

Perineal resuturing versus expectant management following vaginal delivery complicated by a dehisced wound (PREVIEW): protocol for a pilot and feasibility randomised controlled trial

Lynn Dudley,^{1,2} Christine Kettle,^{1,2} Pamela Carter,³ Peter Thomas,⁴ Khaled M Ismail⁵

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For numbered affiliations see end of article.

Correspondence to
Professor Khaled M Ismail;
k.ismail@bham.ac.uk

ABSTRACT

Background: Each year, approximately 350 000 women in the UK experience perineal suturing following childbirth. For those women whose perineal wound dehisces, the management will vary according to individual practitioner's preferences. For most women, the wound will be managed expectantly (healing by secondary intention), whereas others may be offered resuturing. However, there is limited scientific evidence and no clear guidelines to inform best practice. PREVIEW is a two-part study aiming to identify the best management strategy for dehisced perineal wounds, in terms of clinical effectiveness and women's preferences.

Methods/design: The main part of this study is a pilot and feasibility randomised controlled trial designed to provide preliminary evidence of the effectiveness of resuturing versus expectant management for dehisced perineal wounds following childbirth and to feed into the design and feasibility of a larger definitive trial. 144 participants will be randomly allocated to either intervention. The primary outcome is the proportion of women with a healed perineal wound at 6–8 weeks from the trial entry. Secondary outcomes include perineal pain, breast feeding rates, dyspareunia and women's satisfaction with the aesthetic results of the wound healing at 6 weeks, 3 months and 6 months post randomisation. Information will be collected using validated questionnaires. The second part of this study will be to conduct semistructured interviews with 12 study participants, aiming to capture information relating to their physical and psychological experiences following perineal wound dehiscence, assess the acceptability of the research plan and ensure that all outcomes relevant to women are included in the definitive trial.

Dissemination: The results of this study will inform a definitive randomised controlled trial that will provide conclusive evidence of what is the best management of perineal wound dehiscence. This will potentially lead to significant improvements in perineal care and will help to reduce the short- and long-term morbidity experienced by women.

ARTICLE SUMMARY

Article focus

■ This article provides the rationale and protocol for a pilot and feasibility randomised controlled trial, designed to provide preliminary evidence of the effectiveness of resuturing of dehisced perineal wounds, versus healing by expectancy (secondary intention) and to feed into the design and feasibility of a larger definitive trial.

Key messages

■ This study addresses an area of clinical research that has been extremely neglected and has the potential of making a significant impact on women's health and well-being.

Strengths and limitations of this study

■ As both a pilot randomised controlled trial and a feasibility study, this research will test out many of the procedures that will be used to inform the design of a definitive trial.
■ As the definitive trial is likely to require many centres in order to meet sample size requirements, we may use this pilot to identify additional sites and also test out study procedures in those sites. Thus, the actual sample size might be larger than described here.

Clinical trials registration: PREVIEW is registered with the International Standard Research for Clinical Trials (no: ISRCTN05754020) and adopted as a National Institute for Health Research (NIHR) Reproductive Health and Childbirth specialty group portfolio study UKCRN ID 9098.

INTRODUCTION

Perineal trauma affects a vast amount of women both nationally and internationally with more than 350 000 women in the UK per

year needing stitches to facilitate healing of a spontaneous tear or episiotomy.¹ Given that the postpartum management of perineal trauma including the prevention of wound infection and assessing wound healing are core components of routine maternity care,^{2 3} there is limited research evidence available on the management and consequences of wound dehiscence. Furthermore, the available evidence is based on retrospective audit or case reviews and tends to include small numbers of participants hence is subject to bias. Anecdotal evidence suggests that the number of women reporting perineal infections and dehiscence in the community is increasing; however, systems to track these complications following hospital discharge are lacking. It is vital that a true estimate of the problem is established using standardised definitions of wound infection and at the same time determine best practice when treating dehisced perineal wounds. It is apparent that perineal wound dehiscence both locally and worldwide has not been a high priority either in practice or in research, and therefore, management is not based on robust evidence. Due to the lack of evidence-based guidelines, clinical practice varies widely between individual practitioners and institutions.

Perineal wound dehiscence, which is commonly reported to be associated with infection,^{4 5} may lead to major physical, psychological and social problems if left untreated. Although maternal mortality associated with perineal trauma is extremely rare in developed countries, an infected perineal wound is a potential route for systemic infection whereby sepsis and septic shock may ensue.⁶ Indeed sepsis has for the first time been identified as the leading cause of maternal mortality in the UK. The Centre for Maternal and Child Enquiries recently published their eighth Report on Confidential Enquiries into Maternal Deaths.⁷ The report revealed that during the 2006–2008 triennium, sepsis resulted in 26 direct maternal deaths with three further deaths classified as 'Late Direct Deaths' (occurring more than 6 weeks after delivery). Seven women died of sepsis following a vaginal delivery, including one woman with an infected perineum following a second-degree tear. The report clearly illustrates how healthy women with an uncomplicated pregnancy and delivery can become critically ill and die in a very short time.⁷

Moreover, morbidity associated with perineal wound dehiscence can and does pose a serious threat to the general well-being and quality of life of the new mother. Maternal morbidity centres around persistent pain and discomfort at the perineal wound site, urinary retention, defecation problems, dyspareunia and psychological and psychosexual issues from embarrassment and altered body image.^{2 8} Furthermore, the relationship with her newborn baby may become affected, and she may find difficulty in breast feeding due to the distress caused by her perineal problems.⁹

Perineal wound infection and dehiscence is a burden on NHS resources, as quite often women who suffer this

consequence of childbirth, have to undergo corrective surgery, perineal refashioning and excision of excessive scar tissue or other procedures associated with the management of perineal dysfunction.¹⁰

Members of our collaborative team conducted double iteration Delphi surveys in the UK and Brazil to identify childbirth-related perineal trauma outcomes deemed to be important by women.¹¹ These surveys consistently demonstrated that the highest ranked outcome was fear of perineal wound infection and delay in wound healing. Indeed, an outcome that appears to be prioritised by women across different backgrounds and cultures.

Rationale for PREVIEW

This study addresses an area of clinical research that has been extremely neglected and has the potential of making a significant impact on women's health and well-being. For those who suffer from dehisced perineal wounds, it can take up to 16 weeks to heal if treated expectantly and can leave the new mother feeling very traumatised. Some of these women may even request that the mode of delivery for subsequent pregnancies will be via caesarean section to avoid further perineal damage.

Currently, lack of established professionally agreed standards leave clinicians in equipoise as to what is the best management for dehisced perineal wounds following childbirth, hence supporting the need for a clinical trial to answer this question. As both a pilot randomised controlled trial (RCT) and a feasibility study, this research will test out many of the procedures that will be used to inform the design of a definitive trial. Although this is a pilot trial, the sample size is reasonably high ($n=144$), and in the absence of definitive trials, will contribute to the development of evidence-based best practice guidelines by policymakers, clinicians, patients and the public to develop, and to systematic reviews.

METHODS/DESIGN

Study design

PREVIEW is a pilot and feasibility RCT comparing resuturing versus expectant management for the treatment of dehisced perineal wounds following childbirth (figure 1).

The study will provide researchers with a unique opportunity to identify and prepare for the challenges and uncertainties of evaluating the clinical interventions within a larger RCT. Conducting this study will assess the acceptability of the study interventions to women, test the study protocol and facilitate a formal sample size calculation for the definitive study. Ultimately, it will enhance the scientific rigour and value of the full-scale study.

Setting

The pilot and feasibility RCT will be conducted in several maternity centres in the UK in order to assess likely recruitment rates and acceptability across different sites.

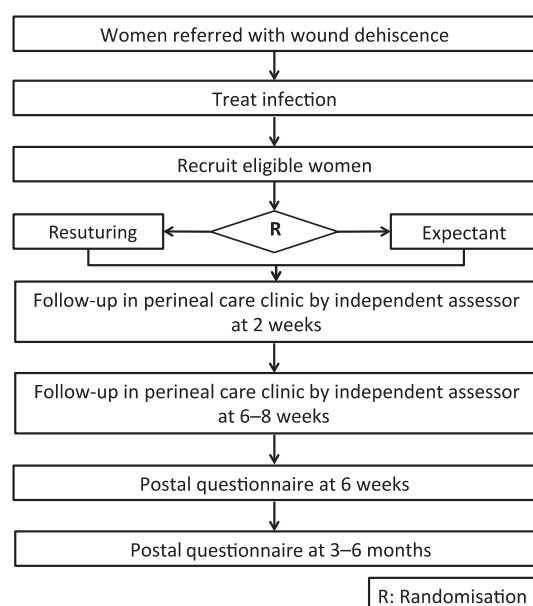


Figure 1 PREVIEW flowchart.

Study population, eligibility criteria

Women, who had a primary repair of a second-degree perineal tear or episiotomy, identified with a dehisced wound within 2 weeks following childbirth, in any of the recruiting sites.

For the purpose of the study, wound dehiscence is defined as separation of both the skin and muscle layers.

Exclusion criteria

- ▶ No valid written consent to participate in the study
- ▶ poor pregnancy outcome (women experiencing a pregnancy loss in current pregnancy)
- ▶ women younger than 16 years
- ▶ women who are considered by the anaesthetist to have an unacceptable anaesthetic, for example, complex cardiac anomalies
- ▶ due to financial constraints in relation to translation services, women who do not understand, read or write the English language will not be able to participate. However, a record of the number of these potential participants and their first language will be kept to help with project planning and resource allocation for the definitive study.

Consent and randomisation

Women eligible for the study will be provided with the study information leaflet, by their community midwife,

hospital midwife or obstetrician and they will be allowed time to ensure that they understand the information and clarify any queries they have. Women who subsequently do not wish to participate in the PREVIEW study will be managed in accordance with local hospital guidelines. Women will be enrolled into the study by a midwife or doctor who is fully aware of Good Clinical Practice guidance. A valid written consent will be obtained from women who wish to participate. The PREVIEW Study integrated web- or telephone-based randomisation, and its treatment allocation service was developed by the Bristol Randomisation Trials Collaboration. The allocation ratio will be 1:1, and randomisation will be in blocks, stratified by study centre. The study participants will be assigned to either resuturing of the dehisced perineal wound preferably within 48 h of randomisation or expectant management (allowing the wound to heal by secondary intention). With the woman's agreement, a letter will be sent to her general practitioner confirming trial entry.

Interventions

Secondary resuturing is being compared with expectancy (healing by secondary intention). Both interventions will be undertaken following trial standardised procedures (not submitted but available from the trial team).

To ensure the standardisation of secondary resuturing, the trial team have provided recommendations for both the methods and materials to be used (table 1). These recommendations are based on clinical expertise and knowledge and will be continually reviewed if new evidence becomes available.

Due to the nature of the interventions, it will not be possible to blind outcome assessors, care providers or participants themselves. Assessment of perineal wounds following treatment allocation, at the agreed time periods, will be undertaken by independent practitioners (ie, not part of the research team); however, it will not be possible to blind participating women, operators and assessors due to the nature of the intervention. Women allocated to the control arm will receive expectant management (current standard intervention), with no additional concomitant care or interventions.

Data collection

Standardised PREVIEW questionnaires are based on those used and tested by members of the research team

Table 1 Methods and materials for resuturing

Methods	Standard surgical procedures for secondary suturing should be followed, including wound debridement if needed
Vaginal mucosa	Continuous technique
Muscle	Interrupted sutures
Skin	Depending on the length of the wound, the skin could be sutured by interrupted or subcutaneous sutures or left unsutured if the edges are approximated by suturing the underlying tissues
Materials	To ensure standardisation of materials, the PREVIEW Study team recommend that standard synthetic polyglactin 910 (gauge 2/0) suture material should be used as the material of choice

in other childbirth-related perineal trauma studies.^{12 13} Participating women for the RCT will be reviewed at 2 and 6–8 weeks. The independent assessor will complete a perineal assessment questionnaire at each visit. For the secondary outcomes, all participating women in the RCT will be asked to complete a prepaid postal questionnaire at 6 weeks, 3 and 6 months following trial entry, respectively.

Data will be scanned into a bespoke database by the Market Research Group at Bournemouth University. By anonymising records and changing treatment allocation to a numeric code, the completed database will be supplied to the research team for analysis, carried out under the supervision of the trial statistician. In this way, analysis will be blinded.

In addition to the pilot RCT, a sample of women (n=12) who are participating in the RCT will be selected to represent age, parity, ethnicity and intervention. In-depth semistructured interviews will be conducted with written consent to capture information relating to their physical and psychological experiences following perineal wound dehiscence at 6–8 weeks following birth. The interviews will be taped, with permission, and transcribed.

Study outcome measures

Primary outcomes

- ▶ Proportion of women with a healed wound at 6–8 weeks following trial entry.

Secondary outcomes

- ▶ Pain at 6 weeks, 3 and 6 months following trial entry (randomisation)
- ▶ Dyspareunia at 6 weeks, 3 and 6 months following trial entry
- ▶ rates of breast feeding at 6 weeks, 3 and 6 months following trial entry
- ▶ woman's satisfaction with the aesthetic results of the perineal wound at 6 weeks, 3 and 6 months following trial entry.

Withdrawal from the PREVIEW Study

Participants may withdraw from the study at any time. Should they choose to withdraw, they will continue to be followed up, in line with current practice within the participating unit, but no further questionnaires will be sent. One reminder questionnaire will be issued to non-responders before they are deemed to have withdrawn. A record of the number of withdrawals will be kept and if applicable their reason for withdrawal.

Statistical issues

Sample size for the RCT

The current literature does not support a robust formal sample size calculation for the primary outcome of interest. One of the purposes of this pilot study is to collect data to inform a sample size calculation for

a full-scale RCT. Three aspects of informing this calculation are to estimate (1) the recruitment rate, (2) attrition rate and (3) the proportion of women whose wound had healed at 6–8 weeks (the primary outcome). Hence, in estimating the sample size of this pilot study, we attempted to ensure a sufficient degree of precision of these estimates (precision defined as twice the SE).

A retrospective study at the host research site has identified that there were 117 women referred to the perineal care clinic with a dehiscence perineal wound during a 4-year period (30 women/year). Hence, we estimate that there will be around 45 eligible women for recruitment per participating centre. Assuming that 45 women will be eligible per centre, with a take up rate of 80% and an attrition rate of 20% in four participating centres, we expect to recruit 144 women and 116 (58 in each arm) of these to complete the pilot study. This would allow for the recruitment rate in each site to be estimated with precision of $\pm 12\%$ (based on n=45), and overall recruitment rate to be estimated with precision $\pm 6\%$ (based on n=180). Loss to follow-up would be estimated with precision $\pm 7\%$ (based on n=144), and healing at 6–8 weeks (assumed to be around 50% from the retrospective study mentioned above) would be estimated to $\pm 13\%$ in each trial arm (based on n=58 per arm). Although the sample size is quite large for a pilot study, we feel that this is necessary in order for recruitment to start bedding down in each of multiple sites.

Estimating effect size is not a specific aim of this pilot, but nevertheless, it is still worth considering precision and power issues given the sample size of 116. Assuming that healing in the secondary intention group will be 50% at 6–8 weeks and that realistic percentages in the secondary resuturing group will be between 10% and 90%, the effect size for the primary outcome will be estimated with a precision of between $\pm 15\%$ and $\pm 18\%$. This will be fed into deliberations regarding plausible effect sizes to be used for future sample size calculations. It is worth noting that with this sample size, the study will have 90% power to detect an increase in healing from 50% to 80% (assuming a 5% two-sided significance level).

As the definitive trial is likely to require many centres in order to meet sample size requirements, we may use this pilot to identify additional sites and also test out study procedures in those sites. Thus, the actual sample size might be larger than described here.

Statistical analysis for the RCT

Recruitment and attrition rates (overall and at each site) and proportion with healed wound at 6–8 weeks will be calculated, and precision of these estimates expressed using 95% CIs. A series of sample size calculations for a definitive RCT will be performed incorporating these interval estimates.

A statistical analysis plan for a full-scale RCT will be developed from and tested upon the data from this pilot

study. We will test out the practicalities of ensuring that the person analysing the data is blinded to group allocation.

Primary analysis will be undertaken on an intention-to-treat basis to limit the possibility of bias associated with women not receiving the intervention they were allocated. Strategies will be developed to ensure that data on primary outcome are as complete as possible (eg, reminder letters and phone calls).

Comparisons will be made between the interventions (secondary repair vs expectant management). Baseline characteristics of the comparative groups will be summarised using standard descriptive statistics. The primary outcome is the proportion of wounds healed at 6–8 weeks; this will be compared between the two groups using a logistic regression model that incorporates study site as a variable (since randomisation was stratified by site). Precision of estimates of effect size (ORs) will be summarised using 95% CIs. The analysis plan for other outcomes will also be developed taking into account the type and distribution of data (eg, logistic regression, multiple regression). If the amount of missing data seems problematic (eg, over 20%), we will assess the robustness of the results by data imputation in tandem with best- and worst-case sensitivity analyses. In addition to looking at each time point separately, we will also test a repeated measures approach to analysis to try and gain insight to whether effect sizes are changing over the course of follow-up (ie, looking at the interaction between intervention group and time). It is anticipated that this will be implemented using a multilevel (mixed) model for binomial or continuous responses as appropriate.¹⁴ These models have the added advantage that they permit analysis of unbalanced repeated measures data, thus avoiding exclusion of participants with incomplete data. No additional a priori adjustment of covariates or subgroup analysis will be performed; these issues will be explored further in supplementary analysis as part of the development of the statistical analysis plan for the larger trial. No interim analyses are planned.

Qualitative analysis

Thematic analysis will be conducted using appropriate software such as N-Vivo. A sample of transcripts will be coded and analysed independently by two researchers and the emerging themes discussed to ensure reliability. While providing the researchers with an opportunity to research women's subjective experiences, the interviews will also offer valuable qualitative insight to aid understanding of the findings generated from the RCT.^{15 16} Additionally, this phase will provide a window of opportunity to view women's unique experiences of an aspect of childbirth, which would otherwise not be known and can facilitate improvement in practice.¹⁷

In relation to the pilot RCT, capturing qualitative data on women's views of the impact of perineal wound infection on their well-being, will help to ensure that the definitive trial captures outcome areas that are relevant

to women themselves. Likewise, it may help us to understand any barriers to participation before embarking on a full-scale evaluation.¹⁸

Patient involvement

Following guidance from INVOLVE,¹⁹ two patient representatives have been recruited to assist with the design of study materials, including the information sheet, trial questionnaires and the qualitative interview schedule. They are also members of the trial steering committee (TSC).

Ethical considerations and safety committee

The PREVIEW protocol has been approved by the North Wales Research Ethics Committee (Central and East), reference number: 10/WNo03/16.

The conduct of the trial at each recruiting site including confidentiality and storage of all personal and research data will be in accordance with all applicable research governance regulatory requirements.^{20–26} All recruiting maternity units will be required to sign a clinical trial agreement document detailing their commitment towards complying with the relevant laws, regulations, codes of practice and obligations to publication.

Site-specific and Research and Development approval is required for each recruiting unit and a Participant Identification Centre agreement is required from the Primary Care Trusts within the recruiting localities. The NIHR Primary Care Trust Research Network have also acknowledged their support for the study and have made a significant contribution towards communicating the study to Primary Care Trusts via individual Practice Managers within the locality of the recruiting sites.

A TSC will be convened to provide overall supervision of the PREVIEW Study and will adhere to the MRC's Guidelines for Good Clinical Practice.²⁴ Any deviations from the clinical trial agreement will be monitored by the TSC who will decide whether further action needs to be considered.

An independent data monitoring ethics committee (DMEC) will be convened for the PREVIEW Study by the sponsor and will act as an advisory committee to the TSC. The DMEC will be the only body involved in the study that will have access to the comparative data. The DMEC will consist of a minimum of three members and will include a statistician and a clinician with expertise in the field of perineal care. The role of the DMEC will be to monitor trial data and make recommendations to the TSC on whether there are any safety reasons why the trial should not continue, including monitoring evidence for treatment harm, for example, serious adverse events (SAE).

The safety, rights and well-being of the trial participants are paramount. The DMEC will consider whether any interim analysis is necessary, will consider data from any analysis and considers requests for its release and will then advise the TSC.

A standardised operating procedure for the DMEC has been developed specifically for the PREVIEW Study based on MRC guidance, the template produced by the DAMOCLES Study Group and the ICH Harmonised Tripartite Guideline, for Good Clinical Practice.^{24–26}

In accordance with NIHR Good Clinical Practice,²⁷ safety reporting guidance for a non-clinical trial of an investigational medicinal product including SAE has been made available for all recruiting sites. The guidance includes definitions of SAE; who the SAE should be reported to, when and how to report the SAE and what information will be needed for the Research Ethics Committee, a copy of the National Research Ethics Service (NRES) SAE reporting form is also provided. Data regarding adverse events, other unintended effects of the trial interventions or protocol violations will be conveyed to the DMEC as and when necessary.

DISCUSSION

This pilot RCT addresses an area of clinical research that has been extremely neglected and has the potential of making a significant impact on women's health and well-being. The evidence gained from the study will inform a definitive RCT that will provide robust evidence of what is the best management of perineal wound dehiscence and hence be used by policymakers, clinicians, patients and the public to develop evidence-based best practice guidelines. This will potentially lead to significant improvements in perineal care and will help to reduce the short- and long-term morbidity experienced by women.

Author affiliations

¹The Maternity Centre, University Hospital of North Staffordshire, Stoke-on-Trent, Staffordshire, UK

²Faculty of Health, Staffordshire University, Blackheath Lane, Stafford, UK

³Arthritis Research UK National Primary Care Centre, Primary Care Services, Keele University, Staffordshire, UK

⁴Clinical Research Unit, School of Health and Social Care, Bournemouth University, Bournemouth, Dorset, UK

⁵School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

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Contributors All authors contributed equally to this work. LD, CK and KMI conceived the idea for the study. PT and LD will perform the statistical analysis for the study. LD is the PREVIEW Study coordinator and the lead research midwife for the study. She is registered as a PhD student at Staffordshire University, and the PREVIEW Study will form part of her doctoral studies. All authors contributed to the design of the study. PC provided qualitative advice and support. All authors helped to draft the manuscript and all authors read and approved the final manuscript.

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(2008–2011). The sponsor organisation in collaboration with the trial management group has overall responsibility for ensuring that the PREVIEW Study is conducted in accordance with the Department of Health Research Governance Framework for Health and Social Care.²³ The sponsor organisation will guarantee that there are appropriate arrangements in place: to initiate, manage and monitor the research; to finance the study and to report the outcomes of the research. The Chief Investigator (CI) and the trial steering committee have a contractual obligation to inform both the NIHR and RIA of any publications, which result from the research study. This relates to all publications generated from the research, including the scientific and lay press, abstracts and conference proceedings. The award holders also have a contractual obligation to submit an end of project report to the NIHR and RIA outlining the outcomes of PREVIEW. The report will detail a comprehensive overview of the work undertaken, summarise the research findings, any variation to the work outlined in the proposal or the research team and describe the next steps to patient benefit and the dissemination strategy. Additionally, the Research Investigators under the conditions of NHS Participant Identification Centre Agreements have a responsibility to share the learning from the research and provide the relevant Clinical Research Networks, Research Management and Governance Consortia with: (1) the literature review from the research protocol, (2) interim findings from the research, when available and (3) a final report or summary of the research.

Competing interests CK and KMI run perineal repair workshops both nationally and internationally and have developed an episiotomy and second-degree tear training model with Limbs & Things, UK. They receive a small royalty fee that contributes towards women's health research funds.

Ethics approval Ethics approval was provided by the North Wales Research Ethics Committee.

Provenance and peer review Not commissioned; internally peer reviewed.

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