducted?**

The aim of the study is to provide high quality and safe automated telephone follow-up for patients after cataract surgery.

2. **Who is conducting the project?**

The study is being led by Dr Eduardo Normando in a consortium led by Imperial College London and including the University of Plymouth and the University of Oxford. The Imperial College Healthcare NHS Trust and the Oxford University Hospitals NHS Foundation Trust are conducting all clinical activity.

3. **Why have I been invited to participate?**

Increasingly hospitals are providing follow up after routine cataract surgery by telephone conducted by a member of the clinical team. Ufonia Ltd has developed an automated system called **DORA**. This system is a computer which can conduct telephone follow up. The aim of this study is to see if this system is safe and that **DORA** makes the same recommendations as a clinician. We are evaluating this for patients who have surgery on certain operating lists which is why you are being asked if you would like to take part.

The study is being conducted as a collaboration between The Imperial College Healthcare NHS Trust and the Oxford University Hospitals NHS Foundation Trust.

4. **Do I have to take part?**

No, taking part is entirely voluntary. It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason.

5. **What will happen to me if I take part in the research?**

If you choose to take part, you will be called on a specific day three weeks after your surgery by **DORA** the automated service. **DORA** will ask you some questions about how you are doing after your surgery and plan the next step in your care as well as what you think of the automated service. This will be overseen by a clinician and if you are not in agreement with the plan you can ask for this to be reviewed.

After your call with **DORA**, you will be provided with a paper or online survey about your experiences using **DORA**. This survey will also ask some optional demographics questions. One week after your call with **DORA**, you may also be invited to take part in a telephone interview for 40-60 minutes, where you will be asked questions about your experience with **DORA**. The interviews will be held privately between you and a researcher. The sessions shall be recorded, subject to your permission, and transcribed by a third-party supplier of the University of Plymouth.

6. **Are there any potential risks in taking part?**

Potential disadvantages are that this is a new system so has not been demonstrated to be effective - this is why the system is currently overseen by a clinician.

7. **Are there any benefits to taking part?**

This safety check is additional to the usual standard of care at the two sites where the study is being conducted. The process will be overseen by a clinician and the system is designed to provide a thorough assessment every time. This study will also benefit future patients through a more convenient follow-up service.

8. What if something goes wrong?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Chief Investigator, Dr Eduardo Normando at e.normando@imperial.ac.uk or 02033123206. The normal National Health Service complaints mechanisms are also available to you.

9. How will we use information about you?

Imperial College London is the sponsor for this study. Imperial College London, the University of Plymouth, The University of Oxford and Ufonia will act as the joint data controllers for this study. This means that all research partners are responsible for looking after your information, using it properly and will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

10. **What happens to the data provided?**

The information you provide during the study is known as the **research data**.

Any research data from where you can be identified or is linked to you is known as **personal data**. This data will be accessed via your digital interactions with **DORA** and stored on an EEA hosted server and on secure university network drives. Audio recordings will be created from interview sessions via a digital recorder. This data will be directly transferred from the device to a secured drive and transcribed by a 3rd party. Once the transcription is completed, the original interview audio interview files will be destroyed.

Other research data (including consent forms) will be stored for ten years after publication or public release of the research and stored on a secure university network drives at Imperial College and the University of Plymouth. Dr Normando and Dr Meinert and their research teams will have access to the research data. Responsible members of Imperial College London, the University of Plymouth and the University of Oxford may be given access to data for monitoring and/or audit of the research.

All data will be stored on a password-protected network drive within the Imperial College London's and University of Plymouth's network. Access to these files will be limited to the study research team. Electronic data shall be coded using a unique participant number and primary critical pseudonymisation (creation of a fictitious name linked to participant numbers) process. Physical copies of consent forms will be stored in a locked folder at Dr Meinert's office in the University of Plymouth at 6 Kirkby Place, Room 2.

We would like your permission to use direct quotes with a fictitious name in any research outputs.

We would like your permission to use pseudonymised data in future studies and to share data with other researchers. All personal information that could identify you will be removed or changed before the information is shared with other researchers or results are made public.

If you consent to take part in the research, any information you provide may be inspected and used by administrators of the study. Each participant will be pseudonymised using a unique identifier to maintain confidentiality, and all data will be securely stored and managed according to sponsor rules and expected practices. Raw, un-anonymised audio data will be securely stored separately from the anonymisation key and deleted when it is no longer needed. The pseudonymised transcripts will be securely stored according to Imperial College London's and the University of Plymouth protocols and regulations.

11. Will the use of my data meet GDPR rules?

GDPR stands for the General Data Protection Regulation. In the UK we follow the GDPR rules and have a law called the Data Protection Act. All research using patient data must follow UK laws and rules.

Universities, NHS organisations and companies may use patient data to do research to make health and care better.

When companies do research to develop new treatments, they need to be able to prove that they need to use patient data for the research, and that they need to do the research to develop new treatments. In legal terms this means that they have a 'legitimate interest' in using patient data.

Universities and the NHS are funded from taxes and they are expected to do research as part of their job. They still need to be able to prove that they need to use patient data for the research. In legal terms this means that they use patient data as part of 'a task in the public interest'.

If they could do the research without using patient data, they would not be allowed to get your data.

Researchers must show that their research takes account of the views of patients and ordinary members of the public. They must also show how they protect the privacy of the people who take part. An NHS research ethics committee checks this before the research starts.

12. **Will what I say be kept confidential?**

All information provided during interviews will be pseudonymised, kept strictly confidential and not attributed to you. Participants will be allocated a study ID number and any information collected will only be seen by the study team. The voice data derived from conversations with DORA will be stored and used by Ufonia, Ltd, the manufacturer of DORA, for up to 10 years to train and improve its system. This data will be stored using a unique ID and will not include your name.

13. **What will happen to the results of the project?**

The results of this evaluation study will be used for the purpose of deciding whether the system is safe to provide autonomous telephone follow-up after cataract surgery without oversight from a clinician. We will publish findings from the study in a medical journal.

14. **Who has reviewed the project?**

The study has been approved by the Health Research Authority, the University of Plymouth, and Imperial College London.

15. Legal Basis

As universities we use personally identifiable information to conduct research to improve health, care and services. As publicly funded organisations, we have to ensure that this work is in the public interest when we use personally identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study.

Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

16. International transfers

There may be a requirement to transfer information to countries outside the European Economic Area (for example, to a research partner). Where this information contains your personal data, Imperial College London will ensure that it is transferred in accordance with data protection legislation. If the data is transferred to a country which is not subject to a European Commission (EC) adequacy decision in respect of its data protection standards, Imperial College London will enter into a data sharing agreement with the recipient organisation that incorporates EC approved standard contractual clauses that safeguard how your personal data is processed.

17. Sharing your information with others

For the purposes referred to in this privacy notice and relying on the bases for processing as set out above, we will share your personal data with certain third parties.

- Other Imperial College London employees, agents, contractors and service providers (for example, suppliers of printing and mailing services, email communication services or web services, or suppliers who help us carry out any of the activities described above). Our third-party service providers are required to enter into data processing agreements with us. We only permit them to process your personal data for specified purposes and in accordance with our policies.

- The following Research Collaborators / Partners in the study:
  - The University of Plymouth – The University of Plymouth will access research and personal data for the purpose of completing an evaluation of **DORA.**
  - The University of Oxford – The University of Oxford will access research and personal data for the purpose of completing an evaluation of **DORA**.
  - Ufonia, Ltd. – Ufonia, Ltd. will access personal data for the processing of conversations with **DORA** and using these conversations to train and improve **DORA**'s ability to conduct automated telephone follow-up.

18. Complaints

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via email at dpo@imperial.ac.uk, via telephone on 020 7594 3502 and/or via post at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

19. **What should I do if I want to take part?**

If you agree to take part, you will be asked to sign a consent form or provide consent verbally and will be given a date to expect a call from DORA.

Contact for further information:

- Dr Eduardo Normando – e.normando@imperial.ac.uk
- Dr Kanmin Xue – kanmin.xue@ouh.nhs.uk
- Dr Edward Meinert – edward.meinert@plymouth.ac.uk

13.2 Appendix 2. Informed Consent Form

Study Title: Autonomous telephone follow-up after cataract surgery

*Informed consent in this study will be taken in written form or recorded.

Participant Identification number for this trial: _____

Name of Principal Investigators: Dr Eduardo M. Normando, Dr Kanmin Xue

Please initial the boxes.

1. I confirm that I have read the information sheet dated..... (Version.....) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from Imperial College London, from University of Oxford, form University of Plymouth, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4. I consent to being contacted regarding potentially taking part in other research studies.	
5. I give/do not give (delete as applicable) consent for information collected about me to be used to support other research in the future, including those outside of the EEA.	
6. I consent to my GP being informed about my participation in the study.	
7. I agree to being contacted for and interview regarding the user experience.	
8. I consent to being audio recorded.	
9. I understand how audio recordings will be used in research outputs.	
10. I give permission to be quoted directly in research outputs against a pseudonym.	
11. I agree to grant access to my follow-up data as specified in the patient information sheet.	
12. I consent to take part in the above study.	

_____	_____	_____
Name of Participant	Date	Signature
_____	_____	_____
Name of Person taking consent (If different from Principal Investigator)	Date	Signature

_____ _____
_____

Principal Investigator Date Signature

You will be given a copy of this consent form to keep (if recorded you will be provided a transcript following consent); one copy will be filed in your medical notes, and one will be filed with the study records within the research folder at the Study Site.

13.3 Appendix 3. SPIRIT-AI Checklist: Recommended items to address in a protocol and related documents for clinical trials evaluating AI interventions

Cruz Rivera S, Liu X, Chan A-W, Denniston AK, Calvert MJ, SPIRIT-AI and CONSORT-AI Working Group. Guidelines for clinical trial protocols for interventions involving artificial intelligence: the SPIRIT-AI extension. Lancet Digit Health 2020 Oct;2(10):e549–e560. PMID:33328049

Section		SPIRIT 2013 Item[a]	SPIRIT-AI Item		Page No[b]
Administrative Information					
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	SPIRIT-AI 1(i) Elaboration	Indicate that the intervention involves artificial intelligence / machine learning and specify the type of model.	Title page
			SPIRIT-AI 1(ii) Elaboration	Specify the intended use of the AI intervention.	Title page
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry			34 - TBD
	2b	All items from the World Health Organization Trial Registration Data Set			Title page, 9
Protocol version	3	Date and version identifier			Title page, 4
Funding	4	Sources and types of financial, material, and other support			34
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors			Title page, 6-7, 10-11
	5b	Name and contact information for the trial sponsor			Title page, 6-7, 10
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities			10
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or			10

		groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)			
Introduction					
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	SPIRIT-AI 6a (i) Extension	Explain the intended use of the AI intervention in the context of the clinical pathway, including its purpose and its intended users (e.g. healthcare professionals, patients, public).	14
			SPIRIT-AI 6a (ii) Extension	Describe any pre-existing evidence for the AI intervention.	14
	6b	Explanation for choice of comparators			19
Objectives	7	Specific objectives or hypotheses			16
Methods: Participants, Interventions and Outcomes					
Trial design	8	Description of trial design including type of trial (e.g., parallel group, crossover, factorial, single group), allocation ratio, and framework (e.g., superiority, equivalence, noninferiority, exploratory)			17
Study setting	9	Description of study settings (e.g., community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	SPIRIT-AI 9 Extension	Describe the onsite and offsite requirements needed to integrate the AI intervention into the trial setting.	17
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (e.g., surgeons, psychotherapists)	SPIRIT-AI 10 (i) Elaboration	State the inclusion and exclusion criteria at the level of participants.	22
			SPIRIT-AI 10 (ii) Extension	State the inclusion and exclusion criteria at the level of the input data.	22
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	SPIRIT-AI 11a (i) Extension	State which version of the AI algorithm will be used.	18
			SPIRIT-AI 11a (ii) Extension	Specify the procedure for acquiring and selecting the input data for the AI intervention.	18-20
			SPIRIT-AI 11a (iii) Extension	Specify the procedure for assessing and handling poor	18, 20

				quality or unavailable input data.	
			SPIRIT-AI 11a (iv) Extension	Specify whether there is human-AI interaction in the handling of the input data, and what level of expertise is required for users.	18- 20
			SPIRIT-AI 11a (v) Extension	Specify the output of the AI intervention.	19-20
			SPIRIT-AI 11a (vi) Extension	Explain the procedure for how the AI intervention's output will contribute to decision-making or other elements of clinical practice.	18
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (e.g., drug dose change in response to harms, participant request, or improving/worsening disease)			19-20
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (e.g., drug tablet return, laboratory tests)			25
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial			N/A
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended			19-22
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)			12 (Fig 1), 17 (Fig 4), 26 (Fig 6)
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations			22-24, App. 7 and 8

Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size			24
Methods: Assignment of Interventions (For Controlled Trials)					
Sequence generation	16A	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions			25
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned			25
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions			25
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how			25
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial			N/A
Methods: Data Collection, Management, And Analysis					
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol			25-26
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols			29-30
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to			31

		where details of data management procedures can be found, if not in the protocol			
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol			26-27
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)			19-20
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)			22-24
Methods: Monitoring					
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed			29
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial			31
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	SPIRIT-AI 22 Extension	Specify any plans to identify and analyse performance errors. If there are no plans for this, explain why not.	19-21
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor			30
Ethics and Dissemination					
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval			28
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)			30
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)			25, 30-31

	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable			N/A
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial			31
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site			34
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	SPIRIT-AI 29 Extension	State whether and how the AI intervention and/or its code can be accessed, including any restrictions to access or re-use.	32
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation			N/A
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions			33
	31b	Authorship eligibility guidelines and any intended use of professional writers			33
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code			N/A
Appendices					
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates			38-41 (App 1 and 2)
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable			N/A

[a] It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items.
[b] Indicates page numbers to be completed by authors during protocol development.

13.4 Appendix 4. Sample Post-Call Survey

Blank, Grant, OxIS 2019 Questionnaire. All Parts (January 30, 2019). Available at SSRN: https://ssrn.com/abstract=3522118

Brooke J. Systems Usability Scale. In: Jordan P, Thomas B, Weerdmeester W, editors. Usability Evaluation In Industry Taylor & Francis; 1996. p. 189–194.

Parmanto B, Lewis AN Jr, Graham KM, Bertolet MH. Development of the Telehealth Usability Questionnaire (TUQ). Int J Telerehabil 2016 Jul 1;8(1):3–10. PMID:27563386

Demographic Questions

1. AGE: In what year were you born?
    a. (If refuse to answer): Would you mind indicating which of these age bands you are in: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+
2. GENDER*: How do you currently describe your gender identity?
    a. *Note: in the OxIS, gender was assessed 'by observation'. The wording of this question is therefore taken from a different source (Hughes, Camden, & Yangchen, 2016)
3. FAMILY:
    a. Are you…? Single, Married, Living together with a partner, Divorced/separated, Widowed
    b. How many adults live in your household (people age 18 or more)? [WRITE IN]
    c. How many children (people age 17 or less) live in your household? [WRITE IN]
4. ETHNICITY: To which of these groups do you consider you belong?
    a. ASIAN: of Indian origin
    b. ASIAN: of Pakistani origin
    c. ASIAN: of Bangladeshi origin
    d. ASIAN: of Chinese origin
    e. ASIAN: of any other origin (WRITE IN) _____
    f. BLACK: of African origin
    g. BLACK: of Caribbean origin
    h. BLACK: of other origin (WRITE IN) _____
    i. WHITE: of British origin
    j. WHITE: of Scottish origin
    k. WHITE: of Welsh origin
    l. WHITE: of any other origin (WRITE IN) _____
    m. OTHER (WRITE IN)
    n. Don't know
5. URBAN: Would you describe the place where you live as a big city, the suburbs or outskirts of a big city, a small city or town, a country village, or, a farm or home in the country?
    a. A big city
    b. The suburbs or outskirts of a big city
    c. A small city or town
    d. A country village
    e. A farm or home in the country
    f. Other
    g. Don't know

6. INCOME: The incomes of households differ a lot in Britain today. Here is a table showing the range of incomes that people have. Which option best represents the total income of your household before tax? Please select one answer only.
    a. Up to £12.500 per year
    b. £12.500 up to £20.000 per year
    c. £20.000 up to £30.000 per year
    d. £30.000 up to £40.000 per year
    e. £40.000 up to £50.000 per year
    f. £50.000 up to £60.000 per year
    g. £60.000 up to £70.000 per year
    h. £70.000 up to £80.000 per year
    i. Over £80.000 per year
    j. Prefer not to say
7. EDUCATION: What is the highest educational or vocational qualification that you have or that you will receive if you complete your next set of exams?
    a. No qualifications
    b. 5 or more GCSE grades A-C
    c. 4 or less GCSE grade A-C
    d. GCSE grade D-G
    e. 5 or more Scottish Standard Grades, grades 1-3
    f. 4 or less Scottish Standard Grades, grades 1-3
    g. 5 or more O Grades, grades 1-3 (Scottish Ordinary Grades)
    h. 4 or less O Grades, grades 1-3 (Scottish Ordinary Grades)
    i. Scottish Standard Grades, grades 4-7
    j. Scottish Highers (either SCE or SQC)
    k. Scottish Certificate Sixth Year Studies
    l. SVQ level 1 or 2 (Scottish Vocational Qualifications)
    m. SVQ level 3 (“)
    n. SVQ level 4 (“)
    o. SVQ level 5 (“)
    p. CSEs
    q. 5 or more O levels
    r. 4 or less O levels
    s. GCE A levels or equivalent
    t. NVQ level 1 or 2
    u. NVQ level 3 or 4
    v. NVQ level 5
    w. GNVQ Foundation
    x. GNVQ Intermediate
    y. GNVQ Advanced
    z. Certificate or Diploma of Higher Education
    aa. HND (Higher National Diploma)
    bb. Bachelor’s degree
    cc. Graduate Certificates and Diploma
    dd. Post-degree professional qualification (eg banking accountancy, architecture, etc.)
    ee. Master’s Degree

ff. Doctoral Degree
gg. Don't know

8. EMPLOYMENT: Which of these descriptions best describes your current situation?
    a. Working Full time (30 hours a week or more)
    b. Working Part time (8-29 hours a week)
        i. If (a) or (b): Apart from working, do you also study? (yes / no / DK)
    c. Retired
    d. Unemployed
    e. Permanently sick or disabled
    f. In community or military service
    g. Undergraduate Student
    h. Post graduate student
    i. In full time education (not higher degree)
    j. In part time education (not higher degree)
        i. If (g)-(j): And apart from studying, do you also work? (yes / no / DK)
    k. Doing housework, looking after children or other persons

<u>System Usability Scale</u>

Rated on a 5-point Likert scale, from 'Strongly Disagree' (1) to 'Strongly Agree' (5)

9. I think that I would like to use this system frequently.
10. I found the system unnecessarily complex.
11. I thought the system was easy to use.
12. I think that I would need the support of a technical person to be able to use this system.
13. I found the various functions in this system were well integrated.
14. I thought there was too much inconsistency in this system.
15. I would imagine that most people would learn to use this system very quickly.
16. I found the system very awkward to use.
17. I felt very confident using the system.
18. I needed to learn a lot of things before I could get going with this system.

<u>Telehealth Usability Questionnaire</u>

Rated on a 7-point Likert scale, from 'Disagree' (1) to 'Agree' (7). It has been adapted slightly to fit the particular context of this study.

19. Telehealth improves my access to healthcare services.
20. Telehealth saves me time traveling to a hospital or specialist clinic.
21. Telehealth provides for my healthcare needs.
22. It was simple to use this system.
23. It was easy to learn to use the system.
24. The way I interact with this system is pleasant.
25. I like using the system.
26. The system is simple and easy to understand.
27. This system is able to do everything I would want it to be able to do.
28. I could easily talk to **DORA**.
29. I could hear **DORA** clearly.
30. I felt I was able to express myself effectively.
31. I think the visits provided over the telehealth system are the same as in-person visits.

32. Whenever I made a mistake using the system, I could recover easily and quickly.
33. The system gave error messages that clearly told me how to fix problems.
34. I feel comfortable communicating with **DORA**.
35. Telehealth is an acceptable way to receive healthcare services.
36. I would use telehealth services again.
37. Overall, I am satisfied with this telehealth system.

13.5 Appendix 5. Topic Guide for Semi-Structured Interviews

The topic guide was developed based on the Theoretical Framework of Acceptability (TFA) [16], which was created to provide a framework for assessing the multiple facets of acceptability of health interventions. The TFA has seven components: "1) affective attitude, 2) burden, 3) ethicality, 4) intervention coherence, 5) opportunity costs, 6) perceived effectiveness, and 7) self-efficacy" [16].

Interview questions

* Before the call
    1. What did you expect the experience of talking to **DORA** to be like before you received the call?
    2. How did you feel about talking to **DORA** before you received the call?
    3. What, if any, concerns did you have before you received the call?
    4. How well did you understand the intervention before you received the call?
    5. What benefits or losses did you think you would experience when you received the call?
    6. How successful did you think **DORA** would be at delivering the follow-up before you had the call?
    7. How confident were you that you would be able to interact with **DORA** before you received the call?
* During the call
    1. How did you feel about your experience interacting with **DORA**?
    2. How much effort did interacting with **DORA** take?
    3. What concerns, if any, did you have while talking with **DORA**?
    4. How well did you understand how the call worked while you were talking to **DORA**?
    5. What benefits or losses did you experience while you were talking to **DORA**?
    6. How much confidence did you have in **DORA's** ability to perform the follow-up assessment while you were talking to **DORA**?
    7. How comfortable and confident were you in your ability to interact with **DORA** while you were on the phone?
* After the call
    8. Looking back on the experience now, how do you feel about using **DORA** to perform follow-up appointments?
    9. Looking back on the experience now, how much effort did interacting with **DORA** take?
    10. Looking back on the experience now, what concerns, if any, do you have about **DORA**?
    11. Looking back on the experience now, how well do you understand how **DORA** worked?
    12. Looking back on the experience now, what do you think you gained or lost by having your follow-up assessment with **DORA**?
    13. Looking back on the experience now, how well do you think **DORA** performed at conducting your follow-up assessment?
    14. Looking back on the experience now, how confident would you be having another interaction with **DORA**?
* General feedback
    15. What would you suggest to make the experience of using **DORA** better?
    16. How willing would you be to use **DORA** again?
    17. If you had the choice between no follow-up / a face-to-face appointment (depending on clinical site) and **DORA**, which would you choose and why?
    18. Is there anything else you'd like to mention?

13.6 Appendix 6. Imperial Historical Recruitment Audit Data

Purpose

To provide real world evidence for assumptions made in modelling of recruitment numbers and study planning.

Audit

We audited all bookings in the cataract one-stop-clinic for the month of October 2020. After discussion with the head of the cataract pathway, it was felt this was the most representative of what the cataract pathway will likely look like in May-July 2021 assuming there is COVID recovery of a similar trajectory to the first wave. It is anticipated there will be 3 consultant-led one-stop clinics running in July to address the backlog. Of note, the general pre-assessment pathways have not been audited.

Key findings

Clinic capacity and utilisation - All October one-stop data

- 33 patients were booked across 4 clinics
- 8.25 patients on average per clinic
- 88% (29/33) attended their one-stop appointments

Conversion rate

- Of all patients booked, 76% proceeded for surgery (25/33)
- Or, of those attending, 86% proceeded to surger**y** (25/29)

Demographics

- Mean age was 71.5
- This was the first eye for 52% of patients

Inclusion/Exclusion

- 100% (29/29) of those attending were listed for routine cataract surgery
- 10% (3/29) required a translator (Tamil, Punjabi, Arabic)
- 1 patient (3%) had dementia and would not have been able to consent
- Overall, of all attending patients, 76% (29/33) would have been eligible for trial inclusion.

Withdrawal

- No patients in this cohort had unexpected surgical complications
- 1 patient (4%) attended AnE before follow up with a corneal abrasion and would have been withdrawn from **DORA** per our current protocol.

Follow up

- **95%** (24/25) of patients attended post-op follow up
- **21%** (7/25) of patients had a documented complication requiring management change at their post-op followup.
    - 6 of these patients were uveitis
        - 4 of which were given maxidex and discharged
        - 1 was given maxidex with phone follow up

        - 1 was given maxidex and listed for 2nd eye.
    - 1 patient has post-op cystoid macular oedema and maxidex requiring medical retina review.

Pathway

- The mean time between one-stop appointment and surgery was **9.88 days.**
    - The range was from 2 days to 62 days
    - **16 patients** had their operations in under 1 week
- Mean time between surgery and first follow up was **24.33 days.**
- A number of patients were followed up under the 21 day point

Comparison with initial estimates

	Imperial One-stop (Projected 3 clinics per week from	**Imperial** One-stop October 2020
Current Numbers Assessed		
Mean Patients assessed per clinic	10	7.25
Clinics per week	3	1
Mean Patients Assessed per week	30	7.25
Eligibility Assumptions		
% proceeding to surgery	80%	86%
% routine cases	80%	100%
% eligible for trial	80%	76%
% dropout due to complicated surgery	5%	0%
Screening		
Compound daily eligibility rate	49%	65%
Number of days screening	2	1
Patients screened per week	10	5
Estimated recruitment		
% consenting to trial	90%	90%
Estimated recruited per week	9	4
Duration of trial (weeks)	26	27
Estimated recruitment over trial	**228**	**115**

Conclusions

- Based on these samples our projections were conservative apart from % eligible for trial
- Based on these projects even 2 clinics per week should allow us to meet a recruitment number of over 200 at Imperial.
- Recruiting from pre-op assessment will be required to meet aim of >400 patients

13.7 Appendix 7. Oxford Historical Recruitment Audit Data

All bookings for cataract surgery pre-assessments at the Oxford University Hospitals NHS Foundation Trust for October were audited to provide evidence for an estimate of the recruitment sample size. Assuming there is a recovery from the Covid-19 pandemic of a similar trajectory to the first way, this was determined to be the most representative of what the cataract pathway will likely look like in May-July 2021. The audit report was produced on 21 January, 2021.

Purpose

To provide real world evidence for assumptions made in modelling of recruitment numbers and study planning.

Audit

We audited the cataract clinic pre-op assessment clinics in October 2020. The clinic numbers were reviewed for the entire month, and the first 50 consecutive patients were reviewed in detail. It was felt this was the most representative of what the cataract pathway will likely look like in May-July 2021 assuming there is COVID recovery of a similar trajectory to the first wave.

Key findings

Clinic capacity and utilisation - all October data

- 160 patients were booked across 21 clinics
- 7.6 patients on average per day
- 96% (50/52) attended their one-stop appointments
- Only 1/160 was booked as a telephone assessment

Conversion rate (reviewing first 50 consecutive patients)

- Of all patients booked, 86% proceeded for surgery (45/52)
- Of all patients that attended, 90% were listed for surgery directly (45/50)
    - 2 were asymptomatic and discharged, 3 were referred to clinic and subsequently listed
    - Including those listed from clinic- 48/50, 96% were listed for surgery.

Demographics

- Mean age was 76.36
- 17 male: 33 female
- This was the first eye for 78% of patients

Inclusion/Exclusion

- 96% (46/48) of those attending were listed for routine cataract surgery
- 2% (1/48) required a translator
- 2 patients (4%) had learning difficulties and would not have been able to consent (the patient with learning difficulties also had surgical complexities)
- Overall, of all attending patients, 92% (44/48) would have been eligible for trial inclusion.

Pathway

- To date 30/44 (68%) of the patients listed have had cataract surgery
- The mean time between one-stop appointment and surgery was 30 days.
    - The range was from 0 days to 79 days
    - 3 patients had their operations in under 1 week

Withdrawal

- 6.6% (2/30) patients in this cohort had unexpected surgical complications – 1 iris prolapse and 1 needing sutures
- The 2 patients with complications attended a planned clinic appointment and were discharged.
- 1 patient attended ED with CMO 10 weeks post procedure, 1 called eye casualty with red eye 6 weeks post procedure but did not need review

Follow up

- Only the 2 patients with unexpected complications had planned clinic appointments

Comparison with initial estimates

	Oxford		Oxford	Oxford
	Pre-assessment October 2020		Pre-assessment (Study projections)	Phone pre-assessment (2nd eye) (Study projections)
Current Numbers Assessed				
Mean Patients assessed per clinic	7.6		12	4
Clinics per week	5		5	5
Mean Patients Assessed per week	39.5		60	20
Eligibility Assumptions				
% proceeding to surgery	90%		90%	90%
% routine cases	96%		80%	80%
% eligible for trial	92%		90%	90%
% dropout due to complicated surgery	6.6%		5%	5%
Screening				
Compound daily eligibility rate	74%		62%	62%
Number of days screening	2		2	2
Patients screened per week	11		15	5

Estimated recruitment				
% consenting to trial	90%		90%	90%
Estimated recruited per week	10		13	4
Duration of trial (weeks)	26		26	26
Estimated recruitment over trial	264		346	115

Conclusions

- The spread between F2F and telephone clinics was different to previously predicted, with only 1 patient in October having a telephone appt booked.
- Similar rates of patients that are potentially eligible in October 2020 compared to previous estimates
- Based on these projections even 2 clinics per week should allow us to meet a recruitment number of over 200 at Oxford