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Title

PINCS-1: protocol for a feasibility study investigating the acceptability and accuracy of cervical screening and self-sampling in women at 6-weeks postnatal

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Abstract

Introduction

Cervical screening rates in the UK are falling, limiting our ability to prevent cervical cancer. Peak incidence of cervical cancer coincides with average age of childbirth and women with young children are less likely to be screened. Current guidelines advise waiting 12-weeks after delivery to perform cervical screening, but this recommendation is not based on evidence from the era of liquid-based cytology (LBC) or high-risk Human Papilloma Virus (hrHPV) testing. New mums suggested that cervical screening could be offered at 6-weeks post-delivery, in conjunction with the postnatal check-up with the general practice team in primary care.

Methods and analysis

A study of 100 participants will be performed to assess feasibility and acceptability of cervical screening at 6- and 12-weeks postnatal, with urine self-sampling at each time point. This will inform whether women are prepared to undergo cervical screening at 6-weeks postnatal and feasibility of a future pair-wise diagnostic test accuracy study, or whether alternative study designs are needed. At each appointment, participants will complete a questionnaire about their experience and thoughts regarding screening. Sub-studies ask participants who withdraw or decline their reasons, to identify barriers. The study will move to a second phase, when 100 participants will be individually randomised to sampling at 6-weeks or 12-weeks, once 100 participants have completed the 6-week screen in PINCS-1, or recruitment is poor, indicating that a paired-sample design is not feasible.

Ethics and dissemination

Ethical approval for PINCS-1 was given by the Stanmore Research Ethics Committee. The results, including participant feedback at each stage, will inform design of large studies to determine accuracy and clinical impact of cervical screening at 6-weeks postnatal, identifying whether giving choice will improve screening uptake. Data will inform sample size needed for future studies to have adequate power. Results will also inform future NHS Cervical Screening Programme management. Results will be shared via scientific publication and via conventional and social media channels accessed by young women.

Strengths and limitations of PINCS-1

Strengths

- The first study to focus on acceptability and reliability of screening, including self-sampling in postnatal women, to test hypothesis and generate data to inform further study design, following recommendations by Elridge et al.[1]
- Multiple points at which acceptability will be assessed by collecting participants' views and participant-reported outcomes.
- Offering self-screening at the time of another appointment was a successful strategy in the YouScreen study.[2]

Limitations

- This study has a limited sample size and is not statistically powered to evaluate the diagnostic test accuracy or the impact of offering screening during postnatal visits on overall screening uptake
- Screening will be performed in secondary care settings throughout this study. However, anticipated changes to screening would be expected to be relevant to primary care in the future studies.

Introduction

Cervical cancer is one of the most preventable malignancies encountered worldwide, due to a combination of primary prevention (HPV vaccination) and secondary prevention (cervical screening) strategies. Global elimination of cervical cancer is a key World Health Organisation strategy.[3 4] By 2022, cervical screening coverage rates in England had fallen to 66% in women/people with a cervix aged 25-49 years, and to less than 50% in some areas. This is markedly below the National Health Service Cervical Screening Programme (NHS CSP) standard of 80%. The majority of cervical cancers now occur in under-screened women [5-7]. Women with young children under 5 years of age are less likely to participate in cervical screening, as are individuals from ethnic minority backgrounds and lower socioeconomic groups, and these groups are also more likely to have had more children and at a younger age.[8]

Peak incidence of cervical cancer in the UK between 2016 and 2019 was in the 30-34-year-old cohort, followed by cases in women aged 25 to 29.[9] This coincides with the average age of mothers giving

birth in England and Wales of 30.9 years.[10] Our local cervical cancer audit between 2016 and 2017 identified that 15% of women diagnosed with cervical cancer were currently, or had recently been, pregnant and had been eligible for cervical screening in pregnancy or postnatally, but none had attended. We found that 50% of women were overdue for cervical screening by the end of their pregnancy and by 6 months postnatal more than half had still not attended screening.[11] This quality improvement (QI) project included canvassed views of new mothers/parents and primary care providers, through focus groups, which identified causes of poor uptake and generated ideas for change.[11] One idea, from both new mothers and primary care practice staff, was to offer postnatal cervical screening at the 6-week postnatal check-up, facilitating easier attendance for women by reducing barriers.[12] Self-testing for high-risk Human Papilloma Virus (hrHPV) was also suggested to improve screening uptake. Interestingly, offering opportunistic self-screening at a GP appointment, was demonstrated to be an effective strategy in the recent YouScreen study, potentially leading to a 7.6% improvement in overall screening rates.[2 13]

There are numerous barriers to screening in young women, including a perception that this age group are not at risk, inadequate knowledge, and fear of pain, discomfort and embarrassment. However, being busy and not getting around to having a test were independent factors, regardless of screening status[14 15] Our work showed that we could improve uptake by 8% in the postnatal cohort, largely by improving education of midwives and women in pregnancy.[11] Detailed quantitative and qualitative feedback in the pre-PINCS acceptability study (unpublished data) alongside the previous QI project focus groups, told us that new parents have many competing priorities and often struggle to address their own health needs.

NICE guidelines recommend a 6-week postnatal check for mothers and babies, which is attended by 78% of eligible people.[16 17] This appointment provides an opportunity for healthcare professionals to discuss multiple topics: infant feeding, lifestyle advice, contraception and health promotion, including discussion of cervical screening.[17 18] New mothers and primary care staff told us that offering to combine this visit with postnatal cervical screening would remove a significant barrier, particularly as 'just putting it off' was the most common reason for younger women being out-of-date for screening in a study by Jo's Cervical Cancer Trust.[19]

National guidance currently advises waiting 12 weeks after childbirth for a routine cervical screening test if it was due in pregnancy.[20] This recommendation is based on one comparison of conventional cytology with Papanicolaou smear testing at 4- vs. 6- vs. 8-weeks postnatal in just 55 participants.[21] There were increased inflammatory changes in Papanicolaou smears taken earlier,

leading to more false-positive, low-grade results. However, this pre-dates hrHPV primary testing (or triage) and liquid-based cytology (LBC), which dramatically improve the ability to test even inflammatory samples, and those contaminated by blood and lochia.

An Irish observational study, including 556 postnatal women, reported no difference in inadequate cervical sample rates when the cervical sample was taken at 6-weeks postnatal using LBC compared to a non-pregnant gynaecological population consisting of 1429 women.[22] Using LBC appears to negate the previously held belief that postnatal cervical samples should be delayed until 12-weeks postpartum. HPV-testing was not conducted in this study and there have been no studies directly comparing LBC cervical screening samples at different postnatal time points in a diagnostic test accuracy (DTA) context. Furthermore, hrHPV infection rates are similar during and outside of pregnancy, although these studies performed hrHPV tests at varying postnatal intervals, ranging from 45 days [23] to 6-months[24] and used swabs rather than clinician-collected LBC samples. This variation limits the applicability of these findings to current UK practice. The current recommendations to delay cervical screening until 12-weeks postpartum are therefore based on long-held perceived wisdom, rather than sound evidence of differences in DTA using current screening methods.

Many women struggle to undergo conventional cervical screening, especially those in higher-risk and socioeconomically disadvantaged groups.[25] hrHPV testing using self-sampling methods offers an alternative and improves screening uptake in under-screened women.[26] However, previous studies have not specifically targeted postnatal women, whose feelings on vaginal sampling may be affected by recent birth experiences. Our project also provides an opportunity to test the feasibility & acceptability[12] of self-testing for hrHPV in urine samples at 6- and 12-weeks postnatal, alongside conventional testing.

We have investigated the acceptability of cervical screening earlier in the postnatal period in a quantitative and qualitative attitudes study (Pre-PINCS – National Institute for Health and Care Research (NIHR) Central Portfolio Management System (CPMS) ID: 55489). Preliminary analyses suggest that over two-thirds of respondents would be willing to take part in a clinical study of 6-week clinician-taken cervical screening and nearly 8 out of every 10 would be willing to take part in a study of self-testing with urine samples (unpublished results; n = 454). Over half of the participants agreed or strongly agreed that they would be more likely to have cervical screening if offered at the time of their postnatal check-up, with only 1 in 13 disagreeing or strongly disagreeing to this (unpublished results).

Aim

PINCS is a two-phase study with a paired-sample study design (PINCS-1) performed at 6 and 12-weeks postpartum, followed by a randomised two-arm feasibility study in phase 2 (PINCS-2, which will be published as a separate protocol), comparing sampling at 6- or 12-weeks postnatal with the overall aim of assessing the acceptability and feasibility of these study designs in comparing cervical screening and self-testing at 6- versus 12-weeks postnatal.

Objectives of PINCS-1

The primary objective is to evaluate a paired-sample study design investigating the acceptability of cervical screening at 6-weeks postpartum, willingness to have repeat screening at 12-weeks postpartum, and to evaluate the feasibility for a larger-scale trial.

The secondary objectives are:

1. To evaluate acceptability of clinician-taken cervical samples and self-collected urine samples for screening tests in those who decline, and in those who consent both at 6- and 12-weeks using questionnaire data.
2. To assess the quality of cervical samples from clinician-taken samples at 6-weeks postnatal.
3. To determine the agreement in hrHPV status at 6- and 12-weeks postnatal between clinician-taken cervical samples and self-collected urine samples.

Methods and analysis

Study design

PINCS-1 is a paired feasibility study to investigate the acceptability of cervical screening and urine self-sampling in postnatal women at 6-weeks and 12-weeks postnatal.

Study setting

The primary study site will be Somerset NHS Foundation Trust. Several study sites across South West England will also collaborate in this study, recruiting participants, completing study visits and data collection. Somerset NHS Foundation Trust act as the study sponsor.

Patient and public involvement (PPI)

This study was instigated following the direct request by stakeholders, when investigating methods to reduce barriers to cervical screening in recently pregnant women/people.[11] Multiple ideas for change were generated through stakeholder groups involving new mothers, young women who had a cervical cancer diagnosed shortly after pregnancy, and primary care staff directly involved in both postnatal care and cervical screening. In addition to suggestions about improving education about cervical screening for midwives and pregnant women/new parents, both public and healthcare participants identified two areas to target: earlier postnatal screening potentially at the time of the postnatal GP appointment and the use of self-screening methods.

We worked with local Maternity Voices groups, whose members included women from marginalised communities, to design study materials, questionnaires and semi-structured interviews for the pre-PINCS study, which is currently undergoing analysis. Pre-PINCS was a two-phase study consisting of a questionnaire and in-depth qualitative analysis of semi-structured interviews. This was performed to gather information, from pregnant women and people within 5-years of their last childbirth, about the acceptability and feasibility of the PINCS studies; these results directly informed the PINCS study design and materials, with specific feedback from participants.

Participants and recruitment

Potential participants will be identified by members of their existing clinical care team including GPs, community or hospital midwifes, health visitors, practice nurses or obstetricians, alongside the local research teams, both antenatally and up to 6-weeks postnatal. Potential participants may also self-identify through publicity literature on recruitment sites and via the social media channels of gynaecological cancer charities (e.g. GO Girls, Eve Appeal) and local and national social media groups for new mothers (e.g. Mumsnet). Publicity will be in the form of posters and leaflets, distributed via social media, at antenatal events, and at routine appointments or shared through the electronic maternity care record. Potential participants will be given a participant information leaflet and, if interested in taking part, they will be referred to a member of the study team. A screening and eligibility questionnaire will be completed with all potential participants and, if eligible and consenting to proceed, an electronic consent form will be completed with an investigator. Participants will be informed of their right to rescind consent at any point during the study and provided with information on how to do this.

Recruitment to PINCS-1 will end when at least 100 recruited participants have attended and completed both clinician-taken cervical sample and urine self-sample at the 6-week appointment and have

attended or declined to attend their 12-week appointment. If participants withdraw prior to the 6-week sample, further participants will be recruited. In the instance of low recruitment, an earlier end point may be initiated following discussion with the Independent Trial Steering Committee (ITSC). Commencement of PINCS-2 will proceed after review of results of PINCS-1 by the ITSC to confirm that differences in testing at 6-week vs. 12-weeks are within acceptable limits to proceed safely.

Inclusion criteria

- 24.5 years (24 years and 183 days or greater on day of consent) to <65 years old
- Female with a cervix (regardless of gender identity)
- Currently pregnant or within 6-weeks of delivery
- Able to give informed consent

Exclusion criteria

- Absence of a cervix
- Not eligible for the NHS CSP
- Unable to give fully informed consent

The study is open to all those eligible for cervical screening, regardless of screening status. To understand the reasons for non-participation and to establish an uptake rate, a cohort of 100 potential participants will be approached and the acceptance rate recorded. All those who decline to participate will be given the opportunity to describe the reasons behind this. All participants who initially consent to the study, but choose to withdraw, will be offered a short electronic questionnaire to identify any concerns and barriers to participation.

Sample size

This study will aim to recruit at least 100 participants to PINCS-1. This sample size was chosen following findings from the pre-PINCS study regarding manageable recruitment in postnatal patients as well as input from statisticians and other experienced researchers with experience in feasibility studies. PINCS-2 will aim to recruit another 100 participants, randomised to either 6- or 12-week testing, with self-sampling with both urine and vaginal swabs at the same visit, allowing direct comparison of acceptability in this cohort. This sample size will provide a standard error on uptake at most 2.5% on each proportion, which we judge to be suitable for assessing acceptability and feasibility of a subsequent paired study design for accuracy. It will inform us as to how prepared women are to undergo cervical screening with a speculum examination at 6-weeks postnatal, and the feasibility of a paired-

sample design using repeat testing in the same participant with clinician- and/or self-samples at both, or either, time points.

Study visits

The study will consist of a screening and consent appointment followed by two study visits (see Figure 1). At each study visit, participants will undergo clinician-taken cervical screening samples using a speculum examination and cervical sample/sweep test, for hrHPV testing and cytology at 6-weeks postnatal. They will also undergo hrHPV testing using urine samples collected in a Colli-pee® device at both time points, to ascertain the agreement with clinician-taken sampling and the acceptability to participants at both time points.[27]

We will perform a patient questionnaire after sampling (web-based or paper), at both 6- and 12- weeks, to ascertain acceptability (concordance with protocol), feasibility (ability to recruit), patient-reported outcomes, including discomfort of testing, preferences regarding timing of screening and attitudes to introducing the option of screening at the 6-week postnatal check up in the GP practice.

Management of cytology and urine samples

Cytology samples performed following a hrHPV positive test will be dual labelled with patient identifying information and study details/study number and stored and managed in accordance with NHS CSP guidance.

Results of the cytological assessment on hrHPV negative samples, which would not ordinarily be performed as part of the NHS CSP, will not be uploaded to the NHS Cervical Screening Administration Service (CSAS), but will be recorded for the purposes of the study and acted on within the study protocol. Cytology samples from hrHPV-negative tests at 6-weeks postnatal will be destroyed at the end of the study period and not made available to CSAS for future audit.

Management of results and further cervical screening will depend upon previous cervical screening history (whether up to date at time of study, or not), attendance for both samples, and results of screening (see Figure 2 and Figure 3). Participants will be contacted with results and management plan, questions about further management answered, and asked about any adverse events, as well as being encouraged to self-report adverse events to the study team.

Urine samples will be labelled with the study details and study ID number and will be destroyed after testing and communication of results with the study team.

Data collection

Each participant will be assigned a unique study ID following consent to participate. All trial data will be uploaded to the secure web application for managing data, REDCap, which will host the electronic Case Report Form (eCRF). The study co-ordinators will be responsible for analysing and monitoring the data from all sites and thus will have full access to the inputted information and local investigators will be able to access the data from their site only.

Statistical analysis

Full details of the statistical analysis will be described in a statistical analysis plan that will be written and finalised before data lock. The primary outcomes are binary variables. We will estimate 95% CIs for each using Wilson's method.

Discussion

Enhancing cervical screening uptake is a healthcare priority, as adequate screening rates lead to reduced incidences of precancerous and cancerous changes in the cervix.[6 7] There is a clear need for research in methods to improve attendance of cervical screening in younger women due to a lack of proven strategies in the current literature.[28] Pregnancy provides several points of contact to engage patients in health promotion through the increased access to healthcare and provides a valuable opportunity to educate and organise cervical screening, especially in 'hardly reached' groups.[10 11 29] Offering opportunistic self-sampling in a healthcare setting during a pre-existing appointment with vaginal swabs to non-attenders achieved uptake rates of 55.9% in a recent study, compared with only 12.9% of those sent test kits via direct-mail.[2] They found that urine self-sampling was preferred to vaginal sampling (41.9% vs. 15.4%), especially among women from ethnic minorities.[13] From our preliminary unpublished attitudes to self-sampling data, this is likely to be even more pertinent to the postnatal cohort. However, this work also highlighted that the idea of self-sampling is not preferable to all. The data from YouScreen support our hypothesis that offering increased choice, and opportunities for testing when people are otherwise attending primary care appointments, is important to improve screening rates. Women have identified making and attending appointments as a significant barrier to

screening and therefore it is essential to minimise process-based restrictions that limit accessibility to screening services.[15 30] Combining screening with postnatal check-ups offers a golden opportunity to inform women, promote self-care and provide low-effort access to screening. This may require increased flexibility of primary care appointments, unless self-sampling is accurate enough to allow this as an alternative and support a redirection to focus of postnatal care on maternal healthcare needs, not just those of their babies.

We outline the protocol for a study evaluating the feasibility and acceptability of cervical screening using pair-wise sampling of clinician-taken cervical screening tests and self-testing with urine samples at 6- and 12-weeks postnatal. Providing there is minimal difference in inadequacy rates of screening and hrHPV positive rates at 6- and 12-weeks in PINCS-1, which is not anticipated based on previous data, we will perform a second feasibility study (PINCS-2) that aims to recruit 100 participants who will be randomised to LBC screening at 6- or 12-weeks postnatal. Urine and vaginal swab self-sampling will be performed at the time of LBC screening. This further study will assess feasibility of individual consent and randomisation. Uptake to the study, and acceptability of LBC screening at 6-weeks in the consented study sample, will inform whether progression to a definitive trial is justified N=50 participants per arm will provide precision of at least 3.5% on the proportion who accept the invitation, which we judge sufficient to determine feasibility. A major amendment to our ethics agreement will be required for PINCS-2 and a separate open protocol will be published once this is in place. For both feasibility study phases (PINCS-1 and PINCS-2) we will invite women to join regardless of screening status at the end of pregnancy, to maximise participation. We will conduct subgroup analyses of uptake by screening status to determine feasibility of then doing the same for the definitive study.

Overall, through the PINCS studies we anticipate establishing the level of acceptability and feasibility to inform design of two further studies and which is best to take forward. First, a DTA study to determine the accuracy of screening for hrHPV and cytological abnormalities at 6-weeks postnatal. This will compare the inadequacy rates, sensitivity and specificity of cervical screening at 6- versus 12-weeks postnatal, informing whether offering earlier postnatal screening is accurate. Provisional power calculations, based on inadequacy rates, estimated requiring over 1000 participants for a formal DTA of cervical screening at 6-week postnatal, hence why this feasibility study is required before embarking on such a significant undertaking. Data from PINCS-1 will inform this study design and size for adequate power.

Second, a randomised control trial (RCT) to examine the effect of earlier postnatal screening on screening uptake rates, as well as the longer-term clinical outcomes, such as rates of high-grade

cervical intraepithelial neoplasia (CIN) at subsequent screening tests. Our proposed feasibility studies will determine whether, in this future RCT, it is reasonable and cost-effective to randomise individual participants to screening at 6- or 12 -weeks. If this design is not feasible, a different design will be needed. For example, randomisation without prior consent, such as through applying for a CAG-251 exemption, or a pragmatic cluster-randomised design, such as that employed with YouScreen.[2]

Self-administered vaginal swabs and urine samples for hrHPV testing are under-evaluation.[2 27 31] However, this research will provide crucial insights into postnatal individuals' experiences with, and preferences for different self-sampling methods. These data will help determine the appropriate sample sizes needed to evaluate the accuracy and safety of these self-sampling techniques in future studies involving postnatal cohorts, as well as and influencing future changes to the NHS CSP.

Ethics and dissemination

Ethics

Ethical approval for PINCS-1 was granted by the Stanmore Research Ethics Committee for this study (IRAS project ID:321696; REC reference:24/LO/0206), was adopted by the NIHR Clinical Research Network (CRN) Portfolio (CPMS ID 60494) and is registered on the International Standard Randomised Controlled Trial Number (ISRCTN) registry (ISRCTN10071810; https://doi.org/10.1186/ISRCTN10071810).

Publication and dissemination plan

Study results will be published as a PhD thesis and high impact peer-reviewed papers, as well as presentations at national and international meetings. They will also be presented to Maternity Voice Groups, gynaecological oncological charities, Mumsnet and local maternity social media sites. Any data arising from this study will be published and presented in an open-access peer-review journal. The manuscript will be deposited with the University of Exeter, according to the University of Exeter's policies and data sharing policies.

Individual participant data sharing statement

To ensure participant anonymity is safeguarded and subject to any reasonable and necessary delay, pseudonymised research data will be securely archived to a repository following publication of the results where they will be stored indefinitely. These data may be used in future research, here or abroad, and shared, subject to reasonable requests, approved by the sponsor, host institution and the regulatory authorities.

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Authors' contributions

All authors contributed to the study conception and design. The first draft of the manuscript was written by VC and revised by JM, HB-R, KC and RN. All authors have approved the final version and JM acts as guarantor.

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Sponsor information

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Conflicting interests statement

VC - none to declare

RN - none to declare

HBR - none to declare

ARB – none to declare

KC – received honorarium and support from SeeGene

KD – received expenses and honorarium from Hologic. Received test kits and consumables from Hologic, Roche, Rovers and Copan for a previous study, now submitted for publication.

LMcW – none to declare

AS- A member of various expert groups providing advice to the English Cervical Screening Programme, including on HPV self-sampling; holds an honorary contract with the University of Manchester to support research into HPV testing in urine samples and Professional Clinical Advisor to the English Cervical Screening Programme.

SS- none to declare

EJC - none to declare

JM – Clinical Advisor to the NHS Cervical Screening Programme Research Innovation and Development Advisory Committee.

Figure legends

Figure 1: PINCS-1 participant flowchart. NTDD = Next Test Due Date.

Figure 2: PINCS-1 study flowchart for those having samples at 6- and 12-weeks. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus; DTA = diagnostic test accuracy; PROM = patient reported outcome measures

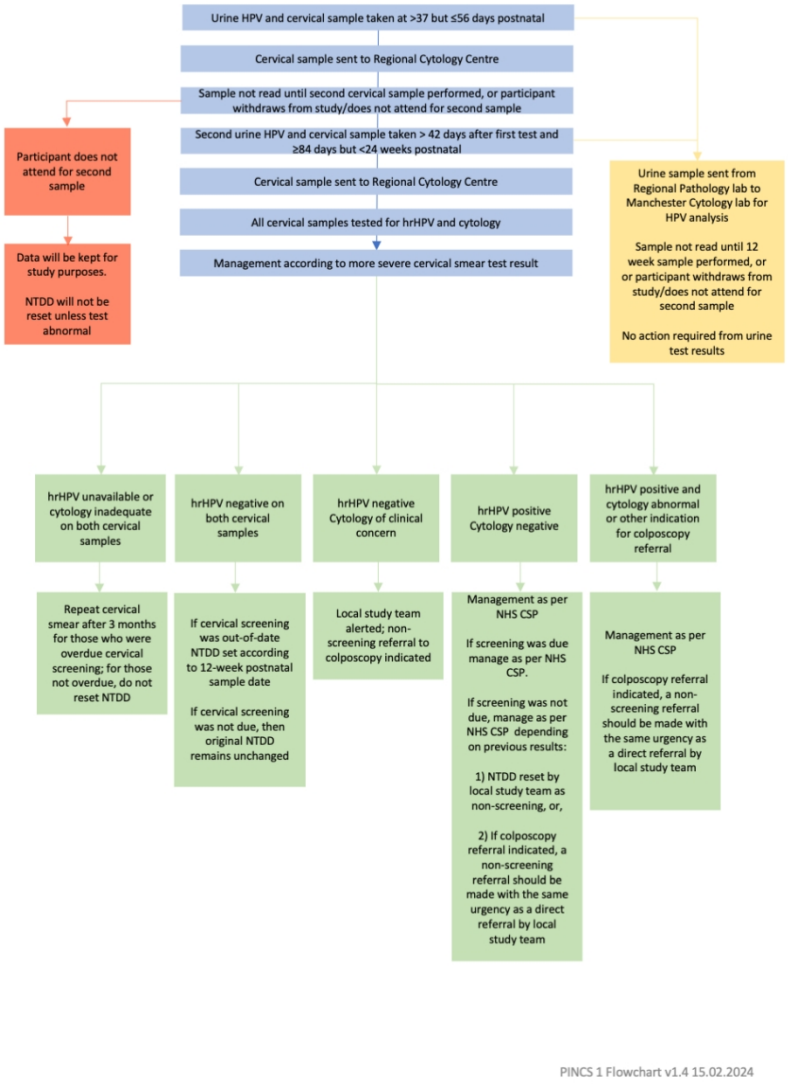
Figure 3: PINCS-1 study flowchart for those having samples at 6-weeks who do not attend for their 12-week sample. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus.

References

1. Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. *PLOS ONE* 2016;11(3):e0150205. doi: 10.1371/journal.pone.0150205
2. Lim AWW, Deats K, Gambell J, et al. Opportunistic offering of self-sampling to non-attenders within the English cervical screening programme: a pragmatic, multicentre, implementation feasibility trial with randomly allocated cluster intervention start dates (YouScreen). *eClinicalMedicine* 2024 doi: 10.1016/j.eclinm.2024.102672
3. World Health Organisation. Cervical cancer 2024 [Available from: https://www.who.int/health-topics/cervical-cancer#tab=tab_1 accessed 23 May 2024.
4. World Health Organisation. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health Organization, 2020.
5. Kitchener HC, Gittins M, Rivero-Arias O, et al. A cluster randomised trial of strategies to increase cervical screening uptake at first invitation (STRATEGIC). *Health Technol Assess* 2016;20(68):1-138. doi: 10.3310/hta20680
6. NHS England. Cervical screening standards data report 2021 to 2022 2023 [Available from: https://www.gov.uk/government/publications/cervical-screening-standards-data-report-2021-to-2022/cervical-screening-standards-data-report-2021-to-2022 accessed 23 May 2024].
7. Landy R, Pesola F, Castanon A, Sasieni P. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. *Br J Cancer* 2016;115(9):1140-46. doi: 10.1038/bjc.2016.290 [published Online First: 20160915]
8. Sabates R, Feinstein L. The role of education in the uptake of preventative health care: The case of cervical screening in Britain. *Social Science & Medicine* 2006;62(12):2998-3010. doi: 10.1016/j.socscimed.2005.11.032
9. NHS Cervical Screening Programme. Audit of invasive cervical cancer: national report 1 April 2016 to 31 March 2019 London2023 [updated 30 November 2023. Available from: https://www.gov.uk/government/publications/cervical-screening-invasive-cervical-cancer-audit-2016-to-2019/nhs-cervical-screening-programme-audit-of-invasive-cervical-cancer-national-report-1-april-2016-to-31-march-2019 accessed 15 June 2024.
10. Office for National Statistics (ONS), released 17 May 2024, ONS website, statistical bulletin, Birth characteristics in England and Wales: 2022 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthcharacteristicsinenglandandwales/2022 accessed 23 May 2024.
11. Coleridge SL, Wiggans A, Nelissen E, et al. Improving the uptake of cervical screening in pregnant and recently postnatal women: a quality improvement project. *BMJ Open Qual* 2022;11(2) doi: 10.1136/bmjoq-2021-001709
12. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Services Research* 2017;17(1):88. doi: 10.1186/s12913-017-2031-8

13. Drysdale H, Marlow LAV, Lim A, Waller J. Experiences of Self-Sampling and Future Screening Preferences in Non-Attenders Who Returned an HPV Vaginal Self-Sample in the YouScreen Study: Findings From a Cross-Sectional Questionnaire. *Health Expect* 2024;27(4):e14118. doi: 10.1111/hex.14118
14. Albrow R, Blomberg K, Kitchener H, et al. Interventions to improve cervical cancer screening uptake amongst young women: a systematic review. *Acta Oncol* 2014;53(4):445-51. doi: 10.3109/0284186X.2013.869618 [published Online First: 20140207]
15. Waller J, Bartoszek M, Marlow L, Wardle J. Barriers to cervical cancer screening attendance in England: a population-based survey. *J Med Screen* 2009;16(4):199-204. doi: 10.1258/jms.2009.009073
16. National Institute for Health and Care Excellence (NICE)and Royal College of Obstetricians and Gynaecologists. Postnatal Care. NICE guideline [NG194]. London: Department of Health and Social Care, 2021.
17. Smith HC, Saxena S, Petersen I. Postnatal checks and primary care consultations in the year following childbirth: an observational cohort study of 309 573 women in the UK, 2006-2016. *BMJ Open* 2020;10(11):e036835. doi: 10.1136/bmjopen-2020-036835 [published Online First: 20201123]
18. Dunphy M. O76 - Midwives can conduct a cervical screen test (CST) at a 6-week postnatal comprehensive health check. Australian College of Midwives National Conference – Be the Change, September 12-14, 2023, Adelaide, South Australia. *Women & Birth* 2023;36:S30.
19. Jo's Cervical Cancer Trust. Barriers to cervical screening among 25-19 year olds 2016 [Available from: https://www.jostrust.org.uk/sites/default/files/ccpw17_survey_summary.pdf accessed 12th May 2020].
20. Royal College of Obstetricians and Gynaecologists. Cervical smears and pregnancy 2013 [Available from: https://www.rcog.org.uk/for-the-public/browse-our-patient-information/cervical-smears-and-pregnancy/#:~:text=This%20appointment%20will%20usually%20be,and%206%20months%20of%20pregnancy.
21. Rarick TL, Tchabo JG. Timing of the postpartum Papanicolaou smear. *Obstet Gynecol* 1994;83(5 Pt 1):761-5.
22. Leahy M, Farah N, Bolger N, et al. Should cervical smears be taken at a postnatal visit. *The Irish Medical Journal* 2006;99(8):244-45.
23. Trottier H, Mayrand MH, Baggio ML, et al. Risk of Human Papillomavirus (HPV) Infection and Cervical Neoplasia after Pregnancy. *BMC Pregnancy Childbirth* 2015;15:244. doi: 10.1186/s12884-015-0675-0 [published Online First: 20151007]
24. Schmeink CE, Melchers WJ, Hendriks JC, et al. Human papillomavirus detection in pregnant women: a prospective matched cohort study. *J Womens Health (Larchmt)* 2012;21(12):1295-301. doi: 10.1089/jwh.2012.3502
25. Gupta S, Palmer C, Bik EM, et al. Self-Sampling for Human Papillomavirus Testing: Increased Cervical Cancer Screening Participation and Incorporation in International Screening Programs. *Frontiers in Public Health* 2018;6
26. Arbyn M, Smith SB, Temin S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ* 2018;363:k4823. doi: 10.1136/bmj.k4823
27. Davies JC, Sargent A, Pinggera E, et al. Urine high-risk human papillomavirus testing as an alternative to routine cervical screening: A comparative diagnostic accuracy study of two urine collection devices using a randomised study design trial. *BJOG* 2024 doi: 10.1111/1471-0528.17831 [published Online First: 20240425]
28. Albrow R, Kitchener H, Gupta N, Desai M. Cervical screening in England: the past, present, and future. *Cancer Cytopathol* 2012;120(2):87-96. doi: 10.1002/cncy.20203 [published Online First: 20120224]
29. Lyonnais E, Vigoureux S, Blondel B, et al. Women's country of birth and failure to catch up an overdue cervical cancer cytological screening participation during pregnancy in France, an observational study based on survey sources. *BMC Cancer* 2024;24(1):595. doi: 10.1186/s12885-024-12335-1 [published Online First: 20240516]

30. Wearn A, Shepherd L. Determinants of routine cervical screening participation in underserved women: a qualitative systematic review. *Psychol Health* 2024;39(2):145-70. doi: 10.1080/08870446.2022.2050230 [published Online First: 20220316]
31. Mills C. HPValidate cervical screening self-sampling study nears completion. In: UK National Screening Committee, ed.: UK Government, 2023.



PINCS-1 participant flowchart. NTDD = Next Test Due Date

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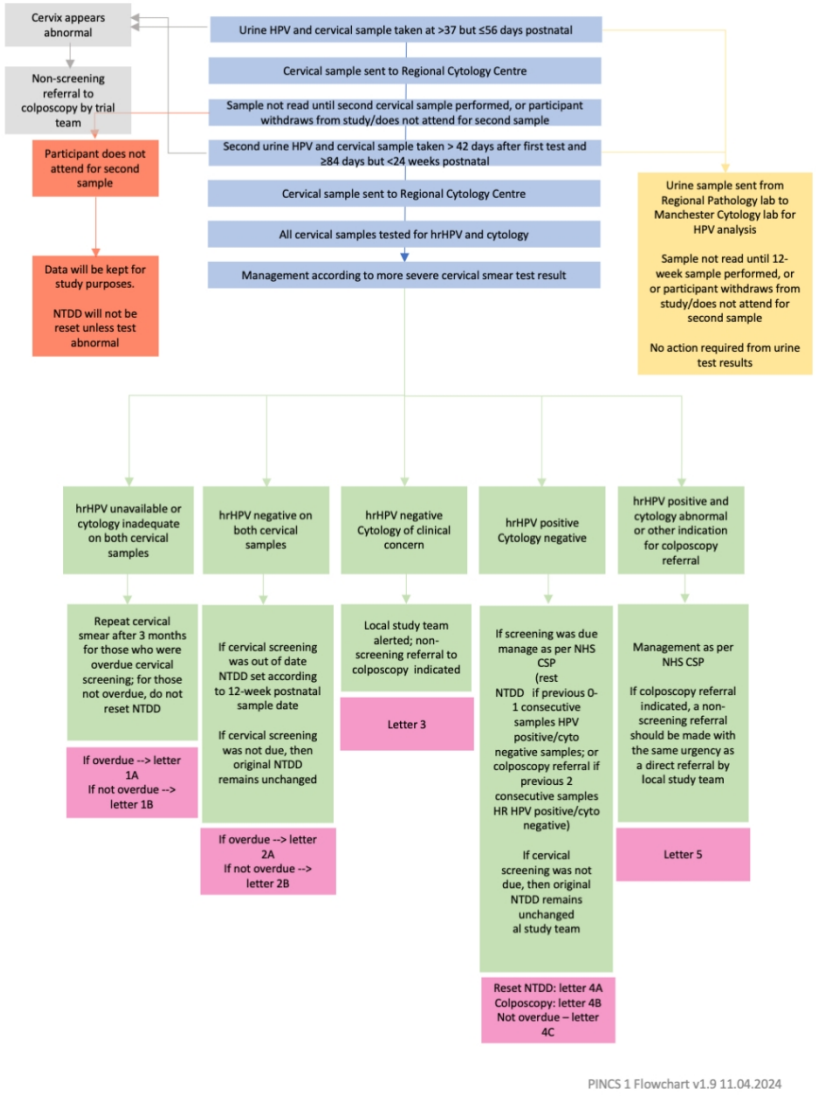
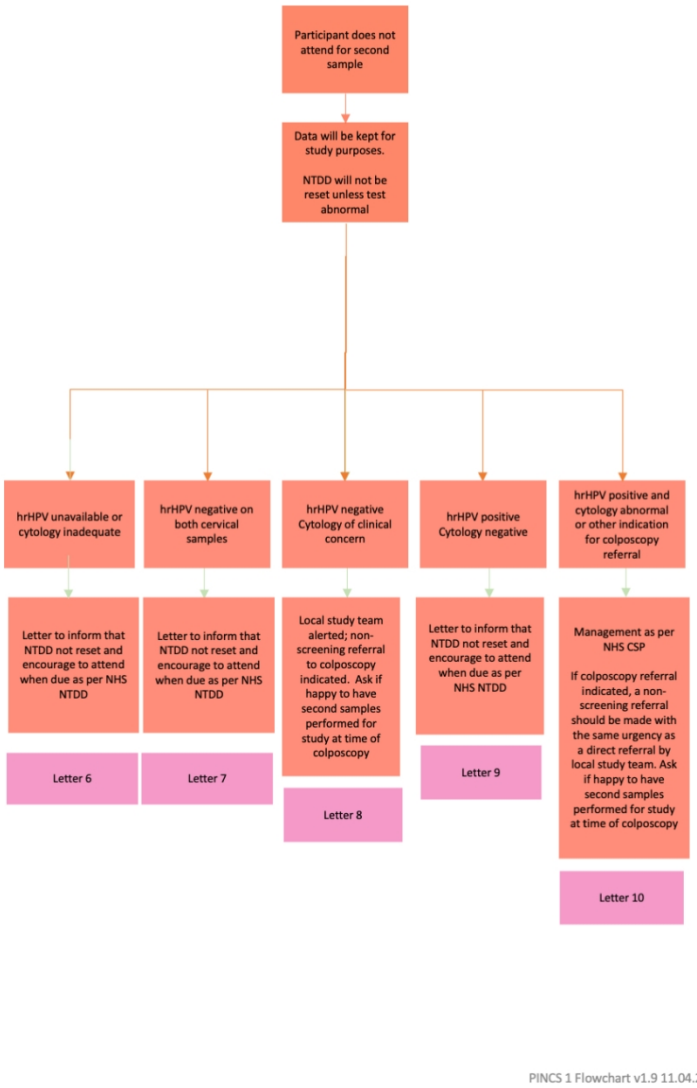


PINCS-1 study flowchart for those having samples at 6- and 12-weeks. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus; DTA = diagnostic test accuracy; PROM = patient reported outcome measures

190x275mm (133 x 133 DPI)



PINCS-1 study flowchart for those having samples at 6-weeks who do not attend for their 12-week sample. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus

190x275mm (133 x 133 DPI)

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Postnatal Instead of Normally Timed Cervical Screening (PINCS-1): a protocol for a feasibility study of paired-sample cervical screening and urine self-sampling at 6- and 12-weeks postnatal in the United Kingdom

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Title

Postnatal Instead of Normally Timed Cervical Screening (PINCS-1): a protocol for a feasibility study of paired-sample cervical screening and urine self-sampling at 6- and 12-weeks postnatal in the United Kingdom

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Postnatal Instead of Normally Timed Cervical Screening (PINCS-1): a protocol for a feasibility study of paired-sample cervical screening and urine self-sampling at 6- and 12-weeks postnatal in the United Kingdom

Abstract

Introduction

Cervical screening rates in the United Kingdon (UK) are falling, limiting our ability to prevent cervical cancer. Peak incidence of cervical cancer coincides with average age of childbirth and women with young children are less likely to be screened. Current UK guidelines advise waiting 12-weeks after delivery to perform cervical screening, but this recommendation is not based on evidence from the era of liquid-based cytology (LBC) or high-risk Human Papillomavirus (hrHPV) testing. New mums suggested offering cervical screening at 6-weeks post-delivery, in conjunction with the postnatal check-up with the general practice team in primary care. This study aims to assess the feasibility and acceptability of a paired-sample study design for cervical screening at 6- and 12-weeks postnatal.

Methods and analysis

A study of 100 participants will be performed to assess feasibility and acceptability of cervical screening at both 6- and 12-weeks postnatal, with urine self-sampling using a Colli-pee collection device at each time point. This will inform whether women are prepared to undergo cervical screening at 6-weeks postnatal and feasibility of a future pair-wise diagnostic test accuracy (of HPV and abnormal cervical cytology) study, or whether alternative study designs are needed. Participants must be aged 24.5 to 64 years-old and eligible for the National Health Service Cervical Screening Programme (NHS CSP). At each appointment, participants will complete a questionnaire about their experience and thoughts regarding screening. Sub-studies ask participants who withdraw or decline to participate their reasons, to identify barriers. The study will close to recruitment once 100 participants have completed the 6-week screen in PINCS-1, or recruitment is poor and not 50% recruited by 6 months, indicating that a paired-sample design is not feasible.

Ethics and dissemination

Ethical approval for PINCS-1 was given by the Stanmore Research Ethics Committee. The results, including participant feedback at each stage. The results and ongoing participant feedback, built into the trial design, will inform the design of large studies to determine accuracy and clinical impact of

cervical screening at 6-weeks postnatal, identifying whether giving choice (e.g., from timing of appointments and/or offering self-sampling) will improve screening uptake. Data will inform sample size needed for future studies to have adequate power. Results will also inform future NHS Cervical Screening Programme management. Results will be shared via scientific publication and via conventional and social media channels accessed by young women.

Strengths and limitations of PINCS-1

Strengths

- To our knowledge this is the first study to focus on acceptability and reliability of cervical screening, including urine self-sampling in postnatal women, to test hypothesis and generate data to inform further study design, following recommendations by Elridge et al.[1]
- There are multiple points at which acceptability will be assessed by collecting participants' views and participant-reported outcomes.
- Data collection tools have been developed using participant responses in the pre-PINCS study,[2] to ensure applicability to the postnatal population.
- Pilot diagnostic test accuracy data will inform the sample size calculation for future studies.

Limitations

- Screening will be performed in secondary care throughout this study, as this study is designed to test the feasibility of a future paired sample diagnostic test accuracy study, not the effect on uptake in a primary care setting; this is a separate question, requiring different study design.

Introduction

Cervical cancer is one of the most preventable malignancies encountered worldwide, due to a combination of primary prevention (HPV vaccination) and secondary prevention (cervical screening) strategies. Global elimination of cervical cancer is a key World Health Organisation strategy.[3 4] By 2022, cervical screening coverage rates in England had fallen to 66% in women/people with a cervix aged 25-49 years, and to less than 50% in some areas. This is markedly below the NHS CSP standard of 80%. The majority of cervical cancers now occur in under-screened women.[5-7] Women with young children under 5 years of age are less likely to participate in cervical screening, as are individuals from

ethnic minority backgrounds and lower socioeconomic groups, and these groups are also more likely to have had more children and at a younger age.[8]

Peak incidence of cervical cancer in the UK between 2016 and 2019 was in the 30-34-year-old cohort, followed by cases in women aged 25 to 29.[9] This coincides with the average age of mothers giving birth in England and Wales of 30.9 years.[10] Our local cervical cancer audit between 2016 and 2017 identified that 15% of women diagnosed with cervical cancer were currently, or had recently been, pregnant and had been eligible for cervical screening in pregnancy or postnatally, but none had attended. We found that 50% of women were overdue for cervical screening by the end of their pregnancy and by 6 months postnatal more than half had still not attended screening.[11] This quality improvement (QI) project included canvassed views of new mothers/parents and primary care providers, through focus groups, which identified causes of poor uptake and generated ideas for change.[11] One idea, from both new mothers and primary care practice staff, was to offer postnatal cervical screening at the 6-week postnatal check-up, facilitating easier attendance for women by reducing barriers.[12] Self-sampling for high-risk Human Papillomavirus (hrHPV) was also suggested to improve screening uptake. Interestingly, offering opportunistic vaginal self-sampling at a GP appointment, was demonstrated to be an effective strategy in the recent YouScreen study, potentially leading to a 7.6% improvement in overall screening rates.[13 14]

There are numerous barriers to screening in young women, including a perception that this age group are not at risk, inadequate knowledge, and fear of pain, discomfort and embarrassment. However, being busy and not getting around to having a test were independent factors, regardless of screening status.[15 16] Our work showed that we could improve uptake by 8% in the postnatal cohort, largely by improving education of midwives and women in pregnancy.[11] Detailed quantitative and qualitative feedback in the pre-PINCS acceptability study (unpublished data) alongside the previous QI project focus groups, told us that new parents have many competing priorities and often struggle to address their own health needs.

National Institute for Health and Care Excellence (NICE) guidelines recommend a 6-week postnatal check for mothers and babies, which is attended by 78% of eligible people.[17 18] This appointment provides an opportunity for healthcare professionals to discuss multiple topics: infant feeding, lifestyle advice, contraception and health promotion, including discussion of cervical screening.[18 19] New mothers and primary care staff told us that offering to combine this visit with postnatal cervical screening

would remove a significant barrier, particularly as 'just putting it off' was the most common reason for younger women being out-of-date for screening in a study by Jo's Cervical Cancer Trust.[20]

UK national guidance currently advises waiting 12 weeks after childbirth for a routine cervical screening test if it was due in pregnancy.[21] This recommendation is based on one comparison of conventional cytology with Papanicolaou smear testing at 4- vs. 6- vs. 8-weeks postnatal in just 55 participants.[22] There were increased inflammatory changes in Papanicolaou smears taken earlier, leading to more false-positive, low-grade results. However, this pre-dates hrHPV primary testing (or triage) and liquid-based cytology (LBC), which dramatically improve the ability to test even inflammatory samples, and those contaminated by blood and lochia.

An Irish observational study, including 556 postnatal women, reported no difference in inadequate cervical sample rates when the cervical sample was taken at 6-weeks postnatal using LBC compared to a non-pregnant gynaecological population consisting of 1429 women.[23] Using LBC appears to negate the previously held belief that postnatal cervical samples should be delayed until 12-weeks postpartum. HPV-testing was not conducted in this study and there have been no studies directly comparing LBC cervical screening samples at different postnatal time points in a diagnostic test accuracy (DTA) context. Furthermore, hrHPV infection rates are similar during and outside of pregnancy, although these studies performed hrHPV tests at varying postnatal intervals, ranging from 45 days[24] to 6-months[25] and used vaginal swabs rather than clinician-collected LBC samples. This variation limits the applicability of these findings to current UK practice. The current recommendations to delay cervical screening until 12-weeks postpartum are therefore based on long-held perceived wisdom, rather than sound evidence of differences in DTA using current screening methods.

Many women struggle to undergo conventional cervical screening, especially those in higher-risk and socioeconomically disadvantaged groups.[26] hrHPV testing using self-sampling methods offers an alternative and improves screening uptake in under-screened women.[27 28] However, previous studies have not specifically targeted postnatal women,[28 29] whose feelings on vaginal sampling may be affected by recent birth experiences. Our project also provides an opportunity to test the feasibility & acceptability[12] of self-sampling for hrHPV in urine samples at 6- and 12-weeks postnatal, alongside conventional testing.

We have investigated the acceptability of cervical screening earlier in the postnatal period in a quantitative and qualitative attitudes study (Pre-PINCS – National Institute for Health and Care

Research (NIHR) Central Portfolio Management System (CPMS) ID: 55489).[2] Preliminary analyses suggest that over two-thirds of respondents would be willing to take part in a clinical study of 6-week clinician-taken cervical screening and nearly 8 out of every 10 would be willing to take part in a study of self-sampling with urine samples (unpublished data).[2] Over half of the participants agreed or strongly agreed that they would be more likely to have cervical screening if offered at the time of their postnatal check-up (unpublished data). Although this current study is set within the well-established NHS CSP, offering opportunistic cervical screening at the time of the postnatal check-up also offers significant advantages to countries without organised call-recall screening programmes.

Aim

PINCS is a two-phase study, this protocol refers to PINCS-1, a paired-sample study design postpartum comparing cervical screening performed at 6- or 12-weeks postnatal. The overall aim will be to assess the acceptability and feasibility of this study design in comparing conventional cervical screening and self-sampling at 6- versus 12-weeks postnatal.

Objectives of PINCS-1

Primary objective:

- To evaluate the feasibility of a paired-sample study design for a future larger scale trial investigating the acceptability of cervical screening at 6-weeks postpartum and willingness to have repeat screening at 12-weeks postpartum.

The secondary objectives are:

- To evaluate acceptability of clinician-taken cervical samples and self-collected urine samples for screening tests in those who decline, and in those who consent both at 6- and 12-weeks using questionnaire data.
- To assess the quality of cervical samples from clinician-taken samples at 6-weeks postnatal through inadequacy rates.
- To determine the agreement in hrHPV status at 6- and 12-weeks postnatal between clinician-taken cervical samples and self-collected urine samples.

Methods and analysis

Study design

PINCS-1 is a paired feasibility study to investigate the acceptability of cervical screening and urine self-sampling in postnatal women at 6-weeks and 12-weeks postnatal.

Study setting

The primary study site will be Somerset NHS Foundation Trust. Two further study sites across South West England will collaborate in this study (Royal Devon and Exeter NHS Trust and Royal Cornwall NHS Foundation Trust), recruiting participants, completing study visits and data collection. Each site is a Gynaecological Cancer Centre. Somerset NHS Foundation Trust act as the study sponsor. The study planned start date is April 2024 (opened August 2024). Recruitment will end when at least 100 recruited participants have attended and completed clinician-taken cervical screening at their six-week appointment and have attended, or declined to attend, their 12-week appointment. If participants withdraw before the 6-week sample, further participants will be recruited, so that at least 100 participants have their 6-week samples performed. The study will end once all participants have completed follow up, as described above, and data have been collected and analysed. In the instance of low recruitment, an earlier end point may be initiated following discussion with the Independent Trial Steering Committee. Anticipated end date is April 2027.

Patient and public involvement (PPI)

This study was instigated following the direct request by stakeholders, when investigating methods to reduce barriers to cervical screening in recently pregnant women/people.[11] Multiple ideas for change were generated through stakeholder groups involving new mothers, young women who had a cervical cancer diagnosed shortly after pregnancy, and primary care staff directly involved in both postnatal care and cervical screening. In addition to suggestions about improving education about cervical screening for midwives and pregnant women/new parents, both public and healthcare participants identified two areas to target: earlier postnatal screening potentially at the time of the postnatal GP appointment and the use of self-screening methods.

We worked with local Maternity Voices groups, whose members included women from marginalised communities to design study materials, questionnaires and semi-structured interviews for the pre-PINCS study, which is currently undergoing analysis. Pre-PINCS was a two-phase study consisting of a questionnaire and in-depth qualitative analysis of semi-structured interviews. This was performed to gather information, from pregnant women and people within 5-years of their last childbirth, about the acceptability and feasibility of the PINCS studies; these results directly informed the PINCS study design and materials, with specific feedback from participants.

Participants and recruitment

Potential participants can be identified by members of their existing clinical care team including GPs, community or hospital midwifes, health visitors, practice nurses or obstetricians, or will be approached if eligible by the local research teams, both antenatally and up to 6-weeks postnatal, in an inpatient or outpatient setting. Potential participants may also self-identify through publicity literature on recruitment sites and via the social media channels of gynaecological cancer charities (e.g. GO Girls, Eve Appeal) and local and national social media groups for new mothers (e.g. Mumsnet). Publicity will be in the form of posters and leaflets, distributed via social media, at antenatal events, and at routine appointments or shared through the electronic maternity care record. Potential participants will be given a participant information leaflet and, if interested in taking part, they will be referred to a member of the study team. A screening and eligibility questionnaire will be completed with all potential participants and, if eligible and consenting to proceed, an electronic consent form will be completed with an investigator. Participants will be informed of their right to rescind consent at any point during the study and provided with information on how to do this.

Recruitment to PINCS-1 will end when at least 100 recruited participants have attended and completed both clinician-taken cervical sample and urine self-sample at the 6-week appointment and have attended or declined to attend their 12-week appointment. If participants withdraw prior to the 6-week sample, further participants will be recruited. In the instance of low recruitment, an earlier end point may be initiated following discussion with the Independent Trial Steering Committee (ITSC). The study will be performed in secondary care, to limit number of sites required and control for variability of cervical sampling from multiple cervical screeners. This is because this study will examine the feasibility of a future large paired-sample study, comparing diagnostic test accuracy of cervical screening at 6- and 12-weeks postnatal. A different study design will be required in a further study to test the effect on uptake of cervical screening, if offered at the 6-week postnatal check-up. This further study will

necessarily be conducted in primary care settings. However, we will need to confirm that this is safe and acceptable to the postnatal population before testing within the wider cervical screening programme.

Inclusion criteria

- 24.5 years (24 years and 183 days or greater on day of consent) to <65 years old
- Female with a cervix (regardless of gender identity)
- Currently pregnant or within 6-weeks of delivery
- Able to give informed consent

Exclusion criteria

- Absence of a cervix
- Not eligible for the NHS CSP
- Unable to give fully informed consent

The study is open to all those eligible for cervical screening, regardless of screening status. To understand the reasons for non-participation and to establish an uptake rate, a cohort of 100 potential participants will be approached and the acceptance rate recorded. All those who decline to participate will be given the opportunity to describe the reasons behind this. All participants who initially consent to the study, but choose to withdraw, will be offered a short electronic questionnaire to identify any concerns and barriers to participation.

Sample size

This study will aim to recruit at least 100 participants to PINCS-1. This sample size was chosen following findings from the pre-PINCS study regarding manageable recruitment in postnatal patients as well as input from statisticians and other experienced researchers with experience in feasibility studies.[2] This sample size will provide a standard error on uptake at most 2.5% on each proportion, which we judge to be suitable for assessing acceptability and feasibility of a subsequent paired study design for accuracy. It will inform us as to how prepared women are to undergo cervical screening with a speculum examination at 6-weeks postnatal, and the feasibility of a paired-sample design using repeat testing in the same participant with clinician- and/or self-samples at both, or either, time points.

Study visits

The study will consist of an eligibility screening and consent appointment followed by two study visits (see Figure 1). At each study visit, participants will undergo clinician-taken cervical screening samples, by a accredited clinician, using a speculum examination and Cervex™ brush for hrHPV testing and cytology at 6-weeks postnatal. They will also undergo hrHPV testing using first void urine samples collected with a 10 ml Colli-pee® device (prior to the clinician-taken sample) at both time points, to ascertain the agreement with clinician-taken sampling and the acceptability to participants at both time points.

We will perform a patient questionnaire after sampling (web-based or paper), at both 6- and 12- weeks, to ascertain acceptability (concordance with protocol), feasibility (ability to recruit), patient-reported outcomes, including discomfort of testing, preferences regarding timing of screening and attitudes to introducing the option of screening at the 6-week postnatal check up in the GP practice. This is based on a questionnaire used in a previous study, following feedback from patients and participants.

Management of cytology and urine samples

All 6-week cervical samples will undergo initial steps in the laboratory, to allow for safe storage, and saved for processing once the 12-week sample is due. If the participant attends for 6-week sampling but subsequently withdraws from the study prior to 12-weeks, their 6-week sample will be processed and the result communicated to themselves and their GP.

All cervical samples will be processed and tested in the regional cervical cytology laboratory (North Bristol Trust) using the Hologic system. All urine samples will be tested at the cytology laboratory in Manchester using the Roche 8800 platform, as the Hologic system was not as sensitive for urine HPV analysis when compared during a previous study.[28]

Cytology samples performed following a hrHPV positive test will be dual labelled with patient identifying information and study details/study number and stored and managed in accordance with NHS CSP guidance.

Results of the cytological assessment on hrHPV negative samples, which would not ordinarily be performed as part of the NHS CSP, will not be uploaded to the NHS Cervical Screening Administration

Service (CSAS), but will be recorded for the purposes of the study and acted on within the study protocol. Cytology samples from hrHPV-negative tests at 6-weeks postnatal will be destroyed at the end of the study period and not made available to CSAS for future audit.

Management of results and further cervical screening will depend upon previous cervical screening history (whether up to date at time of study, or not), attendance for both samples, and results of screening (see Figure 2 and Figure 3; Supplementary material 3). The sample that demonstrates the higher-grade abnormality will determine the ongoing pathway, according to NHS CSP management guidelines. Participants will be contacted with results and management plan, questions about further management answered, and asked about any adverse events, as well as being encouraged to self-report adverse events to the study team.

Urine samples will be labelled with the study details and study ID number and will be destroyed after testing and communication of results with the study team, participants will not be informed of their urine sample result.

Data collection

Each participant will be assigned a unique study ID following consent to participate. All trial data will be uploaded to the secure web application for managing data, REDCap, which will host the electronic Case Report Form (eCRF). The study co-ordinators will be responsible for analysing and monitoring the data from all sites and thus will have full access to the inputted information and local investigators will be able to access the data from their site only. Participants' electronic notes and cervical screening records will be accessed up to one year after recruitment to gather data on attendance to follow-up, subsequent cervical screening results and any colposcopy assessments.

Statistical analysis

Full details of the statistical analysis will be described in a statistical analysis plan that will be written and finalised before data lock. The primary acceptability outcomes are binary variables; the number of participants attending at 6-weeks of those who consent and the number attending at both 6- and 12-weeks. We will estimate 95% CIs for each using Wilson's method. The primary feasibility outcome is the recruitment rate in the sub study of 100 consecutive potential participants. We will compare pain scores on a 10-point scale of testing at 6- and 12-weeks, using paired sample analysis, and other

patient-reported outcome measures. We will compare inadequacy rates of cytology samples at 6- and 12-weeks. We will use 2 x 2 tables to analyse sensitivity and specificity of: combination HPV testing and cytology of LBC samples at 6- and 12-weeks; HPV testing of LBC samples versus urine samples at both 6- and 12- weeks.

Discussion

Enhancing cervical screening uptake is a healthcare priority, as adequate screening rates lead to reduced incidences of precancerous and cancerous changes in the cervix.[6 7] There is a clear need for research in methods to improve attendance of cervical screening in younger women due to a lack of proven strategies in the current literature.[30] Pregnancy provides several points of contact to engage patients in health promotion through the increased access to healthcare and provides a valuable opportunity to educate and organise cervical screening, especially in 'hardly reached' groups.[10 11 31] Offering opportunistic self-sampling in a healthcare setting during a pre-existing appointment with vaginal swabs to non-attenders achieved uptake rates of 55.9% in a recent study, compared with only 12.9% of those sent test kits via direct-mail.[14] They found that urine self-sampling was preferred to vaginal sampling (41.9% vs. 15.4%), especially among women from ethnic minorities.[13] From our preliminary attitudes to self-sampling data, this is likely to be even more pertinent to the postnatal cohort. However, this work also highlighted that the idea of self-sampling is not preferable to all. Women have identified making and attending appointments as a significant barrier to screening and therefore it is essential to minimise process-based restrictions that limit accessibility to screening services.[16 32] Combining screening with postnatal check-ups offers a golden opportunity to inform women, promote self-care and provide low-effort access to screening. This may require increased flexibility of primary care appointments, unless self-sampling is accurate enough to allow this as an alternative and support a redirection to focus of postnatal care on maternal healthcare needs, not just those of their babies.

We outline the protocol for a study evaluating the feasibility and acceptability of cervical screening using pair-wise sampling of clinician-taken cervical screening tests and self-sampling with urine samples at 6- and 12-weeks postnatal. Uptake to the study, and acceptability of LBC screening at 6-weeks in the consented study sample, will inform whether progression to a definitive trial is justified. We will conduct subgroup analyses of uptake based on screening status to determine feasibility of applying these criteria for the definitive study. To maximise participation in PINCS-1, we will invite women to join

regardless of their screening status at the end of pregnancy, since the aim of a subsequent paired-sample study would be to test the DTA of earlier postnatal sampling, not its effect on uptake.

Overall, through the PINCS-1 study and another study (PINCS-2 - to test the feasibility of individual randomisation to 6- versus 12-week study design), we anticipate establishing the level of acceptability and feasibility to inform design of two further studies and how best to take these forward. First, a DTA study to determine the accuracy of screening for hrHPV and cytological abnormalities at 6-weeks postnatal. This will compare the inadequacy rates, sensitivity and specificity of cervical screening at 6- versus 12-weeks postnatal, informing whether offering earlier postnatal screening is accurate. Provisional power calculations, based on inadequacy rates, estimated requiring over 1000 participants for a formal DTA of cervical screening at 6-week postnatal, hence why this feasibility study is required before embarking on such a significant undertaking. Data from PINCS-1 will inform this study design and size for adequate power.

Second, a randomised control trial (RCT) to examine the effect of earlier postnatal screening on screening uptake rates, as well as the longer-term clinical outcomes, such as rates of high-grade cervical intraepithelial neoplasia (CIN) at subsequent screening tests. Our proposed feasibility studies will determine whether, in this future RCT, it is reasonable and cost-effective to randomise individual participants to screening at 6- or 12 -weeks. If this design is not feasible, a different design will be needed. For example, randomisation without prior consent, such as through applying for a CAG-251 exemption, or a pragmatic cluster-randomised design, such as that employed with YouScreen.[14]

Self-administered vaginal swabs and urine samples for hrHPV testing are under-evaluation.[14 28 33] However, this research will provide crucial insights into postnatal individuals' experiences with, and preferences for different self-sampling methods. These data will help determine the appropriate sample sizes needed to evaluate the accuracy and safety of these self-sampling techniques in future studies involving postnatal cohorts, as well as and influencing future changes to the NHS CSP.

Ethics and dissemination

Ethics

Ethical approval for PINCS-1 was granted by the Stanmore Research Ethics Committee for this study (IRAS project ID:321696; REC reference:24/LO/0206), was adopted by the NIHR Clinical Research Network (CRN) Portfolio (CPMS ID 60494) and is registered on the International Standard Randomised

Controlled Trial Number (ISRCTN) registry (ISRCTN10071810; https://doi.org/10.1186/ISRCTN10071810).

Publication and dissemination plan

Study results will be published as a PhD thesis and in high-impact peer-reviewed papers, as well as presentations at national and international meetings. They will also be presented to members of Maternity Voice Groups, gynaecological oncological charities, Mumsnet and local maternity social media sites. Any data arising from this study will be published and presented in an open-access peer-review journal. The manuscript will be deposited with the University of Exeter, according to the University of Exeter's policies and data sharing policies.

Individual participant data sharing statement

To ensure participant anonymity is safeguarded and subject to any reasonable and necessary delay, pseudonymised research data will be securely archived to a repository following publication of the results where they will be stored for 10 years, as per the Sponsor's policy. These data may be used in future research, here or abroad, and shared, subject to reasonable requests, approved by the sponsor, host institution and the regulatory authorities.

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We are grateful to Flo Cullen, Karen Tanner, Laura Courtney-Stamp, Tessa Dean and Richard Innes of the Department of Research and Development at Somerset NHS Foundation Trust; Kath Hunt, Andrzej Karmolinski and Nichole Villeneuve from the North Bristol NHS Trust for invaluable support and advice; and the NHS CSP Research Innovation and Development Advisory Committee for their formal and informal feedback, helpful suggestions and support in setting up this study. We also thank the public and patients involved in our previous QI and qualitative work that instigated and helped design this research.

Authors' contributions

All authors contributed to the study conception and design. The first draft of the manuscript was written by VC and revised by JM, HB-R, KC and RN. All authors have approved the final version and JM acts as guarantor.

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Protocol version

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Trial Registry

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Secondary identifying numbers

CPMS 60494, MR/X030776/1, IRAS 321696

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Conflicting interests statement

VC - none to declare
RN - none to declare
HBR - none to declare
ARB – none to declare
KC – received honorarium and support from SeeGene

KD – received expenses and honorarium from Hologic. Received test kits and consumables from Hologic, Roche, Rovers and Copan for a previous study, now submitted for publication.

LMcW – none to declare

AS- A member of various expert groups providing advice to the English Cervical Screening Programme including on HPV self-sampling; holds an honorary contract with the University of Manchester to support research into HPV testing in urine samples and Professional Clinical Advisor to the English Cervical Screening Programme.

SS- none to declare

EJC - none to declare

JM – Clinical Advisor to the NHS Cervical Screening Programme Research Innovation and Development Advisory Committee.

Figure legends

Figure 1: PINCS-1 participant flowchart. NTDD = Next Test Due Date.

Figure 2: PINCS-1 study flowchart for those having samples at 6- and 12-weeks. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus; DTA = diagnostic test accuracy; PROM = patient reported outcome measures

Figure 3: PINCS-1 study flowchart for those having samples at 6-weeks who do not attend for their 12-week sample. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus.

Supplementary material

Supplementary material 1 - Visit 2 participant questionnaire

Supplementary material 2 - Visit 3 participant questionnaire

Supplementary material 3 - Standard results letters (as per flow chart labels)

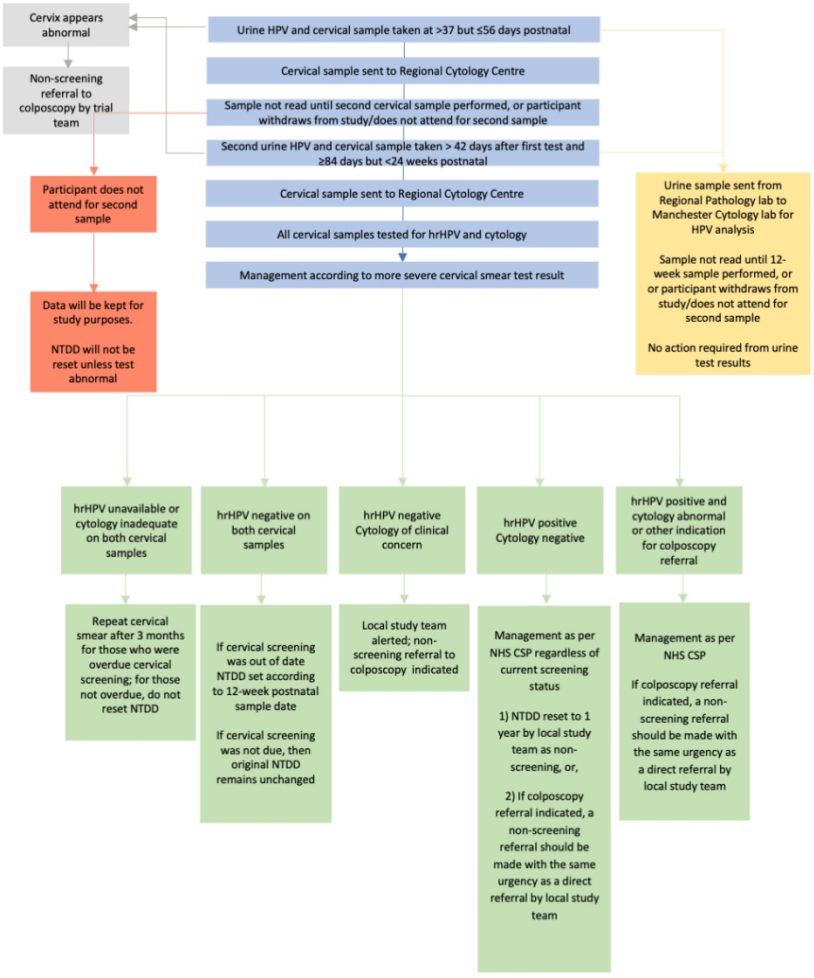
References

1. Eldridge SM, Lancaster GA, Campbell MJ, et al. Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. *PLOS ONE* 2016;11(3):e0150205. doi: 10.1371/journal.pone.0150205
2. Morrison J, Baker-Rand H, Sudha SS, et al. Investigating the acceptability of cervical screening and self-sampling in postnatal women at the 6-week postnatal check London: NHS Health Research Authority; 2023 [Available from: https://www.hra.nhs.uk/planning-and-improving-research/application-

summaries/research-summaries/attitudes-to-postnatal-instead-of-normally-timed-cervical-screening/ accessed 25 Apr 2025 2025.
3. World Health Organisation. Cervical cancer 2024 [Available from: https://www.who.int/health-topics/cervical-cancer#tab=tab_1 accessed 23 May 2024.
4. World Health Organisation. Global strategy to accelerate the elimination of cervical cancer as a public health problem. Geneva: World Health
Organization, 2020.
5. Kitchener HC, Gittins M, Rivero-Arias O, et al. A cluster randomised trial of strategies to increase cervical screening uptake at first invitation (STRATEGIC). *Health Technol Assess* 2016;20(68):1-138. doi: 10.3310/hta20680
6. NHS England. Cervical screening standards data report 2021 to 2022 2023 [Available from: https://www.gov.uk/government/publications/cervical-screening-standards-data-report-2021-to-2022/cervical-screening-standards-data-report-2021-to-2022 accessed 23 May 2024.
7. Landy R, Pesola F, Castanon A, et al. Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. *Br J Cancer* 2016;115(9):1140-46. doi: 10.1038/bjc.2016.290 [published Online First: 20160915]
8. Sabates R, Feinstein L. The role of education in the uptake of preventative health care: The case of cervical screening in Britain. *Social Science & Medicine* 2006;62(12):2998-3010. doi: 10.1016/j.socscimed.2005.11.032
9. NHS Cervical Screening Programme. Audit of invasive cervical cancer: national report 1 April 2016 to 31 March 2019 London2023 [updated 30 November 2023. Available from: https://www.gov.uk/government/publications/cervical-screening-invasive-cervical-cancer-audit-2016-to-2019/nhs-cervical-screening-programme-audit-of-invasive-cervical-cancer-national-report-1-april-2016-to-31-march-2019 accessed 15 June 2024.
10. Office for National Statistics (ONS), released 17 May 2024, ONS website, statistical bulletin, Birth characteristics in England and Wales: 2022 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/livebirths/bulletins/birthcharacteristicsinenglandandwales/2022 accessed 23 May 2024.
11. Coleridge SL, Wiggans A, Nelissen E, et al. Improving the uptake of cervical screening in pregnant and recently postnatal women: a quality improvement project. *BMJ Open Qual* 2022;11(2) doi: 10.1136/bmjoq-2021-001709
12. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Services Research* 2017;17(1):88. doi: 10.1186/s12913-017-2031-8
13. Drysdale H, Marlow LAV, Lim A, et al. Experiences of Self-Sampling and Future Screening Preferences in Non-Attenders Who Returned an HPV Vaginal Self-Sample in the YouScreen Study: Findings From a Cross-Sectional Questionnaire. *Health Expect* 2024;27(4):e14118. doi: 10.1111/hex.14118
14. Lim AWW, Deats K, Gambell J, et al. Opportunistic offering of self-sampling to non-attenders within the English cervical screening programme: a pragmatic, multicentre, implementation feasibility trial with randomly allocated cluster intervention start dates (YouScreen). *eClinicalMedicine* 2024 doi: 10.1016/j.eclinm.2024.102672
15. Albrow R, Blomberg K, Kitchener H, et al. Interventions to improve cervical cancer screening uptake amongst young women: a systematic review. *Acta Oncol* 2014;53(4):445-51. doi: 10.3109/0284186X.2013.869618 [published Online First: 20140207]
16. Waller J, Bartoszek M, Marlow L, et al. Barriers to cervical cancer screening attendance in England: a population-based survey. *J Med Screen* 2009;16(4):199-204. doi: 10.1258/jms.2009.009073

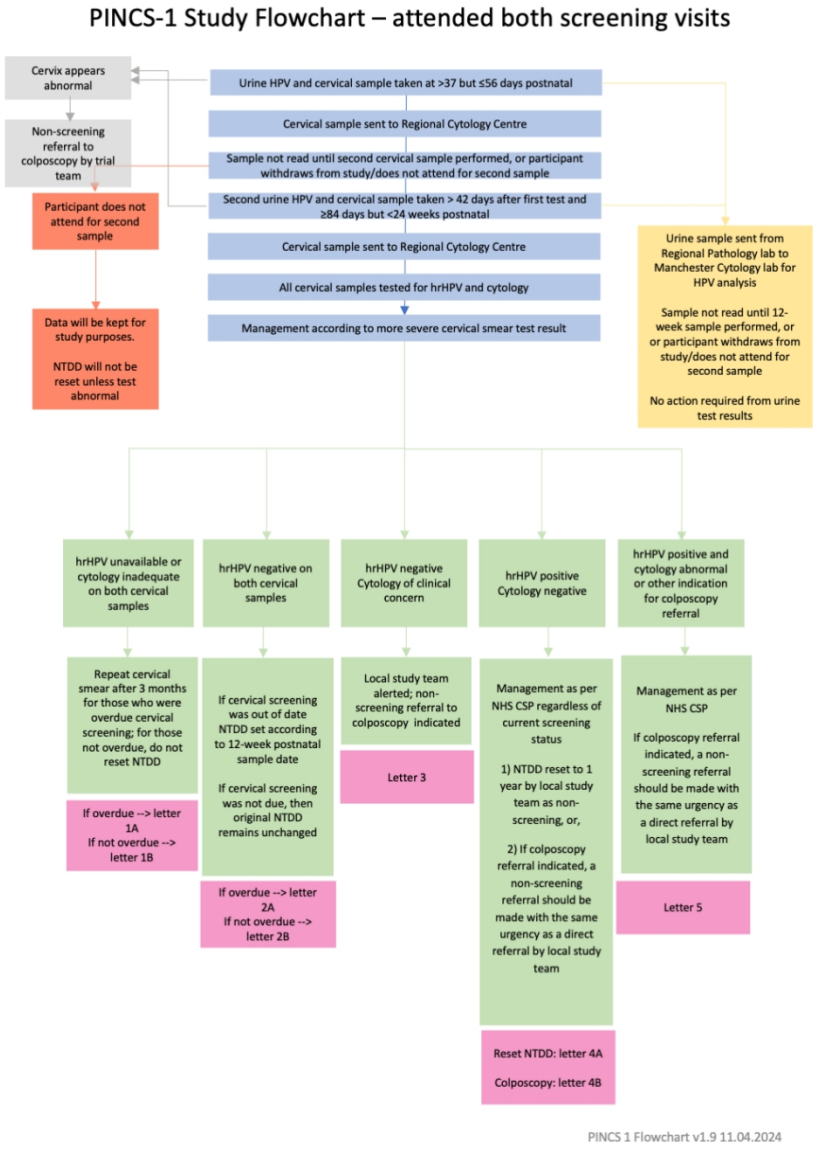
17. National Institute for Health and Care Excellence (NICE) and Royal College of Obstetricians and Gynaecologists. Postnatal Care. NICE guideline [NG194]. London: Department of Health and Social Care, 2021.
18. Smith HC, Saxena S, Petersen I. Postnatal checks and primary care consultations in the year following childbirth: an observational cohort study of 309 573 women in the UK, 2006-2016. *BMJ Open* 2020;10(11):e036835. doi: 10.1136/bmjopen-2020-036835 [published Online First: 20201123]
19. Dunphy M. O76 - Midwives can conduct a cervical screen test (CST) at a 6-week postnatal comprehensive health check. Australian College of Midwives National Conference – Be the Change, September 12-14, 2023, Adelaide, South Australia. *Women & Birth* 2023;36:S30.
20. Jo's Cervical Cancer Trust. Barriers to cervical screening among 25-19 year olds 2016 [Available from: https://www.jostrust.org.uk/sites/default/files/ccpw17_survey_summary.pdf accessed 12th May 2020].
21. Royal College of Obstetricians and Gynaecologists. Cervical smears and pregnancy 2013 [Available from: https://www.rcog.org.uk/for-the-public/browse-our-patient-information/cervical-smears-and-pregnancy/#:~:text=This%20appointment%20will%20usually%20be,and%206%20months%20of%20pregnancy.
22. Rarick TL, Tchabo JG. Timing of the postpartum Papanicolaou smear. *Obstet Gynecol* 1994;83(5 Pt 1):761-5.
23. Leahy M, Farah N, Bolger N, et al. Should cervical smears be taken at a postnatal visit. *The Irish Medical Journal* 2006;99(8):244-45.
24. Trottier H, Mayrand MH, Baggio ML, et al. Risk of Human Papillomavirus (HPV) Infection and Cervical Neoplasia after Pregnancy. *BMC Pregnancy Childbirth* 2015;15:244. doi: 10.1186/s12884-015-0675-0 [published Online First: 20151007]
25. Schmeink CE, Melchers WJ, Hendriks JC, et al. Human papillomavirus detection in pregnant women: a prospective matched cohort study. *J Womens Health (Larchmt)* 2012;21(12):1295-301. doi: 10.1089/jwh.2012.3502
26. Gupta S, Palmer C, Bik EM, et al. Self-Sampling for Human Papillomavirus Testing: Increased Cervical Cancer Screening Participation and Incorporation in International Screening Programs. *Frontiers in Public Health* 2018;6
27. Arbyn M, Smith SB, Temin S, et al. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ* 2018;363:k4823. doi: 10.1136/bmj.k4823
28. Davies JC, Sargent A, Pinggera E, et al. Urine high-risk human papillomavirus testing as an alternative to routine cervical screening: A comparative diagnostic accuracy study of two urine collection devices using a randomised study design trial. *BJOG* 2024;131(11):1456-64. doi: 10.1111/1471-0528.17831 [published Online First: 20240425]
29. Van Keer S, Peeters E, Vanden Broeck D, et al. Clinical and analytical evaluation of the RealTime High Risk HPV assay in Colli-Pee collected first-void urine using the VALHUDES protocol. *Gynecol Oncol* 2021;162(3):575-83. doi: 10.1016/j.ygyno.2021.06.010 [published Online First: 20210623]
30. Albrow R, Kitchener H, Gupta N, et al. Cervical screening in England: the past, present, and future. *Cancer Cytopathol* 2012;120(2):87-96. doi: 10.1002/cncy.20203 [published Online First: 20120224]
31. Lyonnais E, Vigoureux S, Blondel B, et al. Women's country of birth and failure to catch up an overdue cervical cancer cytological screening participation during pregnancy in France, an observational study based on survey sources. *BMC Cancer* 2024;24(1):595. doi: 10.1186/s12885-024-12335-1 [published Online First: 20240516]
32. Wearn A, Shepherd L. Determinants of routine cervical screening participation in underserved women: a qualitative systematic review. *Psychol Health* 2024;39(2):145-70. doi: 10.1080/08870446.2022.2050230 [published Online First: 20220316]

33. Mills C. HPValidate cervical screening self-sampling study nears completion. In: UKNationalScreeningCommittee, ed.: UK Government, 2023.



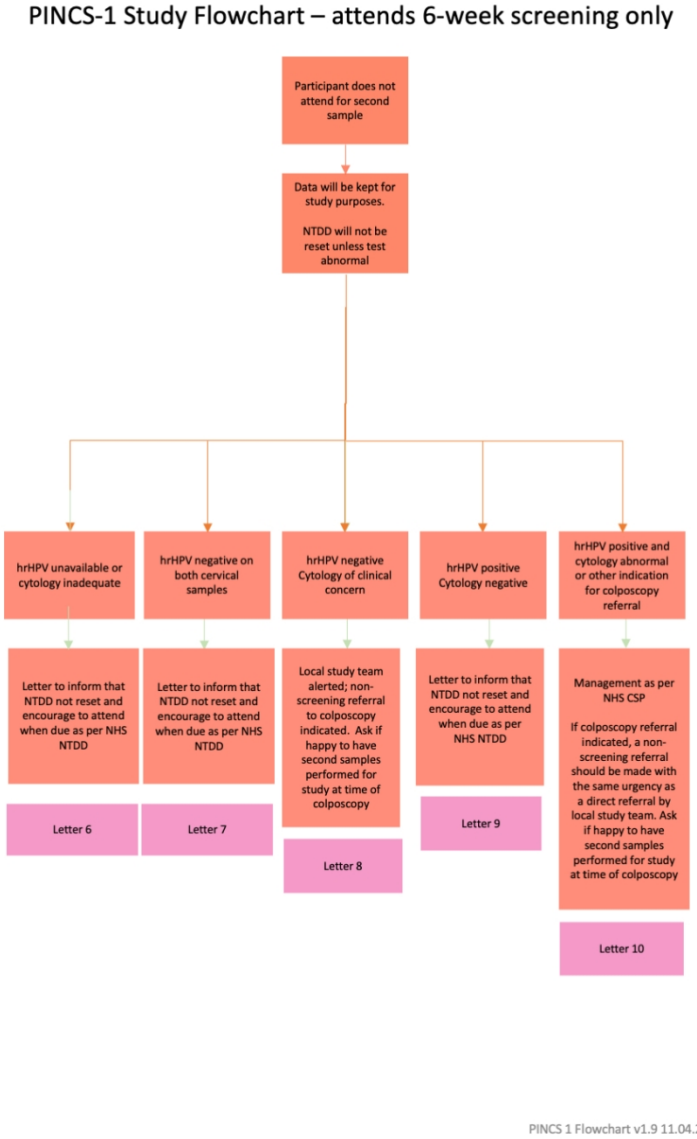
PINCS-1 participant flowchart. NTDD = Next Test Due Date

190x275mm (133 x 133 DPI)



PINCS-1 study flowchart for those having samples at 6- and 12-weeks. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus; DTA = diagnostic test accuracy; PROM = patient reported outcome measures

190x275mm (133 x 133 DPI)



PINCS-1 study flowchart for those having samples at 6-weeks who do not attend for their 12-week sample. NHS CSP = NHS Cervical Screening Programme; NTDD = Next Test Due Date; hrHPV = high risk Human Papilloma Virus.

190x275mm (133 x 133 DPI)

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V.1.4 02/04/24, IRAS:321696 Questionnaire 2(6-week)

PARTICIPANT ID:

Postnatal Instead of Normally-timed Cervical Screening-1 (PINCS-1)

Before completing this questionnaire, please make sure you have read the information sheet.
By completing this questionnaire, you consent to take part in the study.
To complete the questionnaire please circle the answer most applicable to you in each question, tick the correct box or write in the space provided.

Knowledge about HPV

Before we asked you to take part in this study had you heard of HPV (Human papillomavirus)?

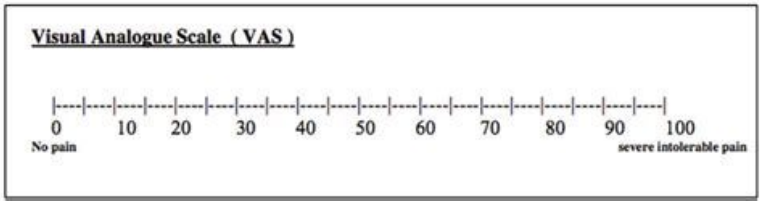
☐Yes ☐No ☐Unsure

About the tests today

Which words describe how you felt about having a clinician take a CERVICAL sample? (Please tick ALL that apply)

☐Uncomfortable ☐It was easy ☐Embarrassed ☐Private ☐Reliable ☐Convenient
☐Comfortable ☐Invasive ☐Unreliable ☐Too soon ☐Reassuring ☐Overwhelming

On a scale of 0 to 100 how uncomfortable was having the cervical sample taken today (0 not at all; 100 extremely painful)? ……..



How much do you agree with these statements? Please circle the appropriate number for each statement.

	Strongly disagree	Somewhat disagree	No opinion	Somewhat agree	Strongly agree
I felt discomfort whilst having a cervical sample	1	2	3	4	5
It felt unpleasant during the cervical sample	1	2	3	4	5
I felt embarrassed during the cervical sample	1	2	3	4	5
I felt anxious during the cervical sample	1	2	3	4	5
I felt reassured by the examination	1	2	3	4	5
I am worried the clinician has not collected the cervical sample correctly	1	2	3	4	5
I am worried how accurate the result from the cervical sample is at 6-weeks after I've given birth.	1	2	3	4	5
I would prefer a clinician to take my sample for cervical screening more than 12 weeks after giving birth.	1	2	3	4	5
I would be happy to have a cervical sample taken 6-weeks after giving birth, at the same time as a routine 6-week postnatal check-up	1	2	3	4	5
I would be happy to have a cervical sample taken 6-weeks after giving birth, but NOT at the same time as a routine 6-week postnatal check-up	1	2	3	4	5
In the future, I would rather delay my cervical screening to more than 12 weeks after giving birth.	1	2	3	4	5
If my cervical screening were due, I would be more likely to have it done, if it were offered at the same visit as the routine 6-week check up	1	2	3	4	5

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V.1.4 02/04/24, IRAS:321696 Questionnaire 2(6-week)

PARTICIPANT ID:

Which words describe how you felt about providing a URINE sample? (Please tick ALL that apply)

☐Uncomfortable ☐It was easy ☐Embarrassed ☐Private ☐Reliable ☐Convenient
☐Comfortable ☐Invasive ☐Unreliable ☐Too soon ☐Reassuring ☐Overwhelming

How much do you agree with these statements about URINE samples? Please circle the appropriate number for each statement.

	Strongly disagree	Somewhat disagree	No opinion	Somewhat agree	Strongly agree
I felt confident collecting a urine sample for cervical screening.	1	2	3	4	5
I felt discomfort whilst collecting the urine sample	1	2	3	4	5
It felt unpleasant collecting the urine sample	1	2	3	4	5
I felt embarrassed collecting the urine sample	1	2	3	4	5
I felt anxious collecting the urine sample	1	2	3	4	5
I am worried I have not collected the urine sample correctly	1	2	3	4	5
I am worried how accurate the urine sample is.	1	2	3	4	5
I would prefer a clinician to take my sample for cervical screening than provide a sample myself.	1	2	3	4	5
A cervical sample taken by a clinician is more reliable.	1	2	3	4	5
I would prefer to take my own urine sample for cervical screening	1	2	3	4	5
I would prefer to take my own vaginal swab sample for cervical screening	1	2	3	4	5
I felt I understood the instructions that were given to me.	1	2	3	4	5
I found it easy to collect a urine sample using the container provided.	1	2	3	4	5
I would prefer to take the urine sample more than 12 weeks after giving birth.	1	2	3	4	5
I would be happy to have a urine sample taken 6-weeks after giving birth, at the same time as a routine postnatal check-up	1	2	3	4	5
I would be happy to have a urine sample taken 6-weeks after giving birth, but NOT at the same time as a routine postnatal check-up	1	2	3	4	5
If my cervical screening were due, I would be more likely to have it done, if it were offered as a urine sample at the same visit as the routine 6-week postnatal check up	1	2	3	4	5

Medical Research Council

NHS Somerset NHS Foundation Trust

V.1.4 02/04/24, IRAS:321696 Questionnaire 2(6-week)

PARTICIPANT ID:

Cervical screening in the future

In the future, would you prefer to do a self-test or have a healthcare professional do the test?

☐ Prefer a self-test with a urine sample
☐ Prefer a self-test with a vaginal swab
☐ Prefer a healthcare professional to do the test
☐ No preference

If you were offered a self-test in the future, would you rather get it…

☐ In the post
☐ In person at the GP surgery
☐ No preference

In the future, the NHS Cervical Screening Programme might offer a choice between using a **URINE or VAGINAL** self test
at home, or going for a cervical screening appointment with a nurse or doctor (we call this '**clinician testing**'). Thinking about this, please tell us how much you agree or disagree with the following statements. (Please circle the appropriate number for each statement)

	Strongly disagree	Somewhat disagree	No opinion	Somewhat agree	Strongly agree
I would like to be offered a choice between self-testing and clinician testing for cervical screening	1	2	3	4	5
I would feel worried about being offered a choice between self-testing and clinician testing for my cervical screening	1	2	3	4	5
I would not want to be offered a choice between self-testing and clinician testing for my cervical screening	1	2	3	4	5
If I was given the choice between self-testing and clinician testing for cervical screening, I would assume it was a way of saving the NHS money	1	2	3	4	5
Being offered a choice between self-testing and clinician testing for cervical screening makes sense to me	1	2	3	4	5
I would find it difficult to choose between self-testing and clinician testing for cervical screening	1	2	3	4	5
Offering a choice between self-testing and clinician testing would improve cervical screening for me	1	2	3	4	5
I would prefer to have a recommendation to do either self-testing or clinician testing rather than having to make a choice myself	1	2	3	4	5
If I tested positive for HPV virus in the urine, I would be more inclined to go for a smear test	1	2	3	4	5

Medical Research Council

NHS Somerset NHS Foundation Trust

V.1.4 02/04/24, IRAS:321696 Questionnaire 2(6-week)

PARTICIPANT ID:

Cervical screening in the past

Is this the first time you have been invited for cervical screening?

☐Yes ☐No ☐Unsure

Have you always attended for cervical screening when invited in the past?

☐Yes ☐No ☐Unsure ☐Not applicable

Have you ever delayed attending for cervical screening?

☐Yes ☐No ☐Unsure

Have any of the following put you off cervical screening?

Embarrassment about having the test	☐ Yes	☐ No	☐ Not sure
Worry about pain or discomfort	☐ Yes	☐ No	☐ Not sure
Difficulty making a convenient appointment	☐ Yes	☐ No	☐ Not sure
Difficulty taking time off work	☐ Yes	☐ No	☐ Not sure
Just not getting round to it	☐ Yes	☐ No	☐ Not sure
Being too busy to go for screening	☐ Yes	☐ No	☐ Not sure
Not feeling at risk of cervical cancer	☐ Yes	☐ No	☐ Not sure
A previous bad experience of screening	☐ Yes	☐ No	☐ Not sure
Not having any symptoms	☐ Yes	☐ No	☐ Not sure
Don't like getting undressed in public	☐ Yes	☐ No	☐ Not sure
Fear of what the test might find	☐ Yes	☐ No	☐ Not sure
Having other health problems	☐ Yes	☐ No	☐ Not sure

Has anything else put you off? -

_____

_____

Medical Research Council

Somerset NHS Foundation Trust

V.1.4 02/04/24, IRAS:321696 Questionnaire 2(6-week)

PARTICIPANT ID:

About you

Which of the following best describes your ethnicity? Please tick your answer below

White	**Multiple ethnic groups**	**Asian/ Asian British**	**Black/African/Caribbean/ Black British**
☐British ☐Irish ☐Gypsy or Irish Traveller ☐White Other, please describe:	☐White and Black Caribbean ☐White and Black African ☐White and Asian ☐Multiple other, please describe:	☐Indian ☐Pakistani ☐Bangladeshi ☐Chinese ☐Asian other, please describe:	☐African ☐Caribbean ☐Black/African/Caribbean other, please describe:
Other ethnic group ☐Arab ☐Other, please describe:		☐Prefer not to say	

How would you best describe your employment status? Please tick your answer below

☐Employed ☐Unemployed ☐Student ☐Full time parent/carer ☐Retired

Which of these qualifications do you have? Please tick all that apply

☐Apprenticeship
☐GCE O-level/GCSE or equivalent
☐ NVQ or equivalent (including BTEC general/national, OND or ONC, City and Guilds Craft)
☐AS, A-level or equivalent
☐Degree or above (including HND or HNC, NVQ level 4 or above, teaching and nurse degree)
☐Postgraduate e.g. second qualification such as masters, PGCERT, PhD
☐None
☐Other (please specify) …….

Which of the following describes how you think of yourself? Please tick your answer below

☐ Woman ☐Man (including trans man) ☐Non-binary
☐ Other (please specify)……
☐ Prefer not to say

Is your gender the same as the gender you were given at birth? Please tick your answer below

☐Yes ☐No ☐ Prefer not to say

Which of the following describes how you think of yourself? Please tick your answer below

☐Heterosexual or Straight ☐Lesbian or Gay ☐Bisexual
☐Other sexual orientation not listed (please specify)……..
☐Prefer not to say

Which of the following describes how you think of yourself? Please tick your answer below

☐I do not consider myself to be disabled ☐Physical disability (including sensory impairment)
☐Learning disability (including development disorders) ☐Another experience of disability
☐Prefer not to say

Medical Research Council

NHS Somerset NHS Foundation Trust

V1.4 02/04/24, IRAS: 321696, Questionnaire 3 (12-week)

PARTICIPANT ID:

Postnatal Instead of Normally-timed Cervical Screening-1 (PINCS-1)

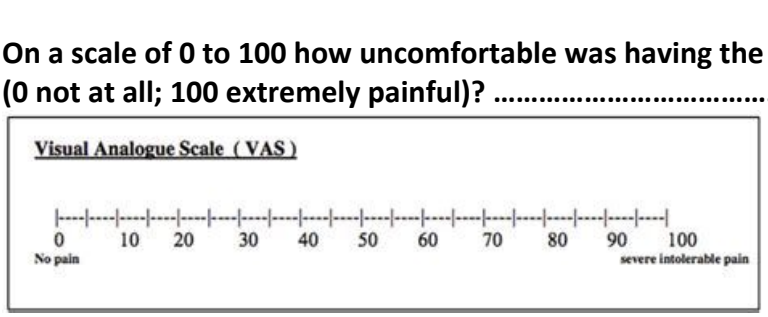
Before completing this questionnaire, please make sure you have read the information sheet.
By completing this questionnaire, you consent to take part in the study.
To complete the questionnaire please circle the answer most applicable to you in each question, tick the correct box or write in the space provided.

About the tests today

Which words describe how you felt about having a clinician take a CERVICAL sample? (Please tick ALL that apply)

☐Uncomfortable ☐It was easy ☐Embarrassed ☐Private ☐Reliable ☐Convenient
☐Comfortable ☐Invasive ☐Unreliable ☐Too soon ☐Reassuring ☐Overwhelming

On a scale of 0 to 100 how uncomfortable was having the cervical sample taken today (0 not at all; 100 extremely painful)? ……..



How much do you agree with these statements? Please circle the appropriate number for each statement.

	Strongly disagree	Somewhat disagree	No opinion	Somewhat agree	Strongly agree
I felt discomfort whilst having a cervical sample	1	2	3	4	5
It felt unpleasant during the cervical sample	1	2	3	4	5
I felt embarrassed during the cervical sample	1	2	3	4	5
I felt anxious during the cervical sample	1	2	3	4	5
I felt reassured by the examination	1	2	3	4	5
I am worried the clinician has not collected the cervical sample correctly	1	2	3	4	5
I am worried how accurate the result from the cervical sample is at 6-weeks after I've given birth.	1	2	3	4	5
I would prefer a clinician to take my sample for cervical screening more than 12 weeks after giving birth.	1	2	3	4	5
I would be happy to have a cervical sample taken 6-weeks after giving birth, at the same time as a routine 6-week postnatal check-up	1	2	3	4	5
I would be happy to have a cervical sample taken 6-weeks after giving birth, but NOT at the same time as a routine 6-week postnatal check-up	1	2	3	4	5
In the future, I would rather delay my cervical screening to more than 12 weeks after giving birth.	1	2	3	4	5
If my cervical screening were due, I would be more likely to have it done, if it were offered at the same visit as the routine 6-week check up	1	2	3	4	5

Which words describe how you felt about providing a URINE sample? (Please tick ALL that apply)

☐Uncomfortable ☐It was easy ☐Embarrassed ☐Private ☐Reliable ☐Convenient
☐Comfortable ☐Invasive ☐Unreliable ☐Too soon ☐Reassuring ☐Overwhelming

How much do you agree with these statements about URINE samples? Please circle the appropriate number for each statement.

	Strongly disagree	Somewhat disagree	No opinion	Somewhat agree	Strongly agree
I felt confident collecting a urine sample for cervical screening.	1	2	3	4	5
I felt discomfort whilst collecting the urine sample	1	2	3	4	5
It felt unpleasant collecting the urine sample	1	2	3	4	5
I felt embarrassed collecting the urine sample	1	2	3	4	5
I felt anxious collecting the urine sample	1	2	3	4	5
I am worried I have not collected the urine sample correctly	1	2	3	4	5
I am worried how accurate the urine sample is.	1	2	3	4	5
I would prefer a clinician to take my sample for cervical screening than provide a sample myself.	1	2	3	4	5
A cervical sample taken by a clinician is more reliable.	1	2	3	4	5
I would prefer to take my own urine sample for cervical screening	1	2	3	4	5
I would prefer to take my own vaginal swab sample for cervical screening	1	2	3	4	5
I felt I understood the instructions that were given to me.	1	2	3	4	5
I found it easy to collect a urine sample using the container provided.	1	2	3	4	5
I would prefer to take the urine sample more than 12 weeks after giving birth.	1	2	3	4	5
I would be happy to have a urine sample taken 6-weeks after giving birth, at the same time as a routine postnatal check-up	1	2	3	4	5
I would be happy to have a urine sample taken 6-weeks after giving birth, but NOT at the same time as a routine postnatal check-up	1	2	3	4	5
If my cervical screening were due, I would be more likely to have it done, if it were offered as a urine sample at the same visit as the routine 6-week postnatal check up	1	2	3	4	5

Medical Research Council

NHS Somerset NHS Foundation Trust

V1.4 02/04/24, IRAS: 321696, Questionnaire 3 (12-week)

PARTICIPANT ID:

Cervical screening in the future

In the future, if you needed a cervical screening test, would you prefer to have the at the same time as a visit to your GP practice for a routine 6-week postnatal check-up?

☐ Prefer at 6-week postnatal check up
☐ Prefer at a separate appointment more than 12 weeks after giving birth
☐ No preference
☐ other – please state ……

In the future, if offered a self-sampling urine test, when would prefer this to be offered?

☐ Prefer at 6-week postnatal check up
☐ Prefer a separate appointment more than 12 weeks after giving birth
☐ No preference

Cervical screening at 6 weeks versus 12 weeks

Have you something you would like to share with us about having cervical screening at 6 weeks postnatal rather than at a later appointment? What would be the benefits of disadvantages to having this at the same visit as the 6-week check up with the GP practice? This might be part of the same appointment or as a double appointment before/after with a practice nurse.

_____

_____

_____

_____

_____

_____

Letters:

Letter 1A:

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

Both of your cervical screening results were inadequate for testing for the human papillomavirus (HPV) and the cell assessment (cytology).

As your cervical screening test is due, as per the normal NHS cervical screening program protocol, we recommend that you have a repeat cervical screening test at your GP practice in three months' time. We have also sent this letter to your GP into this letter to inform them of this.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 1B

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

Both of your cervical screening results were inadequate for testing for the human papillomavirus (HPV) and the cell assessment (cytology).

As your cervical screening test was not due at the time of the study, no action needs to be taken at this time. We recommend you attend for your cervical screening test when it is next due, which you will be informed of by the NHS cervical screening program.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 2A

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

Both of your cervical screening results were negative for HPV (human papillomavirus) and there were no abnormal cells found (negative cytology). This means your risk of cervical cancer is very low.

As your cervical screening test was due, the date for your next test will be reset based upon the date of the second sample that you had as part of the study. You will receive a reminder letter from the NHS cervical screening program closer to the time. If you have not received a letter in three years' time, please contact your GP.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 2B

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

Both of your cervical screening results were negative for HPV (human papillomavirus) and there were no abnormal cells found (negative cytology). This means your risk of cervical cancer is very low.

As your cervical screening test was not due, the date for your next cervical screening will not be changed. You will receive a reminder letter from the NHS cervical screening program when it is due. We recommend you attend as usual, irrespective of your study sample results.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 3

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

Both of your cervical screening results were negative for HPV (human papillomavirus) but at least one sample showed some cells of concern (abnormal cytology). Outside of the study, if a cervical screening test was negative for HPV, we would not have gone on to examine the cells (cytology) and your sample would have been recorded as normal, so these changes are likely to not represent anything significant.

Cervical screening result: ____

However, as a precaution, we recommend a colposcopy examination to look closely at your cervix to see if there is anything that might need a biopsy and/or treatment.

You will receive an appointment for a colposcopy appointment, with a leaflet explaining the procedure.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 4A

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

At least one of your samples was positive for HPV (human papillomavirus). When this result is found, the sample is tested to see if there were any abnormal cells (cytology), this was reassuring (negative) on both of your samples.

As your previous results were normal, the date for your next cervical screening test will be reset to one year's time. You will receive a reminder letter from the NHS cervical screening program when it is due. It is important to attend for this screening.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 4B

Dear _____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

At least one of your samples was positive for HPV (human papillomavirus). When this result is found, the sample is tested to see if there were any abnormal cells (cytology), this was reassuring (negative) on both of your samples.

Because your last two cervical screening tests were also positive for HPV, even though the cells look normal, we recommend a colposcopy examination to look closely at your cervix, to see if there is anything that might need a biopsy and/or treatment.

You will receive an appointment for a colposcopy appointment, with a leaflet explaining the procedure.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 5

Dear ____

I am writing to you regarding your cervical screening results from the PINCS-1 study. Thank you for your participation in our study.

At least one of your samples was positive for HPV (human papillomavirus). When this result is found, the sample is tested for abnormal cells (cytology) and at least one of your samples showed some cells of concern.

Cervical screening result: ____

We recommend a colposcopy examination to look closely at your cervix, to see if there is anything that might need a biopsy and/or treatment.

You will receive an appointment for a colposcopy appointment, with a leaflet explaining the procedure.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 6

Dear _____

I am writing to you regarding your cervical screening result from the PINCS-1 study. Thank you for your participation in our study. As you were not able to attend for the second cervical screening test in the study, this result is from the first sample.

Your cervical screening result was inadequate for testing for the human papillomavirus (HPV) and the cell assessment (cytology).

There has therefore been no change to when your cervical screening test is next due. As this test is not part of the national screening program, if your cervical screening test was due at the time of the study, we recommend you arrange an appointment with your GP to have a cervical screening test.

If your cervical screening test was not due at the time of the study, we recommend you attend when it is next due, you will receive a reminder letter from the NHS cervical screening program closer to the time.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 7

Dear _____

I am writing to you regarding your cervical screening result from the PINCS-1 study. Thank you for your participation in our study. As you were not able to attend for the second cervical screening test in the study, this result is from the first sample.

Your cervical screening result was negative for HPV (human papillomavirus) and there were no abnormal cells found (negative cytology).

As this test is not part of the national screening program, the date for your next cervical screening will not be changed. You will receive a reminder letter from the NHS cervical screening program when it is due. We recommend you attend as usual, irrespective of your study sample results.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 8

Dear _____

I am writing to you regarding your cervical screening result from the PINCS-1 study. Thank you for your participation in our study. As you were not able to attend for the second cervical screening test in the study, this result is from the first sample.

Your cervical screening result was negative for HPV (human papillomavirus) but at least one sample showed some cells of concern (abnormal cytology). Outside of the study, if a cervical screening test was negative for HPV, we would not have gone on to examine the cells (cytology) and your sample would have been recorded as normal, so these changes are likely to not represent anything significant.

Cervical screening result: ____

However, as a precaution, we recommend a colposcopy examination to look closely at your cervix to see if there is anything that might need a biopsy and/or treatment.

You will receive an appointment for a colposcopy appointment, with a leaflet explaining the procedure.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____. Please could you also contact the study team if you would consider having the second cervical screening test for the study at the time of the colposcopy, this is not a requirement and will not affect your care.

Yours sincerely,

Letter 9

Dear _____

I am writing to you regarding your cervical screening result from the PINCS-1 study. Thank you for your participation in our study. As you were not able to attend for the second cervical screening test in the study, this result is from the first sample.

Your sample was positive for HPV (human papillomavirus). When this result is found, the sample is tested for abnormal cells, this was negative on your sample.

As this test is not part of the national screening program, the date for your next cervical screening will not be changed. You will receive a reminder letter from the NHS cervical screening program when it is due. We recommend you attend as usual, irrespective of your study sample results.

If you have any symptoms such as bleeding between periods, after sex or after the menopause, or unusual vaginal discharge, please speak with your GP as soon as possible.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____

Yours sincerely,

Letter 10

Dear _____

I am writing to you regarding your cervical screening result from the PINCS-1 study. Thank you for your participation in our study. As you were not able to attend for the second cervical screening test in the study, this result is from the first sample.

Your sample was positive for HPV (human papillomavirus). When this result is found, the sample is tested for abnormal cells, this identified cells of concern in your sample.

Cervical screening result: ____

We recommend a colposcopy examination to look closely at your cervix, to see if there is anything that might need a biopsy and/or treatment.

You will receive an appointment for a colposcopy appointment, with a leaflet explaining the procedure.

If you have any questions or concerns, or you have experienced any complications or adverse events as a result of the samples taken in the study, please contact your local study team on ____. Please could you also contact the study team if you would consider having the second cervical screening test for the study at the time of the colposcopy, this is not a requirement and will not affect your care.

Yours sincerely,