The Lotus study:
Understanding how surgical procedures and devices are introduced

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Lotus study overview:

- The Lotus study aims to understand how surgical procedures and devices with limited evidence to support efficacy and safety are introduced, used, and modified in the NHS.
- Lotus has been reviewed and approved (HRA and Health and Care Research Wales) by the Frenchay Research Ethics Committee (Ref 18/SW/0277), and the study protocol is published(1).
- It is important to note that the approval is for *studying* the introduction of innovation - it is not approval for undertaking the innovative procedures themselves.
- The study has so far followed nine innovative procedures in eight hospitals, with over 100 patients recruited.
- The findings will aim to support the development of a transparent and safe translational pathway for novel surgical and invasive procedures and devices prior to full evaluation within a phase 3 or similar later phase study and/or to widespread uptake in clinical practice.

Lotus methods overview:

Lotus is a multicentre prospective, observational study. Each case study uses a range of methods, including:

(i) Scene setting 'background' interviews with healthcare professionals to understand the procedure
(ii) Literature reviews to understand the evidence and stage of innovation of a procedure
(iii) Audio-recordings of pre-operative consultations between healthcare professionals and patients
(iv) In-theatre video-recordings and observations of surgery
(v) Post-operative interviews with healthcare professionals to understand modifications over time
(vi) Interviews with patients to understand views on communication, decision-making and, where possible, experiences of recovery
(vii) Clinical and patient data collection
(viii) Governance data collection (e.g., types of approval for the new procedure)
(ix) Feedback meetings with innovators to develop methods for incremental learning about communication, governance, and modifications of new procedures

Scope of this report:

- This report has been prepared for the NICE Interventional Procedure Guidance Review on aortic valve reconstruction using glutaraldehyde-treated autologous pericardium (the 'Ozaki' procedure) and describes the findings of a case study nested within the Lotus study. Specifically, and as requested by NICE's Public Involvement Programme, it only focuses on patients' short-term experiences of recovery from the Ozaki procedure. In addition to this report, linked projects/outputs so far include:
    - A paper has been accepted for publication which syntheses seven case studies to investigate what information patients are provided with (Elliott et al, Annals of Surgery, in press)
    - A descriptive report which summarises key findings from surgeon interviews in relation to views on modifications and patient selection
    - An MD that will be submitted April 2023 which focuses on understanding phase of innovation of surgical procedures and devices. This thesis focusses on the Ozaki procedure.

The Ozaki case study: Overview of methods and analysis

Determining eligibility for the Ozaki procedure as a case study:

- Firstly, an in-depth qualitative interview with the innovator (a 'background' interview) was conducted to learn more about the Ozaki procedure.
- Alongside this, the research team undertook a literature review to identify existing published articles on the procedure.
- Published evidence identified (December 2019):
    - The original case series publications from a single centre in Japan include 850 patients (2-4).
    - Wider adoption of the technique more recently is shown with case series publications from other centres in India (single centre, n=20)(5), Russia (2 centres, n=170)(6).
    - A publication reporting a case series in the United Kingdom (2 centres, n=55, follow up mean 12.5 months)(7), also performed a meta-analytic comparison with other biological valve substitutes.
    - A comparative cohort study of 60 patients in a single centre in Russia has also compared minimally invasive versus full sternotomy Ozaki techniques.
    - Most publications have focused on the feasibility and short-term outcomes and there is limited data on long-term outcomes. One case study describes structural deterioration at 6 years post procedure (8).
- The procedure was therefore deemed suitable for Lotus given the very limited supporting evidence of safety and efficacy.

Summary of data collected so far (December 2019-present):

- Data collection for this case study began in December 2019.
- As of January 2023, 20 patients and six surgeons who are performing the procedure have taken part in Lotus. All data have been obtained from one NHS trust. Note, this does not include all Ozaki procedures being performed during that time.
- At the time, Ozaki was initially being undertaken by the surgeons without formal governance (around 20 procedures performed). Approval from the hospital's Clinical Effectiveness Committee subsequently obtained after this.
- Of the 20 patients, five proceeded to receive alternative procedures (e.g., biological aortic valve replacement, ascending aorta replacement or prosthetic valve) and two are still awaiting surgery.
- Total data collected so far includes:
    - 5 surgeon background interviews
    - 8 pre-operative consultation recordings of 20
    - 10 in-theatre video-recordings of 20
    - 13 post-operative surgeon interviews of 20
    - 17 patient interviews (the focus of this report) of 20

Data collection for patient interviews:

- Interviews with patients explored views on the presentation of information provided about the procedure during consultations, reasons underlying decisions to accept or decline the procedure, views/understanding of innovation and, if relevant, experiences of undergoing the procedure and subsequent recovery.
- Interviews were guided by topic guides to ensure that discussions covered the same core issues, whilst allowing probing questions for each participant to enable new issues of importance to be discussed further. Topic guides were adapted as analysis progressed, to enable exploration of insights identified across and within case studies.
- All interviews were audio-recorded using an encrypted recorder. Interviews were conducted by a range of experienced qualitative researchers (DE, MC, CO, CH).

- Of the 17 patients who were interviewed in total, 13 had received the Ozaki procedure. This report captures the experiences of 12 patients (one interview was pre-surgery so was not included as part of this analysis, although this patient later had the Ozaki).
- Of the 12 patients included, there were six females and six males who had a mean age 44.8 years (standard deviation 20.3). Ages ranged from 23 to 74. Interview dates ranged between 9 days and 11 weeks post-surgery.

Data analyses for patient interviews:

- All audio data were transcribed verbatim in full. Transcripts were de-identified, checked against original recordings, and imported into software (NVivo, QSR International, USA). For this analysis, all data relating to recovery and quality of life were extracted by one researcher (MC). These data were then systematically assigned codes using constant comparison methods derived from grounded theory methodology. Another researcher (DE) read all transcripts to ensure a good fit between coding and representation of participants' experiences.

Preliminary findings: Patients' short-term experiences of recovery

Reflecting on a positive recovery

Patients were generally positive about the inpatient treatment they received, describing a high standard of care from hospital staff:

> *'Honestly my experience in hospital was pretty good, I think all the people that took care of me were really, really kind and really good.' (1029 – 3 weeks post-surgery)*

Patients reflected that the ways that they felt physically different since undergoing the procedure:

> *'I can't see inside my heart what's going on, but I think so far I feel like things have found their place. I do have some niggly, a bit like a stitch when walking up a hill a little bit but I think it's something to do with the diaphragm being a muscle and things have been probably moved about a bit and they need to settle and readjust.' (1029 – 3 weeks post-surgery)*
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> *''I'm all right [...] Today I'm much better, and I walked yesterday, I done two miles yesterday, and I done two miles today. It's okay. And, so I'm okay today, it's just I'm not sleeping very well, but everything else is fine. I haven't got any pain or anything […] I still feel as if my chest is alien to me, I feel as if it doesn't belong to me. Strange feeling but that's the way I feel about it at the moment.' (1023 – 9 days post-surgery)*

Overall, many patients described that they were doing well. These patients described a particularly straightforward and uneventful recovery, and were healing relatively quickly following the procedure:

> *'I'm doing really well thank you, I've been very well throughout, so that's good… I had very little pain, either in hospital or since.' (1022 – 9 weeks post-surgery)*
>
> *'Pretty good. I'm going back to work tomorrow full time. Other than that, okay I've still got some pain in my sternum if I put excessive load on it, but other than that I've got no side effects or anything like that.' (1015 – 8 weeks post-surgery)*
>
> *'I'm doing remarkably well all things considered. I feel a bit achy and a bit- I'm not 100%, but I'm better than I thought I would be.' (1029 – 3 weeks post-surgery)*

Most patients described a steady and positive return to gentle exercise and activity as their recovery progressed. For some this meant a regular regime of walking as their energy levels increased and body continued to heal:

> *'But initially I'm feeling good, I feel like I can walk, for a long time, I was out walking with my parents for the last couple of days, didn't feel breathless or anything, didn't feel fatigued.' (1024 – 4 weeks post-surgery)*

> *'It has been repaired in the best possible way for me. I am walking every day and only walk about a kilometre along the sea front, it takes me 15 minutes which isn't too bad, I could do it quicker' (1025 – 7 weeks post-surgery)*

Nonetheless, patients acknowledged that it was early days in terms of their recovery journey:

> *'It went well but maybe I can't say if it was successful because I am still healing.' (1028 – 5 weeks post-surgery)*

Reflecting on the challenges of recovery

For many, recovery was described as 'a process', with 'ups and downs'. For example, poor appetite was an issue experienced by patients in the immediate aftermath of having the procedure:

> *'I normally have a very good appetite and I eat fairly well, but when I was in hospital after the anaesthetic your appetite is really compromised by that, you feel like under the strong medication they give you straight away doesn't make you feel hungry.' (1029 – 3 weeks post-surgery)*
>
> *'If I hadn't have read the booklet, coz I didn't really eat anything probably five days after the operation, I just couldn't keep anything down, just constantly sick and nauseous. And that would have really worried me if I hadn't read the booklet before which said you might lose your appetite for a few days. That was really comforting to see.' (1026 – 4 weeks post-surgery)*

Several patients described that they were still experiencing breathlessness and chest pain several weeks after the surgery. These symptoms had been expected due to the nature of the surgery, and whilst they did impact quality of life, they were not described as serious or debilitating.

> *'Even just opening a door, a heavy door, something like that, it's really quite challenging and tiring…' (1029 – 3 weeks post-surgery)*
>
> *'It feels like it's getting there, but I don't, I can get like big deep breaths and cough without really any pain, you know. Lying down and, you know whenever I go to bed or get up in the morning it's a little bit sore. Still is. But that pain steadily fades throughout the day. And then by 12 weeks hopefully back to normal in that sense.' (1024 – 4 weeks post-surgery)*
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> *'I thought it was going to be a lot worse than it was. Generally speaking sort of everything else-, eating's fine, no problems with the toilet, I'm able to-, a little bit out of breath still but that's got better… And I think the results so far look quite good. I think coz of how my heart is at the moment yes, I'm still getting out of breath, but my chest is still swollen, there's still a bit of pain there, the heart is going to be adjusting to its new valve.' (1026 – 4 weeks post-surgery)*

Whilst it is important to note that many patients described experiencing pre-existing symptoms linked to the condition that had precipitated the need for the surgery (e.g., chest pains, heart palpitations), they reflected on the ways that such symptoms now felt somewhat *different*. Seeing symptoms change or reduce in their intensity appeared to give a sense of hope that the procedure had been successful:

> *'Yeah, my palpitations- they did get a little bit worse in hospital I have to admit, so after the surgery, maybe like five or six days after the surgery my palpitations were bad. But now they're pretty much you get one, two, a handful, and they're not - the palpitations I used to get before were not sore but they were very uncomfortable. But the palpitations I get now aren't really uncomfortable, you just feel like you're going to have one but it doesn't really happen. So if you like there's some sort of change anyway in terms of the heart function, which I'm pleased about, which is good. But I want to see before I can say that it has been a success or I feel like it's achieved the outcomes for me. Well for me the outcomes were just to alleviate the symptoms I guess I was experiencing, so I guess for palpitations yes, you could say that that's been a success. But as in terms of breathlessness, my breathing's still a little bit restricted just in terms of the bone still hasn't healed yet.' (1024 – 4 weeks post-surgery)*

Complications in the recovery process

Patients described how their hospital stay ranged from overnight to more than two weeks. Longer stays were linked to further treatment following atrial fibrillation (AF) or infection:

> *'I was in intensive care because I had AF, my heart went into AF, and I was given drugs and all that […] So I spent four days altogether I think in critical care, in intensive care.' (1023 – spent 8 days in hospital)*
> *'I was told I'd be out of hospital in like four or five days, but I was in hospital for probably over, just over two weeks post-surgery. But that was to do with an infection in my pleural cavity somewhere. I had water on the lung as well. Yeah, so there was a whole, you know, just complicating factors, but they were worried about an infection being at the site of the operation really, and I think that was established that there wasn't, just through a CT scan [computerized tomography] and echocardiogram.' (1024 – spent 2 weeks in hospital)*

One patient also experienced blood loss that resulted in two transfusions during surgery. This patient described developing anaemia that needed further treatment:

> *'I think they implied that I'd lost quite a lot of blood during the surgery, and so gave me two blood transfusions while I was in ICU (Intensive Care Unit). And I suppose if I'd thought about it I would have thought well I've had blood transfusions, I probably am anaemic.' (1022 – spent 6 days in hospital)*

Several patients had experienced prolonged complications post-surgery linked to infection, lung-related problems, poor wound healing, and blood pressure issues, and were having a more challenging recovery.

> *'I ended up with a collapsed lung, and about three days in, apparently I nearly died.' (1030 – 11 weeks post-surgery)*
> *'One of the small wounds on my chest was not healing very well, and I was going back and forth once or twice a week to have that dressed.' (1022 – 9 weeks post-surgery)*

These patients were being closely monitored, and described how the surgery had impacted their quality of life:

> *'Due to my surgery I had a collapsed lung. It does affect your breath and whatever, so even now I still do get out of breath coming up and down the stairs and things like that. So I'm going back after peak time when things are a bit quieter, and I can settle back into work.' (1030 –11 weeks post-surgery)*
> *'I have some pain in my sternum which will happen with any open-heart surgery, they have to wire you up… It is a very up and down recovery. They told me that it can be quite painful. I am incredibly frustrated by it going backwards, I am fine…my first 3 weeks were absolutely text book and then the sternum pain hit me. It is difficult. But they did warn me that there are complications with recoveries.' (1025 – 7 weeks post-surgery)*

Despite this, they remained positive about the procedure and were optimistic that they would make a good recovery:

> *'I would recommend having the Ozaki over the other ones to be honest with you, I feel the metal one there's a lot more risks involved. When you get through the initial surgery, 'cause it is longer and obviously is a bit more invasive, I think when you come out of it you're a lot better for it.' (1030 – 11 weeks post-surgery)*

Summary of initial results:

- The Lotus utilises multiple methods to understand how innovation is occurring. The Ozaki procedure is one of the nine procedures that Lotus has studied in-depth. Studying innovation in real-time is novel and enables in-depth and contemporaneous insights. We have also found that it is acceptable to staff and patients to use qualitative methods to study the procedure.
- This report provides the findings of post-operative interviews with 12 patients who had recently undergone the Ozaki procedure. The findings are preliminary and subject to further iteration as data analysis is still ongoing. Nonetheless, it provides important insights into patients' short-term experiences of recovery.

- Overall, patients' experiences of recovery and their quality of life varied considerably. Several patients reported a straight-forward and positive recovery. Conversely, others described the ways that the procedure had impacted their quality of life and several patients had experienced complications and were being closely monitored.
- It is important to note that these interviews were conducted relatively soon after surgery (range= 9 days-11 weeks). Therefore, it is imperative that further research is conducted to understand longer term outcomes and experiences. Furthermore, due to the observational nature of the research, we cannot determine patients' quality of life prior to surgery to more accurately understand experiences of recovery.
- Analyses of other data collected in Lotus regarding modifications, patient information and surgeon feedback meetings will be available in the next few months.

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