National Institute for Health Research (NIHR)
Research for Patient Benefit

Final Report Form

IMPORTANT

All projects funded through the Research for Patient Benefit programme are required to submit a report at the end of the funding period in order to:

- Ensure accountability
- Provide quality assurance
- Aid in appropriate dissemination of project results
- Understand the anticipated impact of the research
- Demonstrate the achievements of the research

The report must be a concise, standalone summary of the research; hence including large amounts of copied material should be avoided.

You will also be required to submit a final statement of expenditure at the same time as your report.

Information contained in this report and any related document(s) is of great value as it allows us to review and assess the outcome and outputs of the research we fund. This enables us to ensure that research has been carried out in accordance with our programme objectives and is vital for future planning and strategy setting.

Unless otherwise agreed, a draft report must be provided within two weeks of the project end date. Failure to submit may cause the final payment to be delayed.

The NIHR is committed to making the findings of the research that it funds publicly available. This report or sections thereof, in particular the scientific and plain English summaries, may be published, considering confidential and commercially sensitive information.

For office use only

Region London

Date submitted

1. Project Details

Project Title: Trans-cervical balloon catheter and its comparison to sustained release prostaglandin use for out-patient induction of labour in low-risk women: A feasibility study for a randomised controlled trial.

Reference Number: PB-PG-0815-20022

Contracting Organisation: St George's University Hospitals NHS Foundation Trust

Approved Duration: 24 months Current Duration: 24 months

Extension: 0 months

Start Date: 01 April 2017

End Date: 31 March 2019

Original Award: £216,329.00 Current Award: £216,329.00

2. Chief Investigator

Title: Dr.

Surname: Bhide Forename: Amarnath

Role in Project: Chief investigator, Primciple investigator at St. George's Hospital

Organisation: St. George's Hospital, London

Email Address: abhide@sgul.ac.uk

3. Research Team

Co-investigator 1		
Title: Professor	Surname: McCourt	Forename: Christine
Organisation: City University, London		
Role in project: Co-applicant, Qualitative researcher		
Co-investigator 2		
Title: Dr.	Surname: Sedgwick	Forename: Philip
Organisation: St. George's, University of London		
Role in project: Statistician		
Co-investigator 3		
Title: Dr.	Surname: Barrett	Forename: Barbara

Organisation: King's Clinical Trial Unit		
Role in project: Health economist		
Co-investigator 4		
Title: Ms	Surname: Linton	Forename: Sandra
Organisation: St. George's University Hospital Foundation Trust		
Role in project: Midwife		
Co-investigator 5		
Title: Dr	Surname: Griffin	Forename: Sharon
Organisation: Medway University Hospital		
Role in project: Principle investigator, Medway		
Co-investigator 6		
Title: Ms	Surname: Goode	Forename: Rosie
Organisation: Hypnobirthing works		
Role in project: Patient representative and co-applicant on the grant application		
Co-investigator 7		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 8		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 9		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 10		
Title:	Surname:	Forename:
Organisation:		

Role in project:		
Co-investigator 11		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 12		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 13		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 14		
Title:	Surname:	Forename:
Organisation:		
Role in project:		
Co-investigator 15		
Title:	Surname:	Forename:
Organisation:		
Role in project:		

4. Involvement of NIHR Infrastructure

Please indicate which NIHR Infrastructure organisations were involved in your research.

☐ HTCs	☐ INVOLVE	☐ NOCRI
☐ BRC/BRUs	☐ DECs	☒ CTUs
☒ CRFs	☒ CRN	☐ Other

Please describe the role of each organisation in your research. (***500 words***)

King's CTU provided online randomisation services. It also built the database, maintained the online database to allow data entry and provided data extracts including final extract. South London clinical research network provided midwifery support at Medway Hospital for screening and consenting potential applicants.

5.Changes to Research Team

Please outline any changes that have been made to the research team over the course of the research, including an explanation of why they were required (***750 words***).

Sponsor Representative changed from Debbie Rolfe to Subhir Bedi in May 2018 as Debbie left her position within the Joint Research & Enterprise Office (JRES), St George's Hospital, London.

Regulatory Support Office changed from Sue Cromarty to Joana Sequeira in February 2019 as Sue left her position within the JRES, St George's Hospital, London.

Research team involved in recruitment and follow-up of participants in SGH site started with Amar Bhide (CI), Asma Khalil (Deputy PI), Gina Cupples (Research Midwife (RM)), Louise Shaw (RM), Jessica Davy (RM), Emily Marler (RM), Jude Davies (RM), Yaa Acheampong (RM), Danielle Hake (RM), Nicola Bishop (RM), Helen Perry (Clinical Research Fellow) and Toni Barakova (Clinical Fellow). T. Barakova was replaced by Athenesios Tzepelis (Research Fellow) in November 2017 as she left the trust. A.Tzelepis was replaced by Angela Vinturache (Clinical fellow) in February 2018 as he left the trust. Nicola Bishop and Louise Shaw left for maternity leave in December 2018 and Sophie Robinson (RM) was added to the team in January 2019. H. Perry and A. Vinturache left the trust towards the end of 2018 and Becky Liu (Clinical Fellow), Rosie Townsend (Clinical Research Fellow) and Mohamed Elsayed (Clinical Fellow) joined the team in January 2019.

There were no changes to the research team at Medway site or the City University research team.

6. Scientific Summary

Please provide a structured summary of your work, covering the following points concisely:

- Background
- Original objective(s)
- Methods (including patient and public involvement and, if applicable, study registration number, e.g., ISCRTN and/or PROSPERO)
- Key findings
- Outputs, impact and dissemination
- Conclusions
- Future plans

This summary may be made publicly available, therefore please do not include any information that is confidential or commercially sensitive at the time of submission. If you are in any doubt, please contact your NIHR programme team (***500 words***).

Background – The rate of induction of labour (IoL) has increased steadily over the last decade. Out-patient IoL is considered feasible but there is insufficient evidence about women's preference, or which intervention is the most effective and safe to use in outpatient settings.

Original objectives – The primary objective was to assess the feasibility of conducting a randomised controlled trial (RCT).

Methods - An open-label feasibility RCT (Registration Number: NCT03199820) was conducted in two UK maternity units from October 2017 to March 2019. Women aged ≥16 years, undergoing IOL, ≥37 weeks' gestation, able to give informed consent and deemed suitable for out-patient IoL according to local guidelines were considered eligible. They were randomised to cervical ripening balloon catheter (CRB) or vaginal dinoprostone (Propess). The participants completed a questionnaire and a sub-group underwent detailed interview with a qualitative researcher. Health economics data were collected.

Key findings - During the study period 274 eligible women were identified 230 (83.9%) were

approached for participation in the study of whom 106 (46%) declined participation. In total, 84 women (36.5%) agreed of whom 38 were randomised to dinoprostone (n=20) and CRB (n=18). The intended sample size was not reached due to restrictive criteria for suitability for out-patient IoL.

The intervention as randomised was received by 30/38 (79%) women. Seven of the 38 participants never went home after intervention. Spontaneous vaginal delivery was observed in 9/20 (45%) women in the dinoprostone group, and 11/18 (61%) women in the CRB group. Severe maternal adverse events were recorded in one woman in each group. All babies were born with good condition (5-minute Apgar score >7). The majority of babies (37/38, 97.4%) remained with the mother after delivery. No deaths were recorded.

Full health economics data were available for 36 out of the 38 participants. The service use questionnaire was found to be easy to complete from patient records and the completeness of the data was excellent. 21% of women in the dinoprostone group were readmitted prior to diagnosis of active labour compared to 12% in the CRB group. The biggest difference in resource use was with the mode of birth and the cost was lower by £508.81 for the CRB group.

The patient questionnaire was complete and available for analysis for 37/38 (97.4%) women. Interviews were undertaken for 21/38 women. The interviews suggest that the possibility of not having hormones for IoL was a key reason for participation. Women randomised to Dinoprostone stated varying levels of disappointment. Women were more positive about CRB because it did not involve hormones and appeared a more gentle intervention for IoL.

Output, impact, dissemination - Publication of the study findings, informing pregnant women of their choices, organising dissemination events.

Conclusion - The study is not feasible using existing criteria and that further modifications to the eligibility criteria for out-patient IoL would be needed to make it feasible. Women agreed to randomisation. They were positive about mechanical methods and experiencing starting IoL at home.

Future plans – Larger observational study to assess safety of out-patient IoL.

Keywords (up to eight):

Provide up to eight key words in alphabetical order, which accurately identify the report's purpose, method and focus. Please use the Medical Subject Headings (MeSH®) thesaurus headings where possible.

https://www.nlm.nih.gov/mesh/MeSHonDemand.html

Labour, induced; Cervical ripening; Randomised controlled trial; Cook cervical ripening balloon; Outpatients

7. Plain English Summary

Please provide a plain English summary of your research including where appropriate:

- Aims and objectives
- Background
- Methods
- Key findings
- Dissemination, outputs and impact
- Patient and public involvement
- Conclusions and future plans

A good quality plain English summary providing an easy to read overview of your whole research will help:

a) inform others about your research findings such as members of the public, health professionals, policy makers and the media
b) the research funders to publicise the findings.

It is helpful to involve patients / carers / members of the public in developing a plain English summary.

The plain English summary is not the same as the scientific abstract - please do not cut and paste this or other sections of your application form to create the plain English summary.

Useful links:

INVOLVE http://www.invo.org.uk/resource-centre/plain-english-summaries/

Access to Understanding: http://www.access2understanding.org/guidance/

The Plain English Campaign guide on medical writing: http://www.plainenglish.co.uk/free-guides.html

(***300 words***)

Labour is a natural process, but sometimes it needs to be started artificially (Induction of labour). We compared two methods of preparation for labour induction in low-risk women at term. The first method uses dinoprostone, a synthetic hormone administered as a pessary (Propess) introduced in the vagina that delivers prostaglandin over 24 hours. The second is a catheter - a soft rubber tube with an inflatable balloon at the tip. The balloon is placed in the cervix causing it to soften and release natural hormones (prostaglandins) produced by the woman's body. The aim was to assess the feasibility of conducting a randomised controlled trial (RCT) by exploring if the methods are acceptable to and favoured by women and also explore safety and cost. We invited low-risk pregnant women at term, and who needed their labour to be started artificially to participate in this study. After obtaining consent, women were randomly allocated to one of the two methods. Women were asked to complete a questionnaire about their experiences, and a sub-group were invited for an interview with a researcher. Information regarding the use of resources was also collected. The study was conducted in two UK NHS maternity units over 18 months. Approximately one in three eligible women agreed to participate in this trial. 274 suitable women were identified. Out of these, 230 (83.9%) were approached for participation in the study. Of these 230 women, 84 (36.5%) agreed to participate and 38 were randomised. Women were positive about experiencing the early stages of induction at home. Treatment allocation at random was acceptable. All babies were born with good condition and all, except one, were transferred to the mother after delivery. Severe complications were reported only in a small minority. The results demonstrate willingness of women to participate in a trial.

☒	Please tick the box if this section of the report has been written with members of the public who have been involved in the research.

8. Aims and Objectives

Please describe the original aims and objectives of the research (***250 words***).

The primary objective of the study was to assess the feasibility of conducting a randomised controlled trial.

Secondary objectives were

- to assess the clinical efficacy, cost effectiveness and safety of trans-cervical balloon catheter compared to Prostaglandins (Propess) for out-patient induction of labour in low-risk women,

- to determine women's willingness to be randomised

- to determine the acceptability of using the balloon catheter

- to collect pilot data to plan an appropriately powered randomised controlled trial based on key clinical variables

- to pilot data collection instruments for economic evaluation

- to examine women’s views on out-patient induction of labour

- to assess women's experience with these methods and their preference.

9. Changes to Aims and Objectives

If the aims and objectives changed, please explain in what way and why (***250 words***).

The aims and objectives have not changed during the study period.

10. Description of Research

Please provide a structured summary of your work using the subsections below.

Background (*500 words*)

Describe the problem that was addressed and why this research was important at the time, based on existing evidence.

Methods (*500 words*)

Describe the methods you used to carry out the research and detail any changes from the original plan.

Findings (*1500 words*)

Describe the research findings, detailing how specific objectives, milestones or deliverables were met. If you have not met any of your objectives, please explain why and what measures were taken.

Conclusions (*500 words*)

Describe the conclusions that you can draw from the research findings.

Background -

Over the last decade the rate of induction of labour in the UK has increased steadily to approximately 20% of all pregnant women. Currently, most women undergoing induction of labour are admitted to the hospital prior to commencing IoL. A Cochrane review assessing methods of outpatient labour induction concluded that it was feasible in outpatient settings. However, there is limited evidence as to which induction methods are preferred by women, or the interventions that are most effective and safe to use in outpatient settings. A Cochrane review reported that mechanical methods (trans-cervical balloon catheter) of cervical ripening for induction of labour are as effective as vaginal prostaglandins (Jozwiac et al, 2012). The UK Database of Uncertainties about the Effects of Treatments (UK DUETs) identifies mechanical methods of labour induction as a known uncertainty, and recommends that future studies on mechanical methods for IoL should have larger sample sizes and report on substantive outcomes. The authors reported that the out-patient group had shorter hospital stay prior to birth while vaginal birth rates, total induction to delivery time and total inpatient times were similar. An economic analysis comparing mechanical methods to prostaglandins for cervical ripening, in an outpatient setting, would be beneficial. A recent trial showed that for women with an unfavourable cervix at term, success of induction of labour with a mechanical method is similar to induction of labour with progstaglandins, with fewer maternal and neonatal side-effects, but similar Caesarean section rates (Jozwiac, 2011). Furthermore, (Pennell et al, 2009) reported lower pain scores with the use of mechanical method, as compared to prostaglandins. Both studies were apparently undertaken in an in-patient setting. The OPRA study (Wilkinson et al, 2014) compared clinical outcomes from outpatient with inpatient prostaglandin treatment for low risk labour induction. They concluded that uterine stimulation following prostaglandins may preclude a woman from going home or remaining at home overnight, and may not be the best agent for outpatient ripening. Therefore, it would be beneficial to compare outpatient outcomes of prostaglandin treatment with mechanical methods to determine the most suitable agent. The prostaglandin method is the standard practice for induction of labour at St. George's Hospital, Tooting and Medway Hospitals, Kent. Although the mechanical method is used in some UK hospitals, outpatient use is not common. The Hospital Episode Statistics (HES) database does not record the exact method of induction of labour, nor collect data on efficacy, cost-effectiveness, hospital stay or outcome of labour induction stratified according to the method of induction of labour. Therefore, there

is no readily available data source that can be used to obtain information on the outcomes of induction of labour using mechanical methods in the outpatient setting.

A feasibility trial is therfore required before embarking on a randomised controlled trial. It would permit collection of the variables of interest with sufficient precision and help design a future randomised controlled trial.

Methods –

An open-label RCT (Registration Number: NCT03199820) was conducted in two UK maternity units: St Georges University Hospitals NHS Foundation Trust, South London (October 2017 to March 2019), and Medway Hospital, Kent (February 2018 to October 2018). Inclusion criteria were women aged ≥16 years, undergoing IOL, ≥37 weeks' gestation, intact membranes, able to give informed consent and deemed suitable for out-patient IOL according to local guidelines.

Written information was provided to women regarding the available methods: IOL with sustained release dinoprostone (Propess), or cervical ripening balloon (CRB), both in out-patient setting. Strict eligibility criteria have been developed against which research midwives screened for eligible participants and a medical practitioner confirmed that eligibility was met. An online randomisation service was developed by King's Clinical trial Unit (KCTU). Randomisation was stratified by site and parity using variable block sizes (two and four). A trained member of the study team screened for eligibile participants, explained the study, obtained consent, and entered the data to a secure website which returned a randomisation code. The researcher then administered the treatment method. Following this, clinical care was provided by clinical healthcare practitioners.

Participant demographics, clinical and patient-reported data were collected using an online database developed by KCTU. Feedback was sought from potential partcipants through verbal responses and decliners' questionnaires to gain data on women's willingness to be randomised.

The participants completed a questionnaire and a sub-group underwent detailed interview. Purposive sampling was used whereby all women who took part in the RCT were invited to an interview at least four weeks after the birth. Partners were also invited. An interview guide facilitated semi-structured interviews. Interviews were recorded and transcribed verbatim and rendered anonymous. An interpretivist approach with the intention of understanding women's lived experiences of IOL was adopted. Data were analysed using thematic framework analysis with an inductive/deductive approach.

The purpose of the health economic component was to pilot a data collection instrument for use in a future RCT and to conduct an exploration of the cost of the interventions under evaluation. A data collection instrument was developed according to the standard methods for economic evaluations. All relevant resources were identified via a literature review and from lists developed in collaboration with the clinical research team. The best way to measure these resources was also examined and a data collection instrument was developed. The efficacy of the instrument was judged by the ease of completion by the research staff and it's ability to provide the data needed to generate costs for a full economic evaluation.

The method for estimating the cost of the alternative interventions for this study required work in a feasibility stage because of the need to capture all aspects of induction. Service-use data were reviewed in order to establish the most accurate approach to estimating the cost and alternative methods were compared. The options for sources of unit costs for the intervention and associated resources were also explored, making use of nationally available costs and optimising links with the service use data.

Findings –

Participant characteristics at randomisation – The women had a mean height of 168.9 cm, mean weight 69.1 Kg, and mean BMI 24.2 kg/m2. 25/38 (65.8%) women were nulliparous. The majority of women (29, 76%) were of white European ethnicity. The mean age of women in the dinoprostone group was 34.1 years, compared to 33.2 years in the CRB group. The median Bishop score at study entry for both groups was unfavourable (dinoprostone: 4; CRB: 3).

Feasibility outcomes – In a period of 18 months (16/10/2017 to 31/03/2019), (2167 + Data from Medway not yet available) women underwent IOL and 274 women were found to be eligible for inclusion according to local criteria for out-patient IOL. The recruitment rate was 2/month/site. Of these 230 (84%)

were approached for participation in the trial, of whom 106 women (46%) declined. Reasons for declining participation were preference for a particular method or women not keen on induction of labour itself. During the study, the investigators noticed a shortfall of eligible women. Therefore, inclusion criteria were widened in 2018 at St. George's Hospital to include diabetic women who were originally excluded.

In total, 84 (36.5%) women gave consent to participate. The remaining 40 women did not decline but did not give consent for various reasons. Overall, 38 of the 84 agreeing women were randomised for participation in the trial. 25 women underwent ARM rather than study intervention,13 women delivered and four were no longer eligible after providing consent but before randomisation. Therefore, of the 230 eligible women approached for participation, only 38 (16.5%) were randomised. Of those women randomised, eight (21%) did not receive the intervention they were originally allocated.

Clinical and patient-reported outcomes –

Maternal vital signs were within normal limits at baseline, post-treatment and at follow-up. No uterine activity was detected at baseline in either of the two groups. The device (vaginal pessary or balloon catheter) was expelled only in a minority (4/38, 10.5%) of women. Seven of the 38 participants never went home after intervention. Epidural use for labour analgesia was reported by 20/38 (52.6%) of women. Delivery was by Caesarean section in 14/38 (36.8%) women. Median gestational age at delivery was 41+6 weeks. Median birthweights were similar between groups (Dinoprostone: 3675 gm; CRB: 3670 gm). All babies, except one (37, 97.4%) were transferred to the mother after delivery. No maternal or fetal deaths were recorded.

Health economic outcomes - All unit costs were for the financial year 2017-18. The service use questionnaire was found to be easy to complete from patient records and the completeness of the data was excellent. Monitoring over the data collection period ensured that all relevant resources were included.

Full data at follow-up were available for 36 of the 38 randomised women. In the Dinoprostone group 21% of women were readmitted prior to diagnosis of active labour compared to 12% in the cervical balloon ripening group. The biggest difference in resource use was the mode of birth; nearly two thirds (65%) of the women in the cervical balloon group had a spontaneous vaginal delivery, compared to 42% in the Dinoprostone group. The rates of caesarean section were also lower in the CRB group (12%) compared to the Dinoprostone group (43%).

The cost of induction and readmission prior to delivery were similar between the two randomised groups. However, it is the difference in mode of delivery that generated a substantial difference in total cost between groups; the cost of delivery in the CRB group was on average £2753.53 (SD = 717.04) compared to £3254.16 (SD =1023.94) in the Dinoprostone group generating total costs of £2880.82 in the CRB group and £3389.63 in the Dinoprostone group. Thus, the cost was lower by £508.81 for the CRB group.

Qualitative findings

Twenty one women and three partners took part. Interviews took place between April 2018 and March 2019. Most women (19/21) chose to be interviewed at home and two took part by telephone. Interview duration varied between 18 and 52 minutes.

Women's willingness to be randomised

Data were collected on reasons for declining participation. Overall, 93 women supplied decliners' data with 23 women completing a decliner's questionnaire and 70 women providing verbal responses. The most common reasons for declining to take part were: preferring to have inpatient IOL (24%); declining IOL by any method before 42 weeks (24%) and preferring to have PGE2 pessary (20%).

Data from the qualitative interviews suggest that the possibility of not having hormones to start IOL was a key reason why women took part. Other prominent reasons for participating in the trial included were being able to experience the outpatient IOL and contributing to progress in healthcare.

Following consent, women were aware that they could receive either treatment as all women

considered that the trial processes had been explained to them clearly. It should also be considered that those who consented to the trial at St George's (17/21) would not be able to have the balloon unless participating in trial due to local IOL policy. Many women who were randomised to PGE2 stated varying levels of disappointment. This included feeling disappointed although they knew treatment allocation was random and therefore not certain yet recovered from the disappointment quickly ("It would have been nice but never mind" P08), plus feeling that labour started negatively because of not receiving the balloon.

Acceptability of using the balloon catheter

Women's interviews revealed that few women had prior knowledge of the balloon. One had been informed about the balloon through discussion with the midwife about the trial; they were positive about CRB because it did not involve hormones and appeared a more gentle first IOL intervention.

Four women reported that insertion of the balloon was uncomfortable although not painful. However, for three women the insertion and/or the balloon being in place was a painful experience. This pain continued for two women until they had the balloon removed 24 hours later. Most women reported having the balloon removed was painless and quick. In one woman the balloon fell out at home, leaving her unsure what this meant and what she should do about it.

Five women who had the balloon (including two who found insertion painful) said they would use the method in a future labour. It was largely perceived as a 'natural' way to start the IOL, and even though requiring an IOL, the women in this study wanted to start with a mechanical method as they perceived it as gentler. Contrastingly, all the women who had the pessary said that in a future labour they would either definitely try the balloon, or would take the advice of medical professionals about the current evidence. Women who perceived that the pessary had 'worked' still would prefer to try the CRB in future labours.

Women's views on out-patient induction of labour

All except one of the 21 women who participated in the trial and were interviewed, felt that going home would be beneficial to them. Six women did not go home after receiving the treatment, either because they changed their mind and did not want to, for example if their contractions felt too strong, or because they were recommended not to.

Home was largely viewed as a better place to be at the beginning of an IOL. Reasons why home was preferable fell into three categories. Firstly, home was more comfortable. The possibilities of having a bath, wearing as many clothes as desired, getting into comfortable positions that may not be possible in hospital, lying in one's own bed, and eating chosen foods were all appealing. Secondly, distraction was a strategy employed to get through the first stages of IOL and this was easier at home. Women could keep busy with their usual routines, including looking after older children, or watching television, listen to music or audiobooks, go shopping or walk or do gardening. Thirdly, support was easier to coordinate at home. Partners (and other family members) could all be present at home, could rest better with more space, whilst supporting older children and the mother in labour at the same time.

There were some perceived disadvantages to being at home. A number of women were concerned that the pessary or balloon might have become unplaced, or would not know what to do with it if it came out, or were uncertain whether the pain they were experiencing was 'normal'. However, women were comfortable with calling the hospital to check these matters.

With regards the transition to hospital, most women were not concerned about the time it would take to get from home to hospital, with most having a journey time up to twenty minutes. Time spent at home was variable. Of the 15 women who went home, three were there less than 6 hours whilst eight spent the full 24 hours. Women were clear on, and reassured by, the process of calling the hospital if they felt they needed to, and on the return to hospital. Some women experienced frustration on their return to hospital because of waiting to park, to be seen or getting a room rather than waiting on the ward.

Conclusions –

The number of women eligible for out-patient induction was much less than anticipated. This was the main reason why the desired sample size was not reached. Another reason for under-recruitment was also understaffing and not having the midwife(s) available to screen women every day. Suitability of out-patient induction is dependent on the local criteria. Units with restrictive criteria will have a limited number of women deemed suitable for out-patient induction of labour. A widening of inclusion criteria would increase numbers of women who could be offered out-patient induction of labour. The study is

not feasible using existing criteria and that further modifications to the eligibility criteria for out-patient IoL would be needed to make it feasible.

Approximately a third of all eligible women (84/230, 36.5%) are prepared to participate in a trial where the method of induction of labour in the out-patient setting (dinoprostone or CRB) is chosen at random. The possibility of not having hormones to start IOL was a key reason why women took part. Less than 50% of eligible women declined to participate and the most common reasons for declining to take part were preferring to have in-patient IOL, declining IOL by any method before 42 weeks plus preferring to have PGE2 pessary. Some women declined participation because they had not previously heard of cervical balloon catheter as a method of labour induction. A better education may remove this obstacle and provide eligible women with a wider choice.

A majority of women received the intended intervention and were able to go home, with variable time periods. Delivery was by Caesarean section in 14 (36.8%) women. All babies were born with good condition and only one baby was not transferred to the mother after delivery. Severe complications were reported only in a small minority.

Women were positive about CRB because it did not involve hormones and appeared a more gentle first IOL intervention. Women in the pessary group would prefer to try the CRB in future labours. The vast majority of participants felt that going home would be beneficial to them. The reported advantages of staying at home in the initial stages of IoL included increased comfort, ease of using distractions as a strategy for coping with pain, plus better coordination of help and support. More than 50% of the interviewed women could spend 24 hours at home after starting IoL. However, not all women who desired to go home, could go home.

This trial is acceptable to women and clinicians and can be performed with the developed recruitment and follow-up processes. Collection of health economics data is possible. Although the sample size was very small, no major adverse events were reported relating to the use of either Dinoprostone or cervical balloon catheter for induction of labour in the out-patient setting.

11. Intellectual Property, Commercialisation and Clinical Adoption

Beyond Publications listed in the section above, please provide brief details of IP outputs arising from this research. The term 'IP outputs' refers to any tangible product of the research, not just academic publications. Outputs can include but are not limited to:

- Guidelines (clinical, service or otherwise);
- Copyright (e.g. questionnaires, training aids, toolkits, manuals, software, etc);
- New or improved design of medical devices or instrumentation;
- New or improved diagnostic;
- Trial data that could be used to support a CE mark, market authorisation or equivalent;
- Trial data that could be used to shape or influence a healthcare market or government;
- Potential new drug or healthcare intervention.

If these outputs are different to those anticipated at the start of the research, please briefly outline the reason for any changes.

If you filed any patents as a result of this research, please include the title, number, territories and the current status (pending, published, granted), and outline your further patent strategy, including key territories where protection will be sought. If you have conducted any freedom to operate searches, please describe the results and provide details on who carried them out and when, and explain whether or how they have influenced your research strategy.

Outline the ownership arrangements for the IP outputs arising from the research, and highlight any changes to the original plan. Describe the process by which the research will enter the healthcare environment, including how your IP outputs will be acknowledged, selected and introduced for use in the health and care service or wider society. Where possible consider how the work will be able to be adopted and implemented longer term. Please describe the proposed route to market (commercial or non-commercial) for your IP outputs. Describe who is needed to take it forward and the relationship you currently (or propose to) have with these parties. If your IP outputs are likely to be commercially

exploitable, please include details on how you plan to develop this.

Consider what investment or support is be needed for the next steps in this research to maximise impact (e.g. from NIHR, other Government departments, charity or industry), and explain what such funding would enable.

Describe the difficulties which may be faced in generating impact from your research. These may be difficulties you will face yourself, or challenges faced by those in the implementing context (eg. clinicians). For example:

a) Did the research use data, technology, materials or other inventions that are subject to any form of intellectual property protection (e.g. copyright, design rights, patents) or rights owned by another organisation(s)? If yes, provide brief details of how such third party IP was accessed (e.g. collaboration agreement, drug supply agreement) and any restrictions this may place on future research and/or dissemination/exploitation.
b) What are the key current and future barriers to uptake of any IP output directly in the health and care service, through commercial exploitation or other means, e.g. potential regulatory hurdles?
c) What are the challenges for getting your research implemented in terms of acceptability, accessibility and feasibility? How will you address these?

Please remember that you are contractually obliged to notify NIHR of any plans to enter into commercial agreements. *Please discuss any such plans with the appropriate support function at your institution (e.g. Technology Transfer Office or equivalent) (**1000 words**).*

12. Actual and Anticipated Impact

Please provide a brief impact statement. This should describe the immediate impacts of the study, or the anticipated longer term impacts, i.e. what has changed or what is likely to change as a result of the research and what will the benefit be, for example:

'Our evidence indicates that if this intervention was implemented by the healthcare system then the average patient care costs would be reduced by £x, and the burden of the disease for the people with this condition would be reduced by xxx.'
or
'Our evidence will inform the development of policy to respond to the needs of xxx group of patients/public/healthcare sector.' (***100 words***)

Women consider mechanical methods of IoL favorably as they do not use artificial hormones. A large majority of women intended to go home after starting outpatient IoL process are able to go home, and over half can be at home overnight. Women identify many advantages of being at home, but a small minority prefer to stay in the hospital. A randomised controlled trial of outpatient IoL is feasible.

At one of our PPI events, two trial participants contributed to the project design and suggested breastfeeding and partner acceptability as secondary outcomes in a recently funded study (NIHR127569 [CHOICE Study]).

Describe the impact the research has already achieved or might achieve in the short, medium and long term.

This can include impact on current NHS priorities, clinical guidelines, patient benefit, service provision (for e.g. cost, staff time, hospital bed days, value for money etc), current practice, scientific advances and implications for policy.

Describe who has benefitted from the research activity. Clearly identify who or what user groups were affected as a result of this research. Where possible, give an indication of the size and scale of the different user groups (e.g. less than 1k, over 1m, etc).

Indicate the anticipated timescale for the impact(s) to reach patients/the NHS or the public, providing a quantitative estimate of the scale for these potential benefits, and the extent (e.g. local, national, regional) if possible.

Describe any wider mechanisms/approaches that were used to achieve impact, for example, knowledge engagement, knowledge translation, on-going dialogue with end users/stakeholders.

For research emphasising a clear trajectory into practice, it is important not to 'overclaim' and care should be taken to cover the limitations of the study and any risks associated with implementation.

This should be a comprehensive and realistic, stand-alone summary of the impact of the work. If you include health economic information, please specify the value of the QALY used.

Where actual impact has been achieved, please provide evidence.

NOTE: Negative, definitive findings that could inform disinvestment are also of value. (***750 words***)

13. Dissemination

NIHR is keen that the findings of the research it funds are disseminated effectively to patients, the public, the NHS and the healthcare and research communities.

Please describe how you have disseminated your research findings and what your plans for further dissemination are. Describe your publication strategy (note that individual peer-reviewed publications will need to be listed under Section 12) and describe any major communication and public engagement activities here, including academic workshops and conference presentations, feedback to research participants, meetings or discussions with policymakers or healthcare professionals, and media coverage (***450 words***).

To date, the research team has already taken several steps to disseminate the findings. A PPI event was organised locally (in the antenatal ward at St George's Hospital, London) to invite participants from the trial and anyone interested in the research (including pregnant and labouring women and midwives). Findings of the trial were presented by the team and trial participants openly discussed their experiences. The event was split into three parts: the first part consisted of a quick overview of the project and the summary of the key findings, presented by the research team. The second part consisted of an active discussion group in which mixture of attendees were encourage to discuss how they thought about the key findings. Finally, the third part of the conference consisted a summary of the discussion and focused on how the finding can be utilised in the everyday practice. The event provided an opportunity for participants to explore their experiences and provided a form of feedback and validity for the project team. A second PPI event / focus groups was hosted at City, University of London, where trial participants were invited to help design next-stage research in the area of outpatient IOL.

The study findings will be presented at academic and clinical conferences. An abstract for an oral presentation was presented at the Normal Birth Conference, Cumbria, June 2019, a multidisciplinary conference for academics, researchers, policy makers, clinical staff, service users, parents, and birth activists. A further abstract has been accepted by the Society for Reproductive and Infant Psychology Conference in London, September 2019, where a poster presentation will be provided.

We are preparing a manuscript reporting the main finding of the study in a peer-reviewed open access journal. We have published a systematic review and thematic analysis of women's experiences of induction of labour (Coates R, Cupples G, Scamell A, McCourt C. Women's experiences of induction of labour: Qualitative systematic review and thematic synthesis. Midwifery. 2019;69:17-28). We have drafted a publication of the findings of the postnatal qualitative interviews and plan to submit this to an open access journal for publication in the near future.

14. Publications

Number Published	1	Number in press	0	Number submitted	0	Number in preparation	2

Please provide a link or list here any peer reviewed journal publications which have resulted from the work; forthcoming items should also be included. Please also detail any awards and/or prizes received by the team as a result of undertaking the research.

NOTE: *You are contractually obliged to send one draft copy of the proposed publication to the Authority's Representative at the same time as submission for publication or at least 28 days before the date intended for publication, whichever is earlier. Any published paper directly associated with your award must comply with the NIHR Open Access policy and be made freely available.*

All publications must include the following funding statement:

"This report is independent research funded by the National Institute for Health Research (Research for Patient Benefit programme, PB-PG-0815-20022). The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care"

https://www.midwiferyjournal.com/article/S0266-6138(18)30311-5/abstract

15. Patient and Public Involvement

Please provide a summary of the patient and public involvement in this research using the following sub-headings:

- **Aim**
  Report the aim of PPI in the study
- **Methods**
  Provide a clear description of the methods used for PPI in the study
- **Study results**
  Outcomes – report the results of PPI in the study, including both positive and negative outcomes
- **Discussion and conclusions**
  Outcomes – comment on the extent to which PPI influenced the study overall. Describe positive and negative effects
- **Reflective/critical perspective**
  Comment critically on the study, reflecting on the things that went well and those that did not, so others can learn from this experience

The above list is the short version of GRIPP2 reporting checklist. For more information please visit the Equator Network's website.

If you did not have any PPI in the project, please explain why (***750 words***).

In our initial PPI activity, we had interviewed ten pregnant women to assess their feelings about acceptability to randomisation. Some women expressed their anxiety about not having any control over the method of labour induction. In our previous unsuccessful application, we had included patientpreference arms to the trial. Following the previous NIHR RfPB panel advise that patient preference arm did not add value to the research we held another meeting of the focus group, and explained the proposed study to pregnant women. We realized that the patients' acceptability to randomisation is greatly influenced by the way the study is explained to them. We found that randomisation was acceptable to the majority if properly explained. We also realize the importance of a structured and well-written participant information sheet (PIS). This document was circulated to our patient co-applicant, focus group members and midwives before finalisation, and their comments were useful for modification.

We hed a PPI event in January 2019. The aim of the PPI event held was to explore women's experiences of participating within the trial. Participants who had taken part in the PROBIT-F study, at the St George's Hospital site, were contacted via telephone to inform and invite them to the PPI event. Patients present within the maternity unit, on the day of the event, were also invited to attend. An agenda was developed for the event which included discussion on the experience of being a part of the study

from participants, research midwives and a qualitative researcher.

Two study participants attended the event. Both mentioned that their overall experience of the study was positive and that they felt well-informed throughout. Both participants received a cervical ripening balloon as their first method of treatment and reported that the insertion of the balloon was an uncomfortable experience. It was agreed by both that a support person being present for the procedure would be beneficial. Despite the insertion being uncomfortable, both would like to try this method of IOL again. The women reported that the reasons encouraging them to take part were the opportunity to have an outpatient IoL, the opportunity to have a mechanical method of induction of labour instead of artificial hormones and to "give back to the NHS". Three patients attended who were not participants of the study but were present within the maternity unit on the day of the forum.

The PPI event provided information on women's experiences of participating in the study. The study team could then use this information to improve and enhance the experience for future study participants. There was no representation of participants who were in the Dinoprostone treatment group, whose experience may have been different to those in the mechanical method group. However, feedback reported to the study team, from other participants, was discussed and also reflected some of the points which the present participants made. This suggests that the experiences of the participants present may have been consistent with the experience of other participants. The participants suggested that this was a valuable study as it is exploring a "drug-free" approach to outpatient IoL and they found it surprising this this was not available more extensively within routine care. The feedback is that the study aims and objectives are fitting with the desires of pregnant women.

A total of 5 patients attend the PPI event, 2 of which had participated in the trial and 3 of which were inpatients on the antenatal ward. The mixture of patient backgrounds may have affected the PROBIT-F participants willingness to be open about their experience of the trial. The patients who had not participated in the trial provided limited opinions on the study. This reluctance suggests a possibility these patients may have considered their insight to be less valuable than those who had participated. The agenda included an opportunity for the PROBIT-F participants to discuss their experience. Had we of encouraged non-participating patients to provide their thoughts on the study, we may have been able to expand our knowledge on the patient perspectives on the study from those who have no participated. Those who participate in the trial may not represent the pregnant population as a whole, as those who participated in this study may have a greater interest in the topic of induction of labour. Therefore, encouraging greater feedback from the other non-participant patients may have provided more representative feedback. The relaxed structure of the PPI forum appeared to encourage attendees to feel comfortable participating in discussion and allowed for quite extensive feedback to be shared.

☒	Please tick the box if this section of the report has been written with members of the public who have been involved in the research.

16. Future Research Plans

Please outline your next steps to maximise patient benefit or to further inform policy development/evaluation. If further research and development is needed, such as a definitive trial following a feasibility study, or a programme grant following preparatory work, include details on the likely funder and timetable for submission. If the output(s) from your research are largely commercial, describe the proposed route to market in Section 11 above.

If no further plans are thought necessary, please explain why this is the case (***750 words***).

The current study has shown that the options of induction of labour in the out-patient setting, and the use of mechanical methods for labour induction are acceptable to women. However, the current criteria for eligibility for out-patient IOL are restrictive, so that only a small minority of women undergoing IOL are found suitable for out-patient induction. The qualitative data from the current study shows that women were positive about CRB because it did not involve hormones and appeared a more gentle first IOL intervention. The vast majority of participants felt that going home would be beneficial to them.

A previously published study has shown that for women with an unfavourable cervix at term, success of induction of labour with a mechanical method is similar to induction of labour with progstaglandins, with fewer maternal and neonatal side-effects, but similar Caesarean section rates (Jozwiac, 2011). Pain scores are known to be lower in women using mechanical methods of labour induction in the in-patient setting (Pennell et al, 2009). The present study was not powered to explore differences in clinical outcomes, nor the safety of out-patient IoL. The intended sample size could not be reached due to restrictive local guidelines for out-patient induction of labour. The restrictions were made due to safety concerns about outpatient induction. To overcome this and provide the necessary safety data, a large observational study is necessary. Members of the current study team have been successful in securing funding for such an observational study (CHOICE study, NIHR127569). It is possible to make criteria for suitability of out-patient IoL more permissive if the safety of out-patient IoL is demonstrated with an observational study.

Comparison of clinical outcomes from outpatient with inpatient CRB treatment for low risk labour induction would be a useful study to assess the effect of the setting of IoL (out-patient versus in-patient). For such a study to be feasible, the criteria for suitability for out-patient IOL will have to be more inclusive and many more centres would be needed as the desired sample size will not be easy to reach.

17. Publication of Research Findings

The NIHR is committed to making the findings of the research that it funds publicly available. This report or sections thereof, in particular the scientific and plain English summaries, may be published, considering confidential and commercially sensitive information.We may wish to use the content of this form for contents on our website, to illustrate the work we have funded, share good practice, and make information about research more accessible to the public.

Please indicate if there is any information that you do not wish us to place in the public domain and explain why (***500 words***).

There investigators do not identify any restrictions on placing information from this study in the public domain.

18. Data Sharing

Making clinical data sets available to investigators beyond the original research team can improve patient care, advance medical knowledge and provide better value for money from health research.

Data generated through participation of patients and the public should be put to maximum use by the research community and, whenever possible, translated to deliver patient benefit. Data sharing benefits numerous research-related activities: reproducing analyses; testing secondary hypotheses; developing and evaluating novel statistical methods; teaching; aiding design of future trials; meta-analyses; and helping to prevent error, fraud and selective reporting.

Data sharing achieves many important goals for the scientific community, such as:

- Reinforcing open scientific inquiry.
- Encouraging diversity of analysis and opinion.
- Promoting new research, testing of new or alternative hypotheses and methods of analysis.
- Supporting studies on data collection methods and measurement.
- Facilitating education of new researchers.

Where applicable, please provide a statement about your data sharing and accessibility. It should provide a clear and positive indication:

- Where and when the data will be shared;
- Who can access the data:
- How the data can be obtained (***250 words***).

The trial essential documents along with the trial database will be archived in accordance with the Sponsor (Joint Research and Enterprise Office, St. George's, University of London) SOP

JREOSOP0016. The agreed archiving period for this trial is 15 years. The data will be available for sharing by contacting the Chief applicant. All the co-applicants will have access to the data. Publication policy has been documented in the project protocol. The sponsor should be contacted prior to any publication resulting from the project.

19. Post-Award Monitoring

Please be aware that all NIHR-funded research will be followed up for a period of five years after project completion. Your NIHR Programme Manager will contact you to agree a post-award monitoring plan, including the process and timelines. Our aim is to collect information about further research and development, any further funding obtained, commercialisation, publication and dissemination plans, and any impact achieved.

Please provide the name, address, phone number and email of the individual whom we can contact for post-award monitoring of this project. Usually this will be the Chief Investigator, however, another individual, for example a project manager, may be named instead.

"This report is independent research funded by the National Institute for Health Research (Research for Patient Benefit programme, PB-PG-0815-20022). The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care"