UK National Screening Committee

Cervical screening: HPV self-sampling for the under-screened population

UK National Screening Committee (UK NSC) meeting
27 March 2025

Purpose

To ask the UK NSC members to:

- recommend offering self-sampling for HPV testing to under-screened women and people with a cervix eligible for the NHS Cervical Screening Programme (CSP) in the 4 UK countries, where it is considered a useful approach to improving informed participation in the programme. The option would be provided alongside clinician-collected sampling.

Pre-existing recommendation (prior to March 2025 meeting)

The UK NSC does not recommend the use of HPV self-sampling in the NHS Cervical Screening Programme (CSP), based on a lack of previous evidence.

2019 Rapid review

In 2017-2019, the UK NSC collected and reviewed evidence regarding a series of potential changes to the NHS CSP. While the primary focus was on CSP screening intervals, the UK NSC also reviewed findings from a literature review on the addition of HPV self-sampling as an offer in the programme. At the time, the Committee considered that self-sampling to engage under-screened people needed further study in research projects. Responses from a 3-month UK NSC public consultation agreed that further research and piloting in a UK setting was necessary before formally implementing any HPV self-sampling strategy within the NHS CSP.

2021-2024 YouScreen study

In 2021, the YouScreen study was initiated in the NHS England CSP in north London. The objective of the study was to assess whether introducing the offer of self-sampling to under-screened groups would increase participation in the NHS CSP. The study completed in 2024, and findings have now been published. They

represent an important update to the UK evidence base, alongside other research as outlined below.

The study aimed to assess the feasibility, acceptability, and impact of offering HPV self-sampling to the under-screened (those at least 6 months overdue their routine screening appointment) in practice. Self-sampling was offered opportunistically in-person in a General Practice primary care setting and systematically via direct mailout, with kits usable at home or in the clinic. Self-sampling was offered as an alternative option, with sampling by a healthcare professional still available to those who preferred it.

The study measured impact as the estimated increase in participation in the CSP from the intervention. Secondary impact outcomes were the estimated cervical intraepithelial neoplasia grade 2 or worse (CIN2+) detection rate and the compliance to follow-up in those with self-sampling HPV-positive tests.

The study suggests that offering self-sampling to under-screened people within the north London screening programme was feasible and raised participation by 1.6% during the study period (7.5 months). Routine roll-out was estimated to increase participation in the CSP by 7.4% over a three-year screening round. In England, this could translate to a change in participation from 69.9% to 77.3% (defined as coverage). Adherence to follow-up was 89.2% by the study end, and the CIN2+ yield was 1.0%. Responders were representative of the ethnically diverse and deprived non-responder population (64% ethnic minority groups, 60% from the two most deprived national quintiles).

See the full published results of the YouScreen trial.

2024 Rapid review

As the YouScreen study neared its conclusion in 2024, the UK NSC initiated a re-assessment of the evidence on HPV self-sampling by commissioning a rapid review focused on the under-screened population. The review was conducted by the Glasgow University National Institute for Health and Care Research Evidence Synthesis Group. The aim of the review was to set the YouScreen study results within the context of the international evidence base. The review explored the published evidence relating to key UK NSC criteria on the:

- test accuracy of self-sampling
- effect of self-sampling as a strategy in increasing screening participation in under-screened people
- acceptability of self-sampling

The review concluded that self-sampling is a feasible strategy for reaching under-screened people and should be considered in the national screening programme. However, the review highlighted that understanding the cost-effectiveness, logistics and implementation strategies through country-specific research and local piloting is important.

2024 HPValidate

When the YouScreen study was conducted, no HPV tests were validated for use on self-collected samples. However, as the alternative for under-screened individuals was no test, and as the accuracy of testing self-samples was known to be high, this was considered ethically appropriate. Anticipating broader self-sampling use, the Department of Health and Social Care and NHSE conducted the HPValidate study (2021–2023) to evaluate the accuracy of HPV testing of self-collected samples compared with clinician collected samples, assess user experiences, and explore future attitudes toward self-sampling.

The study identified four effective self-collection device and HPV test combinations in an NHSE CSP colposcopy referral population setting. These can inform kit and platform choices for under-screened people, who face higher risks of HPV and developing cervical cancer and need accessible, innovative screening approaches. The study also found that self-sampling was acceptable to people who provided a self-sample in a primary care setting.

Published after the Glasgow University 2024 rapid evidence review, the HPValidate findings provide UK evidence on self-sample accuracy and acceptability. Its findings complement the 2024 review and the YouScreen study. See report summarising the results of the HPValidate study here.

2024-2025 YouScreen cost-effectiveness analysis

Building on the findings from the YouScreen trial, the YouScreen team collaborated with the University of Sydney to conduct an evaluation of the cost-effectiveness of the YouScreen approach to self-sampling in under-screened groups using the Policy1-Cervix platform.

The Policy1-Cervix platform is a well-established and validated model of sexual behaviour, HPV transmission, natural history, vaccination, cervical screening, diagnosis and treatment. It has been used to evaluate cervical screening programmes in many countries including England.

The evaluation compared the combined direct mail out and GP opportunistic strategy (YouScreen as it occurred) and the individual components of the strategy with the

status quo (HPV based screening with three-year intervals and no additional strategy to reach under-screened groups).

In the context of the YouScreen trial, *GP opportunistic* refers to the offer of a self-sample kit within a General Practice setting when the individual attended for any reason. The *direct mail out* strategy refers to the distribution of self-sample kits sent directly to individuals by post, without the need to request for a kit (opt-in) or for an in-person visit to a General Practice.

Modelled across the lifetime of a cohort of unvaccinated women aged 26 at entry to the programme, the base case estimate for each of these strategies compared to no offer of self-sampling for under-screened groups was:

- GP opportunistic screening alone: £2,284 / additional QALY gained
- Combined strategy: £8,181 / additional QALY gained
- Direct mail out alone: £9,392 / additional QALY gained

Incremental analysis of these strategies resulted in:

- GP opportunistic screening alone: ICER £2,284 / additional QALY gained
- Combined strategy: ICER £24,562 / additional QALY gained
- Direct mail out alone: had higher costs and fewer QALYs than (was dominated by) the GP opportunistic strategy

These relationships remained the same in a limited probabilistic sensitivity analysis (PSA) which varied input values for costs and utilities. The point estimates for the Incremental Cost-effectiveness Ratios (ICERs) were also closely aligned with those of the base case estimates.

- GP opportunistic screening alone: ICER £4,900 / additional QALY gained
- Combined strategy: ICER £26,040 / additional QALY gained
- Direct mail out alone: had higher costs and fewer QALYs than (was dominated by) the GP opportunistic

From the PSA, at a threshold of £20,000 / additional QALY gained, the GP opportunistic strategy had the highest probability of being cost effective. But at a threshold of £30,000, the combined approach had the highest probability of being cost effective. However, the confidence intervals around these results were very wide, ranging from cost saving to not cost effective at a threshold of £30,000.

Although the Policy1-Cervix platform is a very high-quality model, its structure prevented a more comprehensive PSA being undertaken which would vary a broader range of input values. This may under-represent the uncertainty in the estimated costs and QALYs. The effect of a more comprehensive PSA cannot be

predicted. However individual sensitivity analyses resulted in lower ICERs and may provide reassurance about the robustness of the estimates. The exceptions to this were the analyses which increased the costs, lowered the test sensitivity by 20% and assumed no hysterectomies were performed in the modelled population.

In addition, the point estimate of the GP opportunistic strategy is firmly in the cost-effective range in both the base case and the PSA. The direct mail out strategy may also be justified, from a health economics perspective, given the low cost-effectiveness ratio when compared to the status quo. This could be in situations where implementation of the GP opportunistic strategy is not feasible.

The cost-effectiveness of the combined strategy is more uncertain. However, even here, factors which were not considered in the evaluation may lead to a more favourable estimate. For example, the screening programme in Scotland, Wales and, more recently, England has moved to 5-year screening intervals which are likely to be more cost-effective than the 3-year intervals used in the economic evaluation. It was not possible to undertake an analysis of this in the time available.

There are also different views on the discount rate which should be applied to evaluations of screening programmes. For example, a differential discount rate of 3.5% for costs and 1.5% for benefits is applied as standard practice by DHSC as part of an impact assessment. This would also result in a more favourable estimate for this strategy. An analysis of the impact of this differential discount rate on the base case estimate is presented as part of a post meeting addendum to the minutes of the meeting.

2024-2025 Public consultation

The UK NSC launched a public consultation proposing a recommendation to offer self-sampling for HPV to under-screened women and people with a cervix eligible for the NHS CSP. The consultation opened on 4 December 2024 and closed on 26 February 2025.The consultation cover note and supporting documents were circulated and reviewed by the UK NSC Adult Reference Group (ARG) before the consultation.

The following supporting information was published with the consultation:

- a cover note including the proposed recommendation wording
- a rapid review of the national and international evidence on the offer of self-sampling to under-screened people
- findings from the HPValidate study
- findings from the YouScreen study
- a cost-effectiveness analysis based on the YouScreen study strategies

Public feedback was invited on the recommendation as a whole, its wording, and the supporting information provided.

40 cervical screening stakeholders and subscribers were contacted proactively, alongside NHS and laboratory stakeholders. Cervical screening subscriber organisations are listed in Appendix 1.

Stakeholders including the public were invited to:

- make an overall statement of their views on self-sampling in under-screened people as a strategy to improve engagement with the cervical screening offer and on the quality and accuracy of the supporting documentation
- draw attention to disagreements with any aspects of the documents, including their conclusions and / or the proposed recommendation
- highlight potential inconsistencies in the interpretation of the evidence which has been included in the documents
- comment on whether the recommendation is consistent with the evidence which has been presented
- comment on the feasibility of the recommendation
- alert the committee to questions or evidence which may have been omitted by the documents and which may contribute to the recommendation or its revision
- suggest amendments to important errors in the wording of the documents or the proposed recommendation

Consultation cover note and recommendation

The recommendation on which views were sought was:

Self-sampling for HPV testing can be offered to under-screened people eligible for the Cervical Screening Programme in the 4 UK countries, where service commissioners think self-sampling would be a helpful addition to the programme. If implemented, the option would be provided alongside traditional clinician-collected sampling.

Implementation should follow YouScreen's approach to enhance screening participation:

- An under-screened person is an individual who is overdue for their routine cervical screening appointment by at least 6 months or has never attended.
- The self-sampling kit delivery strategy should be based on the approach taken in the YouScreen trial – either as an opportunistic offer, direct mail-out, or both direct mail-out and an opportunistic offer, depending on the feasibility of implementing each strategy. The opportunistic strategy achieved a higher response rate than direct mail-out and is encouraged.

- Any proposals to add alternative self-sampling kit delivery strategies to the CSP should be supported by UK research evidence demonstrating their effectiveness (for example improved uptake and/or improved detection and treatment of CIN2+).
- Tests and associated workflows which have been validated in the UK for use in self-sampling should be used. For example, those included in the HPValidate study can inform the choice of self-sampling kits and testing platforms for under-screened people in the CSP.
- Appropriate information should be developed to facilitate personal informed choice to participate in the screening programme.

Consultation supporting documentation

A draft version of the rapid review was published in the public consultation to ensure the consultation concluded in time for the March 2025 UK NSC meeting. A quality appraisal of the literature and feedback from the consultation has since been integrated into a final version of the rapid review, which is attached to this cover note and is submitted to the UK NSC.

A cost-effectiveness analysis report based on the YouScreen strategies was also published alongside the public consultation. Since the public consultation, there was an update to the probabilistic sensitivity analysis (PSA) in the cost-effectiveness evaluation to reflect a discussion between the authors and the ARG prior to the consultation. The most up to date results are included in the *'2024-2025 YouScreen cost-effectiveness analysis'* section of this 'coversheet' document. Compared to the version published during the public consultation, this updated analysis includes an increase in the Incremental Cost-effectiveness Ratio (ICER) point estimate in the probabilistic sensitivity analysis (PSA) for the combined strategy from under £20,000 / additional QALY gained to over £20,000 / additional QALY gained.

Specifically, since the public consultation, the changes in the PSA were:

- an increase in the upper bound of the self-sampling test costs to align more closely with the main Policy1-Cervix model
- inclusion of wastage costs arising from unused test kits in the direct mail out strategy
- an increase in the standard error of the mean cost values from 1% to 10%
- an increase in the number of runs from 3,000 to 10,000

This increased the ICER point estimates from:

- GP opportunistic screening alone: ICER increased from £597 to £4,900 / additional QALY gained (latter as reported in the cost-effectiveness section of this document)

- Combined strategy: ICER increased from £19,580 to £26,040 / additional QALY gained (latter as reported in the cost-effectiveness section of this document)
- Direct main out alone: costs remained higher and QALYs fewer than (remained dominated by) the GP opportunistic strategy

Therefore, the most significant change was that the ICER for the combined strategy aligned more closely with that of the base case analysis (£24,562). This emphasised the possibility that the combined strategy was less likely to be cost effective at a willingness to pay threshold of £20,000.

The updated cost-effectiveness findings are incorporated into the cost-effectiveness discussion in this document, and the latest report is attached.

Public consultation responses

39 responses were received. 11 responses from individual clinicians, 7 from academics or academic groups, 7 from national charities or organisations, 6 from local clinical and public health groups, 3 from lay members of the public, 3 from industry manufacturers, and 2 from laboratory specialists or centres. All responses can be seen in full in a document accompanying this cover note.

All respondents to the consultation supported the introduction of self-sampling for HPV to the under-screened population, agreeing that its potential benefits were likely to outweigh any risks.

However, several considerations and issues were raised, and the following themes can be identified across the consultation responses.

The main concerns can be broadly split into two categories: (1) concerns about the proposed recommendation and (2) specific concerns about its implementation.

(1) Concerns about the proposed recommendation included:

- the potential for women to delay their appointment to access self-sampling
- lack of adherence to follow-up pathways
- missed opportunities for broader health discussions
- increased colposcopy referrals
- the sensitivity of self-sampling in detecting CIN2+
- its ability to reach all under-screened populations
- the environmental impact of recommending mailing kits to all, whilst a GP opportunistic-only approach might miss those disengaged from healthcare
- clarity on the proposed screening pathway

- the six-month timeframe for identifying non-responders could be potentially too early to reach the ‘true’ non-responder population
- self-sampling should be available to all those eligible for cervical screening rather than just the under-screened
- whether the UK NSC will provide guidance on alternative delivery models beyond YouScreen, including opt-in models and expanding self-sampling beyond primary care to community services and secondary care
- limiting tests to HPValidate could prevent the use of other sufficiently accurate tests in the CSP

(2) Specific implementation concerns included:

- the need for a national implementation strategy with clear timelines within the screening programme
- potential inconsistencies in delivery due to the recommendation wording and a lack of detail on rollout
- accessible screening information in multiple languages and formats
- messaging should reinforce the need for follow-up clinician tests after an hrHPV+ result to prevent loss to follow-up
- the current screening programme is not accessible to certain groups, such as those who are blind or visually impaired, and that barriers to clinician sampling should be addressed along with the implementation of self-sampling
- self-sampling may exacerbate health inequalities, particularly for marginalised groups, such as trans men and non-binary individuals and homeless populations, if not carefully implemented
- healthcare providers require clear guidance on discussing informed choice regarding self-sampling
- the need for inclusion and validation of alternative sampling devices (e.g., urine, tampons), and a device-neutral procurement framework
- further validation of vaginal self-sampling accuracy and laboratory workflows from HPValidate
- sufficient preparation time for labs to scale up ahead of implementation
- strategies must focus on minimising invalid test rates to ensure programme success

Finally, respondents highlighted further research is needed into triage tools, factors influencing participation and non-participation, and decision-support tools or default test options to improve communication and engagement.

To address some of these risks, respondents emphasised the need for clear communication with both women and people with a cervix and healthcare professionals. Recommending a combined strategy – offering home delivery

alongside GP-based self-sampling – was suggested to address a broader range of barriers to screening. Effective programme monitoring with high-quality follow-up data was seen as essential.

Adult Reference Group and follow-up discussions

The Adult Reference Group (ARG) meeting which took place on 20 February 2025 considered the responses which were available at that point in the public consultation process (20 responses), which was still open. Reflecting the consultation feedback, ARG members expressed support for the recommendation, recognising it as a valuable step toward improving the programme. Group members stressed the importance of aligning the recommendation as closely as possible with the evidence – particularly YouScreen, as it represents the most robust UK data available. Members raised concerns about restricting tests to only those validated in the UK, given the evolving international evidence base.

After the ARG meeting and the closure of the consultation, a follow-up meeting with ARG and Research and Methodology Group (RMG) members was held in early March 2025. The purpose of the meeting was to review the full consultation feedback, including separate feedback from the four UK NHSs provided to the UK NSC, and to discuss responses and next steps. The discussions, based on the feedback from the public consultation, led to revised wording for the recommendation. The updated recommendation, now presented to the UK NSC, is outlined below in this document.

After the consultation closed, the UK NSC Secretariat also met separately with HPV testing and laboratory specialists, as well as some cost-effectiveness experts from the reference groups and the UK NSC. These two meetings reflected on the consultation responses and led to revised wording in the recommendation.

Proposal

It is proposed that UK NSC members:

- acknowledge and thank all members of the public and stakeholders who contributed to the consultation
- note that the responses were positive, with broad support for the recommendation to offer HPV self-sampling to improve participation in under-screened groups who are eligible for cervical screening in the four UK countries

- agree that

i. consultation feedback that impacts the recommendation wording has been carefully reviewed and incorporated where appropriate

For example, to address concerns about the six-month timeframe, the importance of using local under-screening data has been emphasised. Clarifications have been made on delivery methods and alternative approaches. The YouScreen model, which includes both opportunistic offers in primary care and direct mail-out, provides the most direct evidence of the effect of self-sampling in a UK setting. However, the recommendation states that alternative strategies can be adopted where these are supported by a reasonable evidence base.

ii. the majority of concerns about the recommendation relate to implementation and should be addressed by service providers

For example, responses emphasising the need for clear and effective communication provision, and robust monitoring offer constructive suggestions to help ensure that self-sampling is implemented in way which improves the screening programme.

iii. the UK evidence supporting self-sampling is limited to under-screened populations

There is insufficient UK evidence to recommend offering self-sampling universally in the NHS CSP. This will be addressed by an in-service evaluation which is currently being commissioned by the National Institute for Health and Care Research. As such, self-sampling should not extend to well-screened populations until further evidence is provided of its effectiveness in a UK setting.

Recommendation

It is proposed that UK NSC members make the following recommendation:

Self-sampling for HPV testing should be offered to under-screened women and people with a cervix eligible for the NHS Cervical Screening Programme (CSP) in the 4 UK countries, where it is considered a useful approach to improving informed participation in the programme. The option would be provided alongside clinician-collected sampling.

Cervical screening is crucial for preventing cervical cancer, but UK participation has declined in recent years. International and UK evidence shows that HPV self-sampling can be an acceptable and effective way to improve informed uptake,

especially among under-screened, high-risk groups. Offering this option could improve participation and may reduce health inequalities. The YouScreen study provides a reference point for CSPs considering the use of self-sampling.

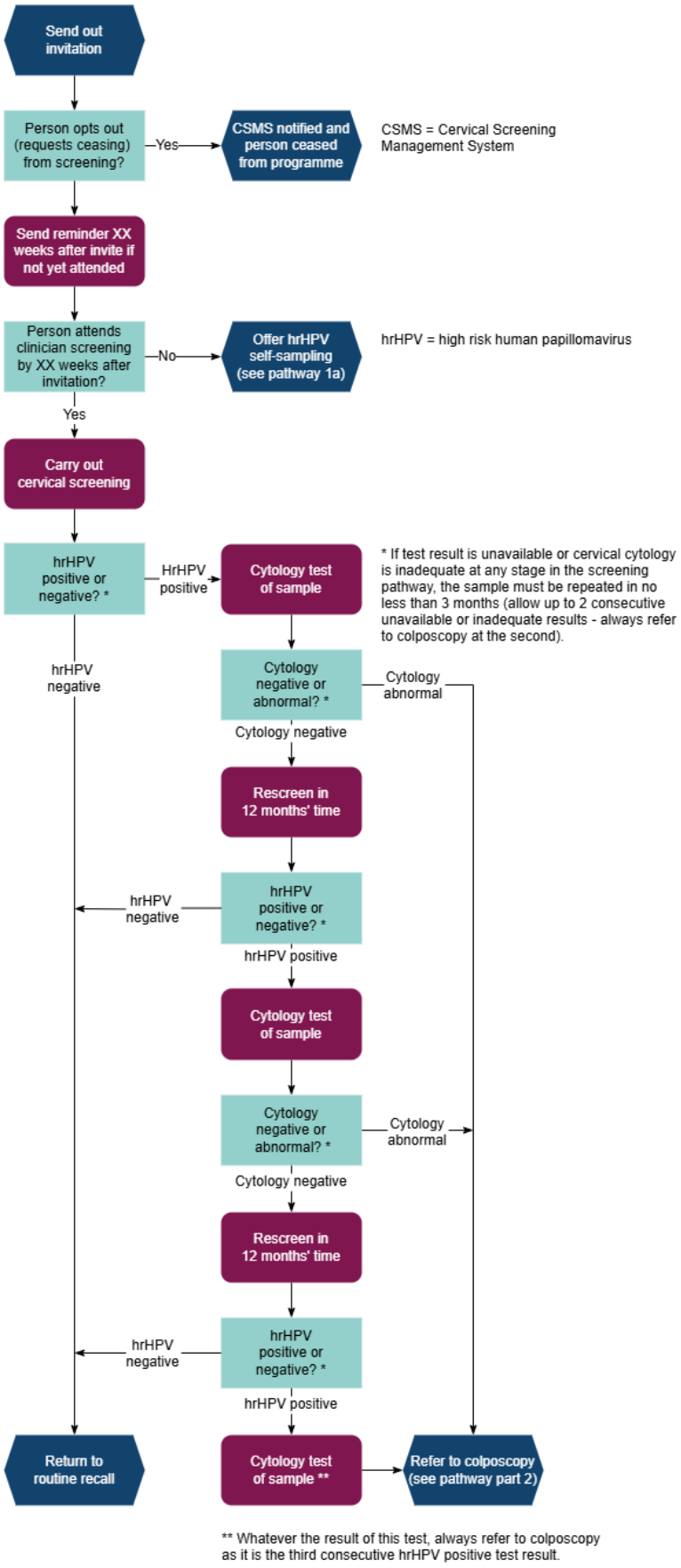
Additional information relating to the recommendation:

The YouScreen study provides a set of delivery approaches with direct evidence of effectiveness in a UK CSP setting and is a reference point for CSPs considering the use of self-sampling:

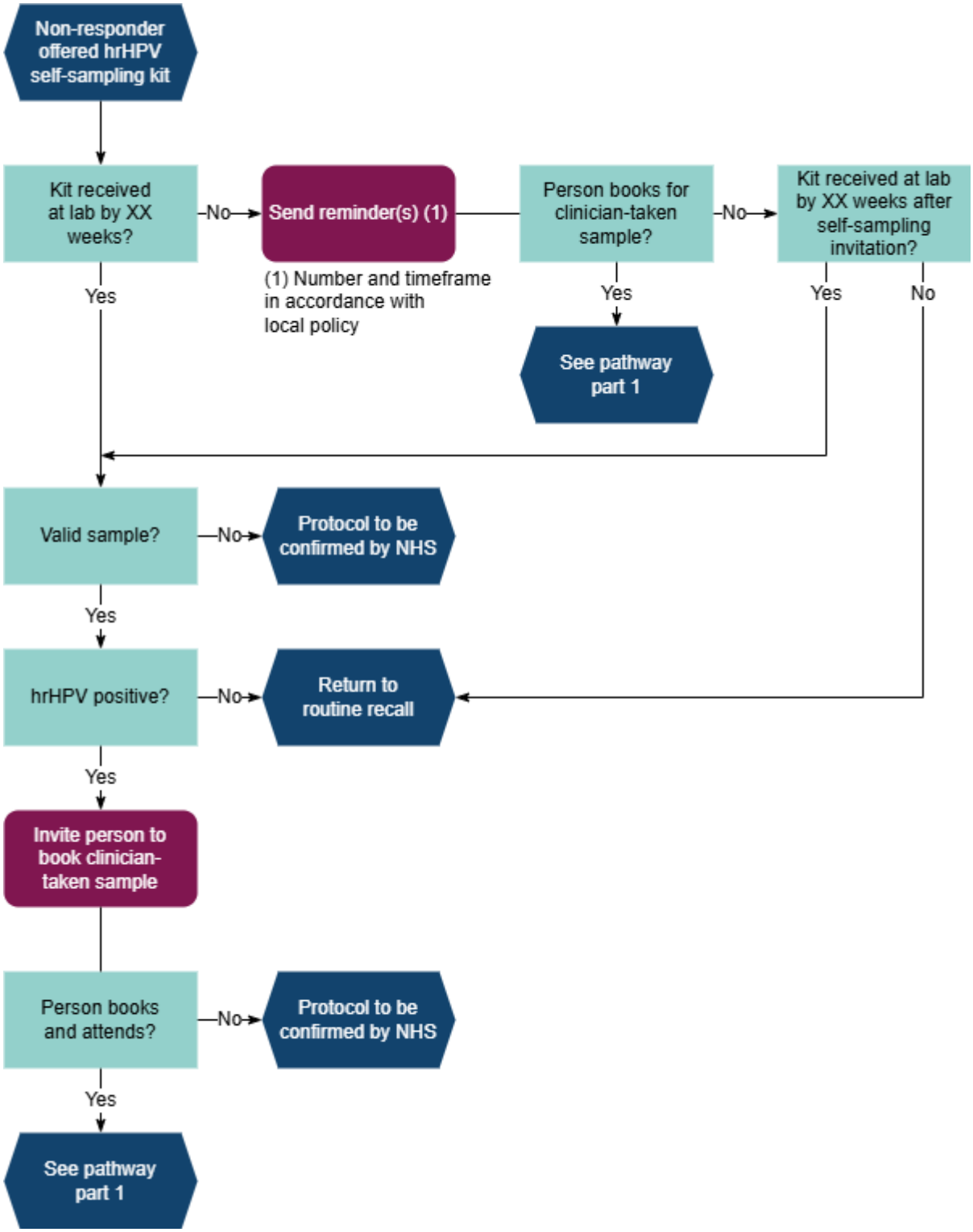
- An under-screened individual is someone who is overdue for their routine cervical screening appointment by at least 6 months or has never attended. The timing of the offer should be informed by local data on participation to ensure it captures individuals who are unlikely to attend for screening.
- The approach to delivering HPV self-sampling kits should follow the model used in YouScreen, using either an opportunistic offer in a General Practice setting, direct mail-out, or a combination of both, depending on the feasibility of implementation. The opportunistic approach had a higher response rate, lower cost, and reached a wider range of people than direct mail-out, making it potentially the most effective option. The cost-effectiveness of delivering both strategies in combination is less certain than delivering them separately.
- Alternative self-sampling kit delivery strategies in the CSP should be supported by robust evidence demonstrating their effectiveness and cost-effectiveness (for example improved uptake and detection and treatment of CIN2+).
- Several self-sample devices and platforms were evaluated through the HPValidate study. Tests should meet or exceed the sensitivity and specificity thresholds demonstrated in HPValidate. The NHS CSP should assure themselves that the test/s and workflows used meet these performance thresholds.
- Accessible evidence-based information should be provided to help individuals make an informed choice about whether to take part in the screening programme.

The self-sampling pathway supporting the recommendation is presented in the two documents below. Pathway 1 reflects the current published cervical screening pathway, while Pathway 1a is an indicative update to include self-sampling.

Pathway 1


Send out invitation
Person opts out (requests ceasing) from screening?
Yes
CSMS notified and person ceased from programme
CSMS = Cervical Screening Management System
Send reminder XX weeks after invite if not yet attended
Person attends clinician screening by XX weeks after invitation?
No
Offer hrHPV self-sampling (see pathway 1a)
hrHPV = high risk human papillomavirus
Yes
Carry out cervical screening
hrHPV positive or negative? *
HrHPV positive
Cytology test of sample
* If test result is unavailable or cervical cytology is inadequate at any stage in the screening pathway, the sample must be repeated in no less than 3 months (allow up to 2 consecutive unavailable or inadequate results - always refer to colposcopy at the second).
hrHPV negative
Cytology negative or abnormal? *
Cytology abnormal
Cytology negative
Rescreen in 12 months' time
hrHPV positive or negative? *
hrHPV negative
hrHPV positive
Cytology test of sample
Cytology negative or abnormal? *
Cytology abnormal
Cytology negative
Rescreen in 12 months' time
hrHPV positive or negative? *
hrHPV negative
hrHPV positive
Return to routine recall
Cytology test of sample **
Refer to colposcopy (see pathway part 2)
** Whatever the result of this test, always refer to colposcopy as it is the third consecutive hrHPV positive test result.

Pathway 1a


Non-responder offered hrHPV self-sampling kit
Kit received at lab by XX weeks?
No
Send reminder(s) (1)
(1) Number and timeframe in accordance with local policy
Person books for clinician-taken sample?
No
Kit received at lab by XX weeks after self-sampling invitation?
Yes
Yes
See pathway part 1
Yes
No
Valid sample?
No
Protocol to be confirmed by NHS
Yes
hrHPV positive?
No
Return to routine recall
Yes
Invite person to book clinician-taken sample
Person books and attends?
No
Protocol to be confirmed by NHS
Yes
See pathway part 1

Action

The UK NSC meeting is asked to consider this paper and the circulated documents and to approve the proposed recommendation.

Attached (circulated) documents:

- Consultation responses
- Glasgow rapid review (final)
- YouScreen cost-effectiveness analysis (final)

Appendix 1

List of cervical screening stakeholders and subscribers proactively contacted: UK NSC cervical screening subscribers:

Belfast Health & Social Care Trust

Brighton and Hove City Council

British Association of Surgical Oncology

British Gynaecological Cancer Society

Camden Council

Canadian Partnership Against Cancer

Cancer Research UK

Cardiff University

Cogora Healthcare Communications Agency

C the signs

Eve Appeal

Faculty of Public Health

Gesundheit Österreich GmbH (GÖG)

GRACE charity

Health and Care Jersey

Hologic

King's College London

Macmillan

Queen Mary's University of London

Northern Ireland Cancer Network

Northumbria University

Owkin

Public Health Agency of Canada

Roche

Society of Radiographers

The Royal College of General Practitioners

The Royal College of Nursing

The Royal College of Pathologists

The Royal College of Physicians

The Royal College of Physicians and Surgeons of Glasgow

The Royal College of Physicians of Edinburgh

The Royal College of Radiologists

The Royal College of Surgeons

The Royal College of Surgeons of Edinburgh

The University of Aberdeen

The University of Leeds

The University of Manchester

The University of Sydney

UK Cervical Cancer

Yorkshire Cancer Research

Appendix 2: YouScreen cost query responses

Response to queries relating to costs in the cost-effectiveness analysis for YouScreen.

Query 1: Cost of the test

Some members thought the rationale for the cost of the HPV test, as laid out in table 3, was not sufficiently explained. This was particularly the case for the mail out and GP opportunistic strategies. In this regard some members would like some more

information to reassure them that the cost was realistic as opposed to that used in the sensitivity analysis exploring the upper bound of the HPV test costs (table 21).

We did some work with XXXXX (Public Health Wales) on the cost of the test in current practice as part of the work on screening in the presence of the vaccination programme. This came out as £28.70 which is very close to the cost of the clinician taken test in table 3. I think that might help to some extent.

But is there any information that can be provided to respond to the concern about the cost of the self-sampling test?

Response 1: Cost of the test

Costs for the self-sampling test were derived from two sources: the YouScreen trial itself, and the costs of supplying HPV testing under the NHS Cervical Screening Programme in England.

The costs used for postage and the self-sampling kit were the actual prices paid by the YouScreen trial.

In the YouScreen trial, the laboratory provided a range to YouScreen for use in the economic analysis in which £29 pounds per person was considered an acceptable midpoint and did not breach any commercial sensitivity. This cost was negotiated with the laboratory by the NHS London procurement team and necessarily needed to account for new process set-up, drafting a manual, quality-control, training, repeat kit management, technology development, administration, additional demands that were specific to a clinical trial, etc. The trial investigators and YouScreen study group were advised by NHS London that these trial lab costs were higher than the usual fee per test in the service contract (but they were unable to disclose the fee per test due to commercial sensitivity of this information). Therefore, for the purposes of the costeffectiveness analysis, the laboratory cost from YouScreen was used as a high-end estimate only, as the study team believed that this cost would not be reflective of what would in practice be achieved under a tender of delivering self-collected HPV testing nationally (an assumption that the lab confirmed was reasonable). A more realistic estimate of laboratory costs per test was used for the base case (£16.09), derived from unpublished (and sensitive) contract award data from NHS England provided to the senior consultant to YouScreen, which included the forecasted number of HPV and cytology tests and the overall funding awarded, and also an LBC price of £25 in London. Collectively, this information allowed region-specific HPV test costs to be estimated, with £16.09 being the cost calculated for the NHSE London region (this cost also being similar to the average cost across 9 regions of £16.39).

The cost of sample collection for a clinician-collected sample is based on inflated values from a prior cost-effectiveness analysis of cervical screening in England led by Mark Jit (Bains 2019 Int J Gynecol Cancer). There was assumed to be no sample collection cost associated with a clinic visit or GP time for the primary HPV test in the

GP Opportunistic self-sampling scenario, because the test was offered during a visit that the participant was attending anyway for other purposes. Both self-sampling delivery approaches (mail-out and GP opportunistic) included a sample collection cost for a clinic visit associated with triage cytology in the event of a positive HPV test.

Query 2: Cost of the GP Opportunistic approach as a whole

Maybe an extension of the above, some members were concerned that the assumption that the GP opportunistic strategy would cost less than the direct mail out strategy was not sufficiently explained.

Is there any information that could be provided to respond to this concern?

Response 2: Cost of the GP Opportunistic approach as a whole

The GP opportunistic approach cost less overall than direct mail-out for 3 reasons:

1. **Wastage**: there is substantially less waste associated with the GP opportunistic pathway, because in the mail-out pathway there are many kits posted to women that are not ultimately returned. As noted in the discussion section of the report: "...approximately 7 to 8 test kits are sent out for each test returned in the first direct mail-out offer (although once people have used self-sampling using direct mail-out, they continue to do so). Therefore, over the lifetime of someone who is first offered and uses self-sampling at age 26 (including at every recommended test thereafter), they will have around 11 HPV tests, but a further 7 to 8 kits needed to be sent for their first test to be returned. Effectively, this means that their 11 tests required 18 to 19 kits in total to be sent plus 11 laboratory tests, so the cost of each HPV test in their lifetime was approximately £29 to £32." In contrast, the tests which are provided for self-collection during GP opportunistic screening are assumed to actually be used, because the return rates were directly based on YouScreen.

2. **Additional mail-out costs**: the direct-mail out pathway has additional costs associated with postage that are not applicable to the GP opportunistic pathway (and there is no analogous cost in the GP opportunistic pathway because, as above, the initial clinic visit is occurring anyway so has no additional cost).

3. **Distribution between self- and clinician-collected HPV tests overall**: as noted in the discussion of the report, on p 62, 'The screening costs for each scenario in the model is affected by the overall cost of HPV screening including delivery, which differs for clinician-collection, direct mailout, and self-samples collected opportunistically at GP visits, and by number of tests which are self-collected versus clinician-collected (which is affected by uptake of self-sampling, as this shifts some people who would have eventually screened with a clinician-collected test to be screened earlier using self-sampling; see Figure 23 in Appendix 3). The GP opportunistic scenario had higher uptake than the direct mail-out scenario, so had

more tests overall, but fewer were clinician-collected tests (as more people had used self-sampling), and in this scenario, the total cost which includes laboratory cost and delivery cost, where the delivery of the clinician-collected tests is substantially more expensive than self-collected tests (£38.80 vs £19.65). In contrast, the lower uptake in the direct mail-out scenario means that a higher proportion of HPV tests overall are the more expensive clinician-collected tests.'

Overall, the GP opportunistic pathway represented a very low-cost way to deliver the HPV test, as there is no cost of postage, and no wasted kits. There is also no additional GP time required per completed test compared to either No YouScreen or the direct mail-out approach.

Appendix 3: YouScreen updated discounting table

Summary

Using a differential discounting rate of 3.5% for costs, and 1.5% for benefits resulted in an increase in quality adjusted life-years (QALYs) overall, and a decrease in ICERs for all strategies. The order of cost-effectiveness of strategies did not change. On the cost-effectiveness frontier YouScreen GP opportunistic (ICER: £1,217/QALY) was more cost-effective than the comparator (No YouScreen Status-quo), the final strategy on the cost-effectiveness frontier was YouScreen (GP opportunistic + Mail out) with an ICER of £17,828/QALY.

Overall, strategies incurred an additional (discounted) cost compared to No YouScreen/ status-quo of between £57,112 (GP opportunistic), and £278,166 (GP opportunistic + Mail out), and resulted in total (discounted) QALY gains of 47-59 QALYs compared to No YouScreen.

These findings are summarised in Table A1. Table A2 is directly equivalent to Table 9 in the original report, but with the updated discount rate of 1.5% used for QALYs.

Table A1. Summary of discounted measures for a cohort of 100,000 women aged 26, with a differential discount rate (3.5% rate for costs 1.5% discounting rate for benefits).

Outcome	No Screening	No YouScreen (status quo)	YouScreen (Mail-out)	YouScreen (GP opportunistic)	YouScreen (GP opportunistic + mail-out)
Total costs	*£4,034,224*	*£33,962,012*	*£34,185,904*	*£34,019,124*	*£34,240,178*
Quality-adjusted life-years (QALYs)	*5,413,905*	*5,418,450*	*5,418,497*	*5,418,497*	*5,418,509*
Relative to "No Screening"					
Difference in total costs	-	*£29,927,788*	*£30,151,680*	*£29,984,900*	*£30,205,954*
QALYs gained	-	*4,545*	*4,592*	*4,592*	*4,604*
CER	-	*£6,585*	*£6,566*	*£6,530*	*£6,560*
Relative to "No YouScreen"					
Difference in total costs	-	-	*£223,892*	*£57,112*	*£278,166*
QALYs gained	-	-	*47*	*47*	*59*
CER	-	-	*£4,737*	*£1,217*	*£4,687*
Incremental^ cost per additional:					
CIN2+ detected	-	-	*£3,065*	*£751*	*£1,806*
CIN3+ detected	-	-	*£6,715*	*£1,428*	*£3,613*
Incremental cost-effectiveness ratio (ICER) (per additional QALY gained)	-	-	*Strongly dominated***	*£1,217*	*£17,828*

*** Any strategy with lower (or equivalent) effectiveness but higher costs than another strategy is said to be "strongly dominated".*

^ *incremental to the next most effective strategy*

Table A2. Summary of all model findings for a cohort of 100,000 women aged 26, with a differential discount rate (3.5% rate for costs 1.5% discounting rate for benefits).

Outcome	No Screening	No YouScreen (status quo)	YouScreen (Mail-out)	YouScreen (GP opportunistic)	YouScreen (GP opportunistic + mail-out)
CIN2+ detected	-	*5,783*	*5,856*	*5,859*	*5,937*
Additional CIN2+ detected	-	-	*73*	*76*	*154*
CIN3+ detected	-	*3,711*	*3,744*	*3,751*	*3,788*
Additional CIN3+ detected	-	-	*33*	*40*	*77*
Cervical cancer cases	*1,316*	*380*	*370*	*369*	*363*
Cervical cancer incidence (ASR*)	*16.6*	*4.4*	*4.3*	*4.3*	*4.2*
Cervical cancer cases prevented compared to					
"No Screening"		*936*	*946*	*947*	*953*
"No YouScreen"	-	-	*10*	*11*	*17*
Cervical cancer deaths	*457*	*119*	*115*	*115*	*115*
Cervical cancer mortality (ASR)	*5.50*	*1.31*	*1.28*	*1.28*	*1.26*
Cervical cancer deaths prevented compared to:					
"No Screening"	-	*338*	*342*	*342*	*342*
"No YouScreen"	-	-		*4*	*4*
Cumulative life risk of cervical cancer: diagnosis	*1.32%*	*0.38%*	*0.37%*	*0.37%*	*0.36%*
Death	*0.46%*	*0.12%*	*0.12%*	*0.12%*	*0.12%*
HPV tests	-	*830,446*	*844,878*	*846,153*	*859,251*
Average lifetime HPV tests per woman	-	*8.30*	*8.45*	*8.46*	*8.59*
Colposcopy evaluations	-	*32,322*	*32,796*	*32,882*	*33,396*
Number of colposcopies needed to prevent one cervical cancer case					
compared to "No Screening"	-	*34.5*	*34.7*	*34.7*	*35.0*
compared to "No YouScreen"	-	-	*46.2*	*50.9*	*63.2*
Number of colposcopies needed to prevent one cervical cancer death					
compared to "No Screening"	-	*95.6*	*96.0*	*96.1*	*97.6*

Outcome	No Screening	No YouScreen (status quo)	YouScreen (Mail-out)	YouScreen (GP opportunistic)	YouScreen (GP opportunistic + mail-out)
compared to “No YouScreen”	-	-	*133*	*140*	*269*
Biopsies	-	*24,231*	*24,556*	*24,626*	*24,987*
Precancer treatments	-	*8,802*	*8,901*	*8,914*	*9,023*
Number needed to treat to prevent one cervical cancer case					
compared to “No Screening”	-	*9.40*	*9.41*	*9.41*	*9.47*
compared to “No YouScreen”	-	-	*9.67*	*10.18*	*13.00*
Number needed to treat to prevent one cervical cancer death					
compared to "No Screening"	-	*26.04*	*26.06*	*26.06*	*26.38*
compared to "No YouScreen"	-	-	*28*	*28*	*55*
Discounted measurements:					
Total costs	*£4,034,224*	*£33,962,012*	*£34,185,904*	*£34,019,124*	*£34,240,178*
Quality-adjusted life-years (QALYs)	*5,413,905*	*5,418,450*	*5,418,497*	*5,418,497*	*5,418,509*
Relative to “No Screening”					
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Relative to “No YouScreen”					
Difference in total costs	-	-	*£223,892*	*£57,112*	*£278,166*
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CER	-	-	*£4,737*	*£1,217*	*£4,687*
Incremental cost per additional:					
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CIN3+ detected	-	-	*£6,715*	*£1,428*	*£3,613*
Incremental cost-effectiveness ratio (ICER) (per additional QALY gained)	-	-	*Strongly dominated***	*£1,217*	*£17,828*

** ASR per 100,000 women standardised to the revised 2013 European Standard population.(Office for national statistics 2016).*

*** Any strategy with lower effectiveness but higher costs than another strategy is said to be “strongly dominated”.*