



UK National  
Screening Committee

## UK National Screening Committee

### Cervical Screening

#### Programme modifications looking at; interval/ surveillance, women over 64 and self-sampling

27 February 2019

#### Aim

1. To ask the UK National Screening Committee (UK NSC) to approve a series of modifications to the NHS Cervical Screening Programme. The modifications relate to:
  - the intervals for primary screening and the surveillance pathway for women with HPV + / cytology – results
  - the strategy for women aged 64 who are exiting the programme
  - self sampling within the screening programme

#### Background

2. The UK NSC recommended the use of primary HPV screening in the cervical screening programme in November 2015. The review document informing this recommendation is attached for information.

Since that point the discussion focused on the national recommendations required on screening intervals for HPV negative women and the surveillance intervals for HPV positive / cytology negative women. The main discussion has focused on:

- whether to extend the screening interval for screen negative women
- a 12 month surveillance interval for HPV positive / cytology negative women and
- whether genotyping should be used to guide the colposcopy referral strategy in the surveillance pathway

In February 2018 the Committee received a report from the HPV pilot sites which suggested that there is little clinical advantage in using genotyping within a surveillance strategy. This was consistent with the results of the ARTISTIC model. The report from the pilot sites also highlighted concern about loss to follow up in women with HPV +/cytology – results if they are recalled for further testing rather than referred for colposcopy following the second surveillance round.

At the Committee's June 2018 meeting it was agreed that a model commissioned by the NHS Cervical Screening Programme should be used as the basis of the core consultation proposals relating to screening intervals and surveillance strategy in the four nations. The results of the model were broadly consistent with those of other models developed in this area. The proposed strategy was:



- an extended , five year, screening interval for HPV negative women irrespective of age
- a 12 month surveillance interval for HPV positive / cytology negative women and that
- women with persistent HPV infection and negative cytology should undergo two surveillance tests. If HPV positive at the second test they should be referred to colposcopy irrespective of cytology result

At the same meeting the strategy for women exiting the programme was also considered. The upper age limit of the screening programme is 64. It was noted that there was an absence of evidence to guide recommendations on women exiting the programme.

A literature search undertaken in October 2016 did not identify any primary studies exploring issues related to women exiting the programme when reaching the upper age limit for screening. Similarly no estimates of outcomes in this group were identified in a summary of modelling studies commissioned by the UK NSC evidence team.

The recommendations for women exiting the programme were proposed by the English Cervical Screening Programme Advisory Group. These were:

- HPV positive / cytology positive women should be managed in the same way as other age groups
- HPV positive / cytology negative women should be recalled at 12 months and, if still HPV positive, be referred for colposcopy. If colposcopy is:
  - i. decisively negative this would prompt discharge from the programme
  - ii. decisively positive this would prompt the offer of loop excision
  - iii. indecisive this would prompt the offer of loop excision or recall a further 12 months later
- as there is an absence of evidence in this area the Programme should work with the relevant national professional or standard setting bodies to produce a clinical consensus statement to guide practice in this area.

In relation to self sampling within the screening programme the proposal was that:

- self sampling as a strategy to address non attendance for screening requires further study in well organised pilots and research projects
- other questions relating to the fit between this approach and the screening programme should also be the subject of research and piloting. For example this would apply to the use of self sampling as an approach to routine screening programme delivery.



## Consultation

3. The UK NSC hosted a three month public consultation exercise which closed in January 2019. Comments were requested on the above proposals. Twenty one stakeholder organisations were contacted directly about the consultation these are listed at the end of this document. **Annex A**

Thirteen responses were received. The responses have been circulated as a zip file.

## Responses

### *Screening intervals and surveillance intervals*

Across the responses there was a broad consensus on the proposal for a five year primary screening interval and the proposal for two surveillance tests at 12 month intervals for women with HPV + / cytology – test results.

Views diverged on the management of women whose results remained HPV + / cytology – at the second surveillance test. It was acknowledged that there was a very limited evidence base relating to this point in the pathway and that the proposed strategy to offer colposcopy to all would be a conservative strategy. However there was also concern that the positive predictive value of colposcopy would be low and that cytology triage may be a realistic and equally safe approach. In addition there was interest in the use of genotyping and other markers to stratify risk at this point in the pathway.

Across the responses there was interest in monitoring and evaluating any strategies that were implemented to manage persistently HPV + / cytology – results.

### *Women aged 64 and over who are exiting the programme*

The absence of evidence in this area was acknowledged across the responses and again there was broad consensus on the basics of the proposed strategy.

Again, views diverged on the management of women with HPV + / cytology – results at the final screening test. In this respect some stakeholders suggested that the number of surveillance test should be the same as in the younger age groups and different combinations of further surveillance, colposcopy and loop excision were suggested.

Given the lack of evidence, stakeholders generally found the proposal to develop a consensus guideline useful and, again, there was interest in monitoring and evaluating any implemented strategies.

### ***Self sampling***

There was broad consensus that further research and piloting was necessary before formally implementing self sampling within the screening programme.

### ***Future developments***

The responses raised a number of issues might be considered as part of the future development of the screening programme. These included:

- use of genotyping at the primary screening test and in the surveillance pathway
- use of novel markers to stratify risk
- revision of the upper age limit for screening
- revision of the screening intervals, for example six years for the under 50s and 10 years for the over 50s
- adjunctive colposcopy
- psychological impact HPV screening
- determinants of non-attendance

Some of these issues might feed into the programme's research agenda along with self sampling. Others might be addressed in the modelling work considering screening in the vaccinated population which is currently being initiated by the UK NSC evidence team.

### ***Programme implementation and QA issues***

The responses also raised a number of issues which are important to the delivery of the proposed changes but which are not strictly UK NSC issues. These included:

- planning to avoid logjams in service delivery
- ensuring an appropriately configured IT system is available
- communication strategy
- ensuring operational rules are in place regarding screening intervals in non attenders
- ensuring clear stopping rules are in place at the upper age limit, for example how to manage late attenders over the age of 64
- arrangements for audit and feedback
- monitoring performance of the test following implementation



## Proposal

4. It is proposed that:
  - an expanded, five year, screening interval for women who test HPV negative at their routine screen, irrespective of age should be implemented
  - a 12 month surveillance interval for HPV positive / cytology negative women should also be implemented
  - women who are HPV positive / cytology positive at their final screen should be managed in the same way as other age groups and those who are HPV positive / cytology negative women should be recalled at 12 months
  - work should be undertaken to develop consensus on the acceptable options for managing women with HPV+ / cytology – test results in the surveillance pathway along with a mechanism to evaluate the impact (for example clinical and logistic) of different strategies
  - self sampling should not be implemented within the screening programme without further research and piloting which demonstrates its value
  - UK NSC activity should be focused on the development of recommendations to guide screening in the vaccinated population

## Action

5. The UK NSC is asked to approve above proposal.



**UK National  
Screening Committee**

## **Annex A**

### **List of organisation contracted:**

- The British Association for Cancer Research
- British Association for Cytopathology
- British Association of Surgical Oncology
- The British Society for Colposcopy and Cervical Pathology
- Cancer Research UK
- Faculty of Public Health
- Jo's Cervical Cancer Trust
- Macmillan
- Northern Ireland Cancer Network
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Nursing- Women's Health Forum
- Royal College of Pathologists
- Royal College of Physicians
- Royal College of Physicians and Surgeons of Glasgow
- Royal College of Physicians of Edinburgh
- Royal College of Radiologists
- Royal College of Surgeons
- Royal College of Surgeons of Edinburgh
- Society and College of Radiographers
- Cervical Screening Programme Advisory Group



*UK National  
Screening Committee*

## **Annex B**

### **Consultation responses**

## **Cancer Research UK response to the UK National Screening Committee consultation on modifying the NHS Cervical Screening Programme**

Cancer Research UK (CRUK) welcomes the opportunity to respond to this consultation. In the UK, around 3,200 women are diagnosed with cervical cancer and over 850 women die from the disease each year. When diagnosed at its earliest stage, roughly 95% of women with cervical cancer will survive for 5 years or more. The cervical screening programme has led to major falls in both incidence and deaths, with roughly 2000 lives being saved each year through screening<sup>i</sup>. Since virtually all cervical cancer cases are preventable<sup>ii</sup>, with the introduction of high risk HPV primary screening and uptake in the HPV vaccine programme, the rate of incidence and number of deaths from cervical cancer should continue to fall.

### **Key Points**

- We support the recommendation to extend standard screening intervals from three to five years for HPV negative women as high risk HPV primary screening, will give longer lasting protection, so the likelihood of developing cervical cancer is highly unlikely in that time frame.
- We are supportive of the proposals for how women aged 64 and over exit the programme. But would like to address the inconsistencies between women with positive HPV results at their exit screen and other HPV positive women in the programme.
- Unless the inconsistencies can be justified through evidence, we suggest the process be the same for all HPV positive/cytology negative women, regardless of age.
- The lack of evidence on exiting the programme should not hinder the rollout of HPV primary testing; provided screen results and diagnostic pathways in older women are monitored for any adverse effects.
- There is a lack of evidence that self-sampling will be the most effective way forward in trying to increase screening numbers. We suggest a pilot on a larger proportion of the population to understand the effectiveness and cost-effectiveness of this intervention.
- Limitations of the current pilot include a lack of cost awareness and knowledge of why people do not attend screening, which will need to be addressed in further studies.

### **Further information**

#### **Issue 1: Screening intervals and surveillance intervals**

HPV primary testing has stronger negative predictive power over cytology and is better able to pick up women with cell changes caused by HPV. Because of this, we agree that the screening interval can safely be extended to five years, as shown by several European trials<sup>iii</sup>. As the vaccinated population grows older, there may be an opportunity to increase screening intervals further. That said, Cancer Research UK has previously commented on suggestions that screening will no longer be necessary in the future, due to HPV vaccination making the risk of being infected so low<sup>iv</sup>. However, we concluded that for now, despite receiving protection from cervical cancer, either from the



screening programme alone, or in combination with HPV vaccination, it is still important to attend cervical screening.

We also support a 12-month surveillance interval for HPV positive, but cytology negative, women believed to be at intermediate risk. The Health Technology Assessment review found this increased the effectiveness of HPV primary screening under all the scenarios considered<sup>v</sup>.

We agree that women with persistent HPV infection and negative cytology should undergo two surveillance tests and if HPV positive at the second test, they should be referred to colposcopy irrespective of their cytology result. This strategy appears to be more cost effective and the absolute number of cancers diagnosed could be reduced due to more pre-cancerous changes being picked up and treated. In Scotland, where HPV vaccination has been shown to exceed 90%, there has been a 50% reduction in CIN2 and a 55% reduction in CIN3 associated with 3 doses of the bivalent HPV vaccination<sup>vi</sup>. Further evidence from vaccinated women who are now reaching screening age, will thus be important to understand whether this will remain an effective strategy in terms of balancing harms, benefits and cost-effectiveness.

## **Issue 2: Women aged 64 and over who are exiting the programme**

In general, Cancer Research UK supports the proposed exit programme recommendation for women aged 64 and over. We agree that the lack of evidence on this proposal should not hinder the rollout of HPV primary testing, provided screening results and diagnostic pathways in older women are monitored and audited to see if there are any adverse effects.

We recommend, in the absence of research, looking at the practices of other countries with comparable health systems to the UK which have already implemented HPV primary testing. For example, Australian guidance on exit screens<sup>vii</sup>.

In the proposed exit strategy, women with a positive HPV result at their exit screen are treated differently from other HPV positive women in the programme and we wish to highlight this inconsistency. Women in the programme who are HPV positive/cytology negative are recommended to undergo two annual surveillance tests before referral to colposcopy (see recommendation 1), but this is reduced to one for women at their final screen. Unless evidence can be used to justify the different treatment of older women, we would suggest that the process be the same for all HPV positive/cytology negative women, regardless of age.

We are concerned that, without clear evidence to guide either way, women who are HPV positive, but cytology and colposcopy negative will be discharged completely from the programme. These women could have a persistent HPV infection and so may be at higher risk of cervical cancer. We'd like the NSC to consider whether these women need to be managed differently and need to be offered further recall tests. It could be useful to analyse the proportion of women from HPV pilot sites who test HPV positive/cytology and colposcopy negative at their final screen, and their diagnostic pathways following this. We also advise that the audit of the cervical screening programme should be set up to monitor diagnostic pathways for these women.

### **Issue 3: Self-sampling as a strategy to address non-attendance for screening**

We understand the potential that self-sampling could have in reducing the barriers to screening. However, Cancer Research UK supports the proposal that further studies for self-sampling are required. This would need to focus on certain practicalities, highlighted below.

We recommend that due consideration is given to the timing of when self-sampling is offered, to ensure that it is effective in reaching under-screened women, whilst not encouraging women who would normally attend screening to miss clinician appointments. Evidence suggests that the accuracy of HPV testing is lower in self-collected samples than in clinician-collected samples<sup>viii</sup>. It is vital that women understand the comparative advantages of clinician-collected screening and that these are preferable to self-sampling. It is important to communicate, that only if they do not attend screening appointments, will self-sampling be offered as a screening option, to lessen the impact of women switching screening strategies. We argue that more research should be carried out and insight gathered, to guarantee individuals understand this choice.

If self-sampling is being considered as a failsafe for women who do not respond to screening invitations due to fear or embarrassment of the appointment, research needs to be carried out to ensure that fear of a cancer diagnosis or low understanding of HPV and cervical cancer does not similarly lead to a low uptake of self-sampling. Hence, there is a need to understand why women do not conduct clinician led screening or self-sampling and how best to combat this focusing on which women to target with self-sampling. Anecdotally, our nurse helpline is reporting high volumes of calls from women worried about an 'HPV diagnosis'. Research has also demonstrated that in certain communities with lower uptake of screening, like some Asian groups, women report barriers around attributing the disease with sexually transmitted infections and promiscuity<sup>ix</sup>. Fear of embarrassment and rejection from one's own community could result in women not attending screening invitations or partaking in self-sampling. Thus, specific types of non-responders need to be targeted by self-sampling as the reasons for non-attendance between non-responders is quite diverse. Educational campaigns to generate better understanding of what HPV is, what causes it and how it is treated, is essential to make more impact.

The substantial economic cost that sending self-sampling kits to all women as a routine approach would require, when uptake is so low, attention. We suggest a further self-sampling pilot with a large study population to help build the evidence base and understand the impact self-sampling would have for non-responders across a national screening programme. Further information would be useful to establish the best possible pathways to increase informed uptake of screening, whether that be through self-sampling kits, or by sending individuals another invitation for clinician sampling. We would also like to see that the planned Public Health England campaign is thoroughly evaluated. Should a self-sampling pilot prove successful, an educational campaign would be vital in increasing understanding of what HPV is, what causes it and how it is treated and, run should run alongside the introduction of self-sampling screening. As well as raise greater awareness of clinician screening, health marketing campaigns could help reduce stigma and fear of the process and result in more individuals attending screenings or successful self-sampling being undertaken.

## About us

Cancer Research UK is the world's largest independent cancer charity dedicated to saving lives through research. We support research into all aspects of cancer and this is achieved through the work of over 4,000 scientists, doctors and nurses. In 2017/18, we spent £423 million on research institutes, hospitals and universities across the UK.

For more information, please contact XXXX XXXX Policy Advisor XXXX XXXX XXXX

---

<sup>i</sup> Landy, R., Pesola, F., Castañón, A. and Sasieni, P. (2016). Impact of cervical screening on cervical cancer mortality: estimation using stage-specific results from a nested case-control study. *British Journal of Cancer*, 115(9), pp.1140-1146.

<sup>ii</sup> Cancer Research UK, <https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/cervical-cancer>, Accessed [November] [2018].

<sup>iii</sup> C Kitchener, H., Canfell, K., Gilham, C., Sargent, A., Roberts, C., Desai, M. and Peto, J. (2014). The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. *Health Technology Assessment*, 18(23).

<sup>iv</sup> Cancer Research UK, <https://scienceblog.cancerresearchuk.org/2017/11/10/the-hpv-vaccine-and-cervical-screening-how-many-tests-do-you-need/>, Accessed [November] [2018]

<sup>v</sup> C Kitchener, H., Canfell, K., Gilham, C., Sargent, A., Roberts, C., Desai, M. and Peto, J. (2014). The clinical effectiveness and cost-effectiveness of primary human papillomavirus cervical screening in England: extended follow-up of the ARTISTIC randomised trial cohort through three screening rounds. *Health Technology Assessment*, 18(23).

<sup>vi</sup> Cameron, R. (2017). The impact of the human papillomavirus vaccine in Scotland: a changing landscape *Clinical Pharmacist*, 9

<sup>vii</sup> Cancer Council Australia Cervical Cancer Screening Guidelines Working Party. Women undergoing exit testing, <https://wiki.cancer.org.au/australiawiki/index.php?oldid=190204>, [November] [2018].

<sup>viii</sup> Arbyn, M., Verdoodt, F., Snijders, P., Verhoef, V., Suonio, E., Dillner, L., Minozzi, S., Bellisario, C., Banzi, R., Zhao, F., Hillemanns, P. and Anttila, A. (2014). Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. *The Lancet Oncology*, 15(2), 172-183.

<sup>ix</sup> Marlow, L., Wardle, J. and Waller, J. (2015). Understanding cervical screening non-attendance among ethnic minority women in England. *British Journal of Cancer*, 113(5), 833-839.

We welcome the opportunity to comment on the UK NSC consultation on modifying the NHS Cervical Screening Programmes in the four UK nations.

We have based our comments on a general view of the literature not only on the documentation included as supporting the NSC recommendations.

### **Issue 1: screening intervals and surveillance intervals**

- **An expanded, five-year, screening interval for HPV negative women**

We support extending the screening interval when HPV primary testing is rolled out. However

- 1) There is no extension of the screening interval in women aged 50 to 64 who test HPV negative. Why was this not considered?  
We ask for clarification because the NSC had in their previous recommendations considered 6 yearly screening as supported by the ARTISTIC trial (among others) The modelling work detailed in supporting document (3a) did not consider the possibility of strategies other than the current one (3y and 5y) or (5year to all ages). Hence it provides no evidence of the impact of other strategies and does not allow for comparison to longer intervals. Ideally the modelling should look at the ICER, and to find the correct ICER there is a need to compare to a large number of alternatives not simply the existing test and interval.
  - 2) The committee should emphasise that extended intervals should only apply to those who are screened with HPV **and test negative**. Those invited but not screened should remain on three yearly intervals.
- **A 12-month surveillance interval for HPV positive/cytology negative women**
  - **Women with persistent HPV infection and negative cytology should undergo two surveillance tests. If HPV positive at the second test they should be referred to colposcopy irrespective of cytology result.**

We support a 12-month interval for HPV positive/cytology negative women and the proposal for surveillance of women with persistent HPV positive results. This recommendation is a good starting position and key for allowing the programme to implement the new primary test. However,

- 1) We would encourage the NSC to use less prescriptive language to allow flexibility on the exact nature of the surveillance in the future. Further there should be an option to optimise the strategy by encouraging research into HPV typing, methylation and on appropriate intervals for triage.
- 2) We suggest that the different nations within the UK be allowed to vary what they do within limits.
- 3) A detailed discussion should be provided to address the need to mitigate dramatic fluctuations in workload. For example, there will be an increase in colposcopy 2 years after HPV primary screening is introduced; and the huge drop in primary screening in years 4 and 5 following a screening interval extension to 6years).

To get roughly similar numbers of women attending each year (while the roll-out is on-going) there is a need to stagger the screening intervals in the first two years following implementation. As an example, 60% of women would transition to 5-yearly, 20% would remain at 3-yearly and 20% would transition to 4-yearly screening.

## **Issue 2: women aged 64 and over who are exiting the programme**

- 1) There is mention of 'estimates of outcomes in this age group' in this section of the consultation. It is not clear what age-group this refers to. We assume it is 60-69. The NSC should specify that there is a need to evaluate and record outcomes that occur beyond age 64 to allow both for a screen that is a few months late and for surveillance testing at 65 and 66.
- 2) The recommendation would benefit from clarification of what happens to women who attend routine screening late (i.e they are now over age 65); do they get turned away?
- 3) Any woman who tests HPV positive but has no colposcopy abnormalities should be invited again not discharged. For example, in this age group women who test HPV positive and cytology positive but for whom nothing is detected at colposcopy could potentially be returned to primary care and at this age they would then be discharged from the programme without further follow-up.
- 4) It is unclear what is meant by a "decisively positive colposcopy".
- 5) There should be monitoring of what happens in practice among women with an indecisive colposcopy. Potentially all these women could receive a LLETZ rather than surveillance. There should be a record of the proportion of treated women that have CIN2+ present in their excision cone.

Given the level of uncertainty on certain issues, it is essential that data are collected and made available for analysis to ensure that outcomes are as desired. In fact, this is an area where views from lay members would also be beneficial. PPI should be sought to understand the pros and cons of continuing to screen/investigate older women.

## **Issue 3: self-sampling as a strategy to address non-attendance for screening**

We would welcome a recommendation that makes it easier to pilot/research self-sampling. National screening programmes should encourage local programmes to implement pilots of self-sampling— on the condition that they are properly evaluated.

Key needs in this area which are unaddressed include:

- 1) When self-sampling is done within a properly evaluated pilot, these test results should be considered as screening and the next test due date changed accordingly.
- 2) There is a need for research related to reflex (triage) tests using self-samples.
- 3) The question of whether a self-sample HPV test must have a negative control should be addressed.
- 4) The 10-20% improvement in screening uptake needs clarification. There is absolutely no suggestion that we could improve uptake from 70% to 77-84%. At best they mean that 10-20% of those who do not uptake conventional would uptake self-sampling – this means increasing the uptake from 70% to 73-76%. What is key is the proportion of those who test positive on a self-sample who subsequently attend for clinical sampling. Fortunately, this is high (~80%) in most studies.
- 5) It should not be forgotten that urine could be an alternative to swabs.

## **Forthcoming work**

We agree that it is currently premature to consider changing screening intervals for vaccinated women. However, to be in the best position possible to evaluate screening intervals in vaccinated women it is imperative that the national statistics bulletins allow for results to be reported by school year cohort (i.e. in single year of age from September to August). The data by single year of school year cohort should include cervical screening test

results, HPV typing where available; colposcopy referral; CIN2 and CIN3+ in screened women.

Sincerely,

Peter Sasieni, Alejandra Castanon, Anita Lim and Matejka Rebolj

Cancer prevention group | School of Cancer & Pharmaceutical Sciences | Faculty of Life Sciences & Medicine| King's College London

Innovation Hub, Guys Cancer Centre, Guys Hospital, Great Maze Pond, London SE1 9RT

<b>Name:</b>	Professor Peter Sasieni and colleagues	<b>Email address:</b>	XXXX XXXX
<b>Organisation (if appropriate):</b>	King's College London		
<b>Role:</b>	Professor of Cancer Prevention		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	Dr Paul Cross	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	British Association for Cytopathology		
<b>Role:</b>	President BAC		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
General points	Supporting documents	The consultation is around three specific potential changes as listed in the NSC covering letter. The BAC would support the three proposals re interval/age changes and self testing, with the provisos below.  A general point about any such changes as those advocated in this consultation is that the call/recall IT system used for the	

		<p>CSP must be robust and able to cope with such changes in a safe and reliable manner. Given recent issues with screening IT systems and concerns over IT system delivery in the CSP this must be established and confirmed before any such changes are implemented.</p> <p>The psychological impact of these changes does not seem to have been considered, and again literature on this exists.</p>
Interval and age changes	Evidence papers 2, 3a and 3b	<p>It is surprising that some of the evidence put forward for this consultation appears the same as that put forward previously by the NSC to support the change to primary HPV testing within the cervical screening programme in 2015, and as such does not appear to have been updated. Whilst it would support a change to screening intervals, the addition of more recent evidence which is available would have been of value. Possible UK based data, from the English pHPV pilot sites which may have used aspects of the changes in follow up, would have been of value. The changes suggested seem warranted on the available evidence, but good follow up/failsafe mechanisms are essential to ensure this policy is correct.</p>
Self testing	Evidence papers 4 and 5	<p>These two papers appear specifically sourced for this consultation. They do support the use of self testing as a way of encouraging “hard to reach” women to submit samples. Some countries have already moved to this in areas, e.g. Holland, Denmark. Issues as highlighted in paper 5 (page 22) area round how this could be introduced, and if such a sample is hrHPV positive whether it is repeated after a primary care sample and if still positive referred or whether direct referral is advocated. Whilst this may increase coverage the cost effectiveness and practicalities of this still need resolving. A recent paper in the BMJ (Arbyn et al, BMJ 2018; 363; 396)</p>



		suggests pilot studies first to help resolve these points. There are several other peer reviewed papers from 2017/2018 which would support the general points made around this topic also.
--	--	--

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	Dr Timothy PALMER	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	Scottish Cervical Screening programme		
<b>Role:</b>	Scottish Clinical Lead for Cervical Screening		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
Issue 1; question 1		<i>It is proposed that the Cervical Screening Programmes in the four UK nations should implement the following: an expanded, five year, screening interval for HPV negative women</i> <b>Agree; no further comments. Information systems used to support cervical screening must be capable of easy adaptation to changing screening intervals.</b>	

Issue 1; question 2		<p><i>It is proposed that the Cervical Screening Programmes in the four UK nations should implement the following: a 12 month surveillance interval for HPV positive / cytology negative women</i></p> <p><b>Agree; no further comments.</b></p>
Issue 1; question 3		<p><i>It is proposed that the Cervical Screening Programmes in the four UK nations should implement the following:</i></p> <p><i>(a) women with persistent HPV infection and negative cytology should undergo two surveillance tests.</i></p> <p><b>Agree; no further comments</b></p>
Issue 1; question 3		<p><i>(b) (b) If HPV positive at the second test they should be referred to colposcopy irrespective of cytology result</i></p> <p><b>Proposal: Cytology triage should be implemented at 24 months. This will allow triage-negative women to be managed in a manner commensurate with their risk of high grade disease, either by early (less than 5 year) recall or colposcopy as indicated by the evidence. The UK NSC should commission studies to investigate the appropriate management for HPV+/trriage negative women at this stage and gather evidence on the most effective triage strategy. The UK NSC should advise on the acceptable levels of risk for CIN3+ that would allow return to routine recall, lead to early recall or mandate referral for colposcopy.</b></p>
Issue 2		<p><i>Exit strategy for women aged 64 and over</i></p> <p><b>Proposal: The UK NSC should commission studies in the UK that provide information that will lead to the formation of consensus guidelines. The information systems underpinning the cervical screening programmes should be set up to facilitate gathering such information. In the absence of guidelines, Scotland is proposing to replicate the assessment process for other HPV+ women.</b></p>

Issue 3		Inclusion of self-sampling in the UK Cervical Screening program <b>Proposal: The UK NSC should commission studies, outlined above, that provide information that will inform the implementation of self-sampling into the UK cervical screening programmes. Scotland is well-placed to host and deliver such studies.</b>
---------	--	--

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	Dr Mary McMenamin	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	Department of Cellular Pathology, Altnagelvin Hospital, Western Health and Social Care Trust, Northern Ireland		
<b>Role:</b>	Biomedical/Research Scientist		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b> <i>Please use a new row for each comment and add extra rows as required.</i>	
<b>Issue 1: screening intervals and surveillance intervals</b>	A 12 month surveillance interval for HPV positive / cytology negative women and that women with persistent HPV	In these instances, consideration should be given to the inclusion of other triage tests and HPV genotyping to improve specificity with respect to underlying CIN2+. According to ARTISTIC and data from the UK HPV Primary Pilots, around 8%-9% of screened women will be HPV positive/cytology negative. The Primary Pilots also reported that 'cytology negative/HPV positive women will harbour undetected CIN, amongst whom at least 3% will have CIN2+'.	

	<p>infection and negative cytology should undergo two surveillance tests. If HPV positive at the second test they should be referred to colposcopy irrespective of cytology result.</p>	<p>There are potential biomarkers available that could provide risk stratification in this group thus stratifying those who require immediate colposcopy referral (thus expediting the detection of CIN2+) from those who can safely be rescreened.</p> <p>This new class of abnormal result will also have implications for colposcopy as referrals could increase by 2.5% according to the Primary Pilots. However, the specificity of HPV positivity with respect to underlying CIN2+ could be increased by restricting 12-month referral to women with the highest risk types (HPV16/18) and further recall at 24 months for the other high risk HPV positives. This will allow the highest risk women to be assessed earlier and allow further clearance to occur in those with lower risk types. Indeed, economic modelling from ARTISTIC suggested that selective referral to colposcopy at 12 months was found to be more cost effective than delaying referral for all until 24 months.</p> <p>The Cellular Pathology Department at Altnagelvin Hospital in Northern Ireland is currently conducting a study which evaluates the combined p16 and ki67 biomarkers for triage in HPV primary screening. The Department will publish the findings of this study when they become available.</p>
<p><b>Issue 3: Self sampling as a strategy to address non attendance for screening</b></p>	<p>It is proposed that self sampling as a strategy to address non attendance for screening requires further study in well organised pilots and research projects.</p> <p>Other questions relating to the fit between this approach and the screening programme should also be the subject of research and piloting. For example this would apply to the use of self sampling as</p>	<p>It is widely accepted that screening coverage is declining in the UK, particularly in younger women. It is also known that not being screened is one of the highest risk factors for cervical cancer. There are a number of reasons why women do not attend for screening including; embarrassment, inconvenience, and discomfort associated with obtaining cervical samples, and non-attenders have consistently reported that self-sampling would be a preferable option for them. Furthermore, as the rates of cervical cancer in women aged 25-29 years have been increasing steadily since 2005 [1, 2] it is important to explore strategies to increase cervical screening uptake, particularly in this age group.</p> <p>As the review has established, self-sampling has demonstrated sensitivity to detect cervical disease that is equal to clinician-collected samples, and that offering women the opportunity to collect a self-sample to test for HPV could increase screening coverage.</p> <p>Self-sampling should therefore be explored as a means of maximising screening coverage. The HPV primary cervical screening programme in The Netherlands has included self-sampling for HPV testing in non-attenders and could therefore provide a useful model.</p> <p>It is also worth mentioning that if there is a lack of options for those who choose not to avail of cervical screening in its current form, this could create an opening for possible private sector</p>

	<p>an approach to routine screening programme delivery.</p>	<p>involvement to satisfy demand for self-sampling and this could subsequently undermine the screening programme as individual clinical information may be lost.</p> <p>The Cellular Pathology Department at Altnagelvin Hospital in Northern Ireland is currently piloting offering vaginal self-sampling to women aged 25y-29y and 55y-64y who do not attend for cervical screening. The Department will publish the findings of this study when they become available.</p> <ol style="list-style-type: none"> <li>1. <a href="http://www.cancerresearchuk.org/health-professional/cancerstatistics/statistics-by-cancer-type/cervical-cancer/incidence#heading-Two">http://www.cancerresearchuk.org/health-professional/cancerstatistics/ statistics-by-cancer-type/cervical-cancer/incidence#heading-Two</a></li> <li>2. <a href="http://www.ncin.org.uk/publications/databriefings/cervicalincidenceandscreening">http://www.ncin.org.uk/publications/databriefings/cervicalincidenceandscreening</a></li> </ol>

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	Dr Paul Cross	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	On behalf of Cytopathology SAC of RCPATH		
<b>Role:</b>	Vice Chair RCPATH SAC Cytopathology		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
General points	Supporting documents	The consultation is on three specific potential changes as listed in the NSC covering letter. The RCPATH support the three proposals re interval/age changes and self testing, with the provisos below.  It is essential that the call/recall IT system used for the CSP	



		must be robust and able to cope with age/interval/ modality changes in a safe and reliable manner.
Interval and age changes	Evidence papers 2, 3a and 3b	Some of the evidence put forward for this consultation appears the same as that put forward previously by the NSC to support the change to primary HPV testing within the cervical screening programme in 2015, and as such does not appear to have been updated. We would endorse the proposed interval/age changes, but safe and reliable follow up/failsafe mechanisms are essential to ensure this policy is correct.
Self testing	Evidence papers 4 and 5	The NSC clearly recognises that the case for self-sampling is less clear, and we would endorse this view. We are particularly concerned around the lack of quality control of the sample being submitted, and the lack of evidence on a potential negative impact for usual responders. We would highlight that reference is made to a low 'inadequate' rate for HPV testing amongst a self-testing cohort, but scientifically the interpretation of this is extremely difficult. A HPV test would only flag as inadequate if there was a technical problem with the assay or the quantity of human DNA fell below the set threshold. This is very different from saying this is an adequate sample of potentially abnormal material that will give a reliable negative result. A reliable failsafe for such women is also essential. Such issues need resolving, and we endorse the suggestion in the consultation that a pilot be developed before any potential roll out of this approach.

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	xxxx xxxx, on behalf of xxxx xxxx	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>			
<b>Role:</b>			
<p>Do you consent to your name being published on the UK NSC website alongside your response?</p> <p>Yes <input type="checkbox"/> No <input checked="" type="checkbox"/></p>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b> <i>Please use a new row for each comment and add extra rows as required.</i>	
		Audit trails were not clearly described and need to be appropriately thought out.	
		Lessons learnt should be fed back continuously. The feedback mechanism was not well described in consultation.	
3		Self Sampling will be useful in increasing uptake in groups	

		which have historically had low uptake due to issues such as embarrassment, religion or culture

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



**UK National  
Screening Committee**

**UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations**

**Consultation comments pro-forma**

<b>Name:</b>	Gillian Holdsworth	<b>Email address:</b>	XXXX XXXX
<b>Organisation (if appropriate):</b>	SH:24		
<b>Role:</b>	Managing Director, Consultant in Public Health Medicine		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
	We submit evidence about the design and delivery of a digital sex and reproductive health service which we believe are applicable to this consultation – including a number of learning points from our experience..		


Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.

# SH:24

## HPV Self-Sampling Strategy Consultation

---

### Context

In 2016-17, it was estimated that more than 1.2 million women – around 1 in 4 of those eligible – didn't take up their screening invitation, with the proportion increasing to 1 in 3 among those aged 25 to 29 and to 1 in 2 in some more deprived regions of the UK. HPV self-sampling has been proposed as a strategy to address non-attendance for screening.

A recent survey conducted by Jo's Cervical Cancer Trust found the main barriers preventing women from taking up screening were twofold: 1) embarrassed about their body shape and appearance of their genital area, and 2) difficulty taking time off work and making appointments.

These barriers are very similar to those faced by users of sexual health services. Our experience of the digital transformation of sexual health services in recent years to improve access and reduce stigma is directly applicable to the challenges the NHS cervical screening programme currently faces over population coverage and addressing non-attendance.

### Transforming sexual health services

SH:24 is the leading online sexual and reproductive health service in the UK. Working as a collaborative team of public health and GUM doctors, designers, and developers, SH:24 believes that a significant proportion of sexual health activity can be delivered remotely. We believe that information, education and signposting enable people to manage their own sexual and reproductive health, with access to remote clinical support and referral into partner clinics for specialist care as required. Similarly, HPV self-sampling using postal kits could enable the management of patients remotely through an online service and improve population screening coverage.

#### SH:24 model

SH:24 built the online STI testing service using an agile, design-led approach. We worked closely with users on every element of the service, from the website, the kit packaging and instruction leaflets, to the delivery of remote clinical support, resulting in a product that is simple to use and a service that is accessible and which service users want and like to use. Not only does SH:24 improve access for people who lead busy lives but also, for many, avoids the embarrassment and stigma of going to a clinic.

Figure 1. SH:24 user journey for STI testing and treatment



Our design-led and user-centred approach means that the service has evolved and improved over time. For example, based on service user feedback we re-modelled the instructions which accompany our blood test. This increased the return rate from 65% in July 2015 (at the launch of the service) to 82% in September 2017. This is significantly higher than the return rate of 51% achieved by the National HIV testing programme.

### Impact of SH:24

Feedback from service users has been overwhelmingly positive (Figure 2) and our service has had a significant impact on STI rates. Since the launch of SH:24 in the London Boroughs of Lambeth and Southwark, STI testing has almost doubled and there has been an 8% reduction in STI rates at a time when testing rates decreased across London and STI rates increased (Figure 3). A randomized trial demonstrated that individuals signposted to SH:24 were almost twice as likely as those signposted to clinics to have an STI test (Wilson et al., 2017<sup>1</sup>), and this increased access is observed irrespective of characteristics such as age, ethnicity, gender and deprivation.

Figure 2. User feedback for STI testing.

<sup>1</sup> Wilson, E. et al. (2017) 'Internet-accessed sexually transmitted infection (e-STI) testing and results service: A randomised, single-blind, controlled trial.', *PLoS medicine*. Public Library of Science, 14(12), p. e1002479. doi: 10.1371/journal.pmed.1002479.

"My life has changed overnight because of the service you provide as I was concerned about my health and didn't have the confidence to go to a clinic in person. I can move forward knowing I'm fine thanks to you."

"Can't rate the service highly enough! Super-fast delivery. Easy to complete test. Fool proof instructions. Great communication. Super-fast results. Highly recommend."

"...as a full time working single mum it's almost impossible to get to an appointment or even book an appointment so this service is truly amazing and really appreciated."

"I live in an area where STI testing is otherwise only available from a clinic that's open for 3 hours once a month. I'm physically disabled and can't get there easily. Being able to get tested at home is so much less taxing on my health, and I appreciate it being an option."

**SH:24**

Figure 3. STI testing rate and new STI diagnosis rate per 100,000 population (excluding chlamydia in under 25s)



## Overcoming barriers

One in five SH:24 services users have never attended a sexual health clinic before, approximately half of whom are over 25 years. In these first time users of sexual health services aged 25 years and over, 14.5% tested positive for an STI (almost double the rate seen in SH:24's service overall). This demonstrates that SH:24 enables people to test who, perhaps due to fear, stigma or access issues, are not attending face-to-face clinics but probably should be.

## Service expansion

Since 2013 SH:24 has grown to operate in 18 regions across the country. SH:24 launched in Germany in collaboration with AIDS Hilfe in July 2018 and we are building a platform for adolescent sexual and reproductive health in Kenya. Taking the same user-centred approach, we have successfully expanded our service offer to include home STI treatment, online oral contraception, and remote photo-diagnosis for genital warts and herpes. Running in parallel, all of our interventions have been independently evaluated with our academic partners including King's College London, London School of Hygiene and Tropical Medicine and the University of Bristol.

## Towards a new approach to HPV testing



SH:24 has a wealth of knowledge and experience of digital sexual health provision and service transformation which it would be willing to share with the HPV self-sampling pilot. Our model aligns with the 2019 NHS plan opening a 'digital front door to the health service' and 'early detection and treatment'.

We know from our experience of developing and delivering online services in partnership with the NHS that there are a number of things that are essential to quality assure digital services:

1. Human centred design to ensure that services are intuitive and easy to use. Many digital interfaces within the NHS are complex and difficult to navigate and unresponsive resulting in inequalities in access.
2. Excellent information provided in a range of online formats developed in collaboration with service users, remote clinical support as required with a clear referral pathway.
3. A continued process of service development and optimisation after implementation.
4. Academic evaluation to develop an evidence base for the impact of online services in comparison to clinic-based services, both in terms of health outcome and value for money.
5. Standards of good practice that are agreed by the relevant professional bodies and those with experience of digital health provision



UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	XXXX XXXX	<b>Email address:</b>	XXXX XXXX
<b>Organisation (if appropriate):</b>	XXXX XXXX		
<b>Role:</b>	XXXX XXXX		
<p>Do you consent to your name being published on the UK NSC website alongside your response?</p> <p>Yes <input type="checkbox"/> No <input checked="" type="checkbox"/></p>			
Issue number (1, 2 or 3)	Document, page number and text to which comments relate (optional)	Comment	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
1	"An expanded, five year, screening interval for HPV negative women."	We acknowledge the view of the UK NSC to extend the screening interval from 3 to 5 years. The consultation document 3a. (p.13) recognises that the cost saving includes QALY loss, thereby, putting women at an increased risk compared to the 3-year interval strategy.	

		<p>The HPV assays currently on the list of approved tests by the NHS CSP are not all equivalent. Some assays do not have a control for adequacy of cellularity, and/or use biomarkers, such as HPV RNA, which are backed up by fewer clinical trials with collectively only a small number of CIN2/3 cases compared to trials with HPV DNA assays.</p> <p>Should the NHS CSP expand the screening interval for HPV negative women, then more stringent criteria for approval of HPV tests should be adopted to be able to deliver the best available long term safety over a 5-year interval. These criteria should be modelled on the Australian guidelines (<a href="http://www.health.gov.au/internet/main/publishing.nsf/Content/npaac-cervical-screening">http://www.health.gov.au/internet/main/publishing.nsf/Content/npaac-cervical-screening</a> ) or the US FDA (<a href="https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm458179.pdf">https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-meddev-gen/documents/document/ucm458179.pdf</a>).</p>
1	“An expanded, five year, screening interval for HPV negative women.”	<p>We would suggest that there is some uncertainty around whether the number of women attending the test appointment (hereafter referred to as the recall “return rate”) will remain the same when extending the screening interval from 3 to 5 years. We would recommend additional modelling around the recall rate to determine the impact, in addition to the modelling recommendations made by YHEC in section 5.</p>
1	“An expanded, five year, screening interval for HPV negative women.”	<p>Patient awareness on the clinical value of the test could be improved to prevent negative perception that expanding the screening interval is based only on cost saving. The messaging must reinforce that HPV testing is a ‘test of risk’ rather than a ‘test of disease’.</p>

<p>1</p>	<ul style="list-style-type: none"> <li>- “A 12 month surveillance interval for HPV positive / cytology negative women.</li> <li>- Women with persistent HPV infection and negative cytology should undergo two surveillance tests. If HPV positive at the second test they should be referred to colposcopy irrespective of cytology result.”</li> </ul>	<p>New technologies should be considered to improve management and reduce risk for HPV positive / cytology negative women, which is a population still bearing a significant risk of developing cervical cancer.</p> <p>In particular triage with CINtec® PLUS Cytology p16/Ki-67 dual-stain (DS) testing has consistently shown high sensitivity for underlying CIN2+ and CIN3+ (Abridged list: Wright et al., 2017 <a href="http://www.ncbi.nlm.nih.gov/pubmed/28094038">www.ncbi.nlm.nih.gov/pubmed/28094038</a>; Wentzensen et al., 2012 <a href="http://www.ncbi.nlm.nih.gov/pubmed/22675168">www.ncbi.nlm.nih.gov/pubmed/22675168</a>; Schmidt et al 2011 <a href="http://www.ncbi.nlm.nih.gov/pubmed/21442767">www.ncbi.nlm.nih.gov/pubmed/21442767</a>; Uijterwaal et al., 2014 <a href="http://www.ncbi.nlm.nih.gov/pubmed/24518601">www.ncbi.nlm.nih.gov/pubmed/24518601</a>)</p> <p>In a recent publication (Clarke et al., JAMA Oncol 2018 <a href="http://www.ncbi.nlm.nih.gov/pubmed/30325982">www.ncbi.nlm.nih.gov/pubmed/30325982</a>) the authors went beyond and evaluated the longitudinal performance of CINtec® PLUS Cytology p16/Ki-67 DS triage for detection of cervical precancer in HPV-positive women over 5 years of follow-up in the context of clinical management thresholds.</p> <p>This study demonstrates that CINtec® PLUS Cytology provides better long-term risk stratification compared to cytology over 5 years. This means that CINtec® PLUS Cytology is a more accurate HPV positive triage test compared to cytology.</p> <p>Interestingly and particularly relevant to this point of the consultation, women who were HPV positive and CINtec® PLUS Cytology negative could safely wait 3 years before their next follow-up screening. These results suggest a new way of</p>
----------	--	--

		<p>managing women which will be safer than the standard of care based on cytology triage.</p> <p>In the real world, not all women with HPV positive / cytology negative results will comply with the surveillance tests. The percentage varies depending on the site and has been explored by publications. Therefore, there is additional benefit in adopting a test which provides a clear diagnosis and mitigates the risk of diminishing compliance with the surveillance tests.</p>
2	<p><b>Issue 2: women aged 64 and over who are exiting the programme:</b> HPV positive / cytology negative women should be recalled at 12 months and, if still HPV positive, be referred for colposcopy. If colposcopy is:</p> <ul style="list-style-type: none"> <li>i. decisively negative this would prompt discharge from the programme</li> <li>ii. decisively positive this would prompt the offer of loop excision</li> <li>iii. indecisive this would prompt the offer of loop excision or recall a further 12 months</li> </ul>	<p>We know that the risk of cancer is higher in older (&gt;50) women (Peto et al., 2004 <a href="https://www.sciencedirect.com/science/article/pii/S0140673604166749">https://www.sciencedirect.com/science/article/pii/S0140673604166749</a>) and is related to HPV persistence. As such, it is important to continue monitoring older women who are HPV-positive to prevent them from developing cancer. These women should not be discharged from the programme until their infections have been resolved.</p> <p>Furthermore, colposcopy might have a poorer performance than previously recognised: “Colposcopic examination including directed biopsies has been proposed as the gold standard in the evaluation of abnormal cervical cytology. However there is increasing evidence demonstrating its poor performance with only 54.8% of women with CIN3 being diagnosed in the colposcopy arm of the ALTS study. Various new technologies, usually employing optical spectroscopy, have been investigated to improve the detection of CIN and have reported sensitivity to detect high grade CIN in the range of 70%–95% and specificity of 50%–83%.” (Balasubramani et al., 2009</p>

		<p><a href="https://www.sciencedirect.com/science/article/pii/S0090825809005988?via%3Dihub">https://www.sciencedirect.com/science/article/pii/S0090825809005988?via%3Dihub</a>). This reinforces the argument of not discharging women over 64 from the programme based on an uncertain result (Macdonald et al., 2017 <a href="https://www.ncbi.nlm.nih.gov/pubmed/28292693">https://www.ncbi.nlm.nih.gov/pubmed/28292693</a>).</p>
2	<p><b>Issue 2: Forthcoming work on genotyping</b></p>	<p>The use of partial genotyping should also be explored to provide better stratification in the older women population to detect whether they have HPV 16/18 as opposed to other lower risk HPV types. For instance, the Australian National Cervical Screening Programme (NCSP) is using partial genotyping for HPV16 and 18 (<a href="http://www.health.gov.au/internet/main/publishing.nsf/Content/npaac-cervical-screening">http://www.health.gov.au/internet/main/publishing.nsf/Content/npaac-cervical-screening</a>).</p> <p>Additionally, once disease prevalence decreases, there is a rationale for using better tests, such as CINtec® PLUS genotyping (McMenamin et al., 2018, <a href="https://doi.org/10.1093/ajcp/aqy073">https://doi.org/10.1093/ajcp/aqy073</a>; Clarke et al., 2018 <a href="https://jamanetwork.com/journals/jamaoncology/fullarticle/2705607">https://jamanetwork.com/journals/jamaoncology/fullarticle/2705607</a>).</p> <p>As disease prevalence decreases, colposcopy will also become more difficult: “With the increased sensitivity of HPV testing in comparison to cytology alone, many women with high-grade disease are likely to be seen in colposcopy much earlier, before the disease is visible with acetic acid. This highlights the need for an assessment that does not rely on visual inspection of acetowhite changes alone.” (Macdonald et al., 2017, <a href="https://www.ncbi.nlm.nih.gov/pubmed/28292693">https://www.ncbi.nlm.nih.gov/pubmed/28292693</a>).</p>

3	<p><b>Issue 3: Self sampling as a strategy to address non-attendance for screening</b></p>	<p>Implementing self-sampling into the Cervical Screening programme presents a great opportunity for the UK to aspire to the ambition set out by the Government in the NHS Long Term plan to seize the opportunities of the future. At the heart of this plan is the principle that prevention is better than cure, screening programme participation improvement through introduction of self-sampling would be an excellent way to deliver of this plan.</p> <p>Yet the UK is already lagging behind other countries in implementation of HPV as a primary screening test with countries such as Australia and The Netherlands fully implementing HPV as a primary screening test in 2017 and 2016, respectively, despite the evidence for the clinical and cost effectiveness of this approach being available as early as 2010.</p> <p>In this fast moving area of self-sampling there is new evidence emerging around the globe. We would therefore urge that due consideration is given to existing evidence so that any further UK pilots or research required can be non-duplicative and undertaken with a view to swift implementation nationally.</p> <p>There may also be useful learnings and parallels that could be gleaned from sexual health self-testing programmes, the uptake for which is rapidly increasing across the UK. Consideration should be given to patient cohorts that may intersect and who would also benefit from a self-sampling alternative to encourage them to participate in the Cervical Screening programme.</p> <p>There are some great examples of where Self Sampling has</p>
---	--	---

		<p>been evaluated. For instance, a Danish initiative demonstrated how it could successfully increase compliance converting 24,000 screening non-attenders to self-sampling, which could be the basis for future routine implementation. (Lam J.U.H. al et., 2017 <a href="https://www.ncbi.nlm.nih.gov/pubmed/28195317">https://www.ncbi.nlm.nih.gov/pubmed/28195317</a>). The study used self-sampling brushes with a novel RFID-chip for secure patient identification, eliminating inconveniences for the women to fill out forms on returning the brush and loss of brushes due to missing identification. Women could easily request a home test through different communication platforms including regular mail, phone and a custom-made web/mobile-app.</p>
3	<p><b>Issue 3: Self sampling as a strategy to address non attendance for screening</b></p>	<p>Peter Sasini and colleagues in Castañon et al., 2018 (<a href="http://www.ncbi.nlm.nih.gov/pubmed/30280637">www.ncbi.nlm.nih.gov/pubmed/30280637</a>) take an innovative approach to consideration of new technologies asking whether “a delay in the introduction of human papillomavirus-based cervical screening is affordable”.</p> <p>The results of their analysis show that a one-year delay in the implementation of human papillomavirus screening would miss the opportunity to prevent cases of cervical cancer, and lead to a loss quality-adjusted life years. These measurable losses should be considered in prioritising decision-making in screening and this method should be applied to consideration of self sampling as a strategy to address non attendance for screening.</p> <p>It should also be considered that cervical cancer mortality rates are higher in underscreened populations (Musselwhite et al., 2016 <a href="http://www.ncbi.nlm.nih.gov/pubmed/27825171">www.ncbi.nlm.nih.gov/pubmed/27825171</a>).</p>



		<p>Furthermore, non-attenders could have a higher proportion of cytological abnormalities upon follow-up and higher detection rates of <math>\geq</math>CIN2 than women attending routine screening (Enerly et al., 2016 <a href="https://www.ncbi.nlm.nih.gov/pubmed/27073929">https://www.ncbi.nlm.nih.gov/pubmed/27073929</a>; Lam J. U. H. et al., 2017 <a href="https://www.ncbi.nlm.nih.gov/pubmed/28724554">https://www.ncbi.nlm.nih.gov/pubmed/28724554</a>; Lam J. U. H. et al. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29136403">https://www.ncbi.nlm.nih.gov/pubmed/29136403</a>). Therefore, the implementation of self-sampling, even with a small uptake, could bring disproportionate value in terms of increase in quality-adjusted life years.</p>
3	<p><b>Issue 3: Self sampling as a strategy to address non attendance for screening</b></p>	<p>Not all assays currently approved by NHSCP for HPV testing have been proven suitable in self sampling.</p> <p>For example, HPV DNA testing has been proved more efficacious in self-sampling compared to RNA-based testing. Better performance of HPV DNA testing in this context could be due to higher stability of the DNA Biomarker and higher sensitivity of DNA testing compared to RNA (Chernesky et al., 2014 <a href="https://www.ncbi.nlm.nih.gov/pubmed/24825332">https://www.ncbi.nlm.nih.gov/pubmed/24825332</a>; Arbyn et al., 2014 <a href="https://www.ncbi.nlm.nih.gov/pubmed/24433684">https://www.ncbi.nlm.nih.gov/pubmed/24433684</a>).</p> <p>The Dutch cervical screening programme currently run self sampling as an integral part of the programme. The self sample device is offered to women who do not respond to the first invitation letter to get a pap smear taken. Within the second letter they receive there is a link to a website to apply for a self sample device.</p> <p>The Dutch cervical screening programme has decided to use an assay based on a validated PCR method for their</p>

		population screening for cervical cancer, which includes self-collected material, based on the higher sensitivity of the PCR method. (see list Arbyn 2012, update list IPVS congress Seattle 20-25 August 2014).
n/a	Forthcoming work for screening the vaccinated population	As part of the work initiated by the UK NSC, we would suggest considering options to screen the vaccinated population as these women are now entering the screening age. As per comment on issue 2, genotyping might prove a useful strategy to monitor the success of vaccination.

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



**UK National  
Screening Committee**

**UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations**

**Consultation comments pro-forma**

<b>Name:</b>	Neil Cooper	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	Preventx Ltd		
<b>Role:</b>	Managing Director		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b> <i>Please use a new row for each comment and add extra rows as required.</i>	
3	"It is proposed that self sampling as a strategy to address non attendance for screening requires further study in well organised pilots and research projects."	Any plans for additional research and pilots should take full account of the considerable body of knowledge which has been built-up over the last decade in the area of sexual health self-sampling in England. Pilots in this sector started in 2003 and services are now successfully operating at scale. Many learnings from sexual health programmes could potentially be leveraged to "fast-track" HPV self-sampling.	

3	<p>“It is proposed that self sampling as a strategy to address non attendance for screening requires further study in well organised pilots and research projects.”</p>	<p>Any plans for additional research and pilots should also take advantage of the sophisticated research and testing programmes which are already part of standard business operations for integrated sexual health self-sampling providers i.e. providers managing website, IT, test kit logistics and pathology functions in-house. Preventx’s assessment is that our own integrated platform could meet 90% of NSC’s requirements today, with the remaining 10% of requirements addressed through straightforward customisation of platform and processes.</p> <p>Many learnings from the sexual health sector may be immediately applicable to HPV e.g. factors impacting test kit return rates. Beyond this, the research and testing programmes described above, if applied to HPV, would yield highly cost-effective results for many of the questions considered by this consultation far more quickly than smaller scale pilots due to:</p> <p><b>Scale.</b> Providers are delivering tests at scale e.g. in the 6 months to December 2018, Preventx processed 90,927 vaginal self-samples for chlamydia alone. High volumes enable us to run sophisticated comparative tests as part of “business as usual”. These tests present one group of patients with a defined experience and a second group with a slightly different experience e.g. different wording on communications. The benefit is the ability to generate robust findings very quickly, at minimal cost. By contrast, the largest test population cited in the consultation documentation was 5,202 patients, equating to around a week of testing for Preventx and too small (over a protracted period) for rapid comparative testing.</p> <p><b>Availability of fit-for-purpose IT and skilled resource.</b> Purpose-built IT systems enable data-driven insights (including through comparative testing) for sexual health self-sampling services. These insights have enabled enormous strides in service performance. For example, services such as our own routinely generate kit return rates of 75%+. This level of performance has been achieved by; 1) using data driven analysis to identify the key factors which impact kit return rates and; 2) in light of this information, flexing operational delivery appropriately to maximise return rates.</p>
---	---	--

	<p>“However, the review highlighted a number of limitations: Cost effectiveness of the strategy had not been evaluated”</p>	<p>This form of process optimisation demands both highly flexible IT systems and the availability of dedicated, skilled resource e.g. to organise consistent despatch of test kits within 24 hours of receipt of any request. It would be very challenging for NSC to replicate these conditions within a smaller scale pilot. However, without them, it is difficult to see how some research requirements could be delivered. For example, to assess cost-effectiveness, it would be crucial to understand the scope for flexing operational KPIs such as kit return rates and sample completion rates, given their impact on overall financial performance.</p>
3	<p>“However, the review highlighted a number of limitations: Cost effectiveness of the strategy had not been evaluated”</p>	<p>For comparison, within a fully integrated chlamydia self-sampling service, the typical cost per completed screen for chlamydia is £23. This is based on test kit return rates of 75%, is inclusive of all set-up costs, overheads and wastage (the unreturned 25%) and exclusive of treatment costs.</p> <p>Today, a similar, integrated service for HPV would cost under £40 per completed test at launch, falling to under £30 per completed test at volume. This is based on Preventx’s list pricing, realistic assumptions e.g. for kit return rates and includes kit costs and the cost of establishing a fully integrated technology pathway.</p> <p>The research and testing techniques described above could be used to assess the cost-effectiveness of various options including:</p> <ul style="list-style-type: none"> <li>• Different sample collection methodologies e.g. via Evalyn HPV Brush</li> <li>• Different distribution methodologies e.g. unsolicited mailing of test kits vs requiring patients to submit a request for test kits.</li> </ul>
3	<p>“However, the review highlighted a number of limitations: Cost effectiveness of the strategy had not been evaluated”</p>	<p>From the numbers in the consultation documents, 10%-20% of non-attenders subsequently accepting an offer for self-sampling equates to an additional 450,000 completed screens at a total cost of <math>450,000 * £30 = £13.5</math> million. At a 0.1% cancer diagnosis rate, this suggests a cost of around £30k per cancer diagnosis.</p>

		<p>Overall cost effectiveness of HPV self-sampling could be even greater given the higher prevalence of CIN2 and CIN3 compared to cervical cancer and the correspondingly greater opportunities to reduce cost of treatment and to improve quality of life through the early identification of lesions.</p> <p>(Petry et al., 2013 <a href="http://www.ncbi.nlm.nih.gov/pubmed/23497108">www.ncbi.nlm.nih.gov/pubmed/23497108</a>, Petry et al., 2003 <a href="http://www.ncbi.nlm.nih.gov/pubmed/12771924">www.ncbi.nlm.nih.gov/pubmed/12771924</a>, <a href="https://digital.nhs.uk/data-and-information/publications/statistical/cervical-screening-programme/england---2017-18">https://digital.nhs.uk/data-and-information/publications/statistical/cervical-screening-programme/england---2017-18</a> (Cervical Screening Programme, England - 2017-18: Data Tables: Table 18)</p>
3	<p>“It is proposed that self sampling as a strategy to address non attendance for screening requires further study in well organised pilots and research projects.”</p>	<p>Preventx would be very willing to contribute to the design and implementation of an appropriate, large scale pilot. We are keen to support development in this area and would be willing to contribute learnings, skills and IT resources at cost including access to the test and research platform and capabilities described above, to accelerate progress.</p> <p>Our suggestion would be implementation of a single, large pilot (potentially covering England, Scotland, Wales and Northern Ireland) as the most cost-effective solution. An integrated diagnostics provider (with in-house website, IT development, test kit logistics and pathology functions) could manage all the key systems and process to support such a pilot, greatly simplifying logistics and set-up. There is no reason why such a pilot could not be launched comfortably in the second or third quarter of 2019.</p> <p>If a reduced geographical scope would be preferable for a pilot, we would recommend targeting Scotland, where we understand that the IT infrastructure with which an HPV self-sampling service may need to integrate is well developed and robust.</p> <p>We are also aware of major pharmaceutical, diagnostic and third sector partners including Jo’s Cervical Cancer Trust who are equally keen to see progress in this area and we would also be very willing to test their appetite for supporting such a pilot.</p>

3	<p>“ii) there is a low rate of inadequate samples for HPV testing”</p>	<p>This reflects experience in sexual health self-sampling. For example, of 90,926 self-sampled vaginal swabs received by Preventx for chlamydia testing in the six months to December 2018, only 0.24% could not be successfully tested.</p> <p>We recommend that the self-sampling programme explores the use of assays which incorporate a cellularity control to differentiate specimens which are genuinely HPV negative from specimens which do not exhibit HPV signal due to insufficient cell mass i.e. false negatives.</p>
3	<p>“iii) there was an improvement in screening uptake, in most studies, of between 10% and 20% when compared to invitations to clinician sampling”</p>	<p>This mirrors experience from sexual health self-sampling. Some women are very reluctant to visit a GP/health centre to allow a clinician to take a sample, due to embarrassment, perceived inconvenience or negative associations (e.g. fear of pain or fear of a positive diagnosis), but a proportion of this cohort will agree to self-sample.</p> <p>35% of young women are embarrassed to attend smear tests because of their body shape, according to a recent survey of survey of 2,017 women aged 25-35 <a href="http://www.jostrust.org.uk/node/1073042">www.jostrust.org.uk/node/1073042</a>.</p> <p>Importantly, this group may well be higher risk due to lack of screening history. This may translate into a higher cancer diagnostic rate.</p> <p>While self-sampling will unquestionably help the NSC to address non-attendance, it should also be viewed as the vehicle through which the NSC can engage more broadly with this cohort. This should include learning more about the causes of non-attendance and identifying the messages and triggers which will encourage non-attenders and self-samplers to trial testing in-clinic.</p>
3	<p>“there was insufficient information on the circumstances in which the approach should be used. This might</p>	<p>Different forms of approach, the impact of communication timing and content and many related factors could be quickly and cost effectively researched via comparative testing as described above.</p>

	<p>include the overall level of uptake, length of time following the initial invitation and the number of subsequent prompts”</p> <p>“the review suggested that it would be useful to understand more about how to approach women regarding self sampling. However higher uptake was reported when sampling kits were directly mailed to women compared to an offer to collect or order a kit”</p>	<p>Testing should also be used to review the cost effectiveness of mailing sampling kits directly (unsolicited) to women versus asking women to order kits. For example, a voucher code for an online kit order could easily be sent out with a second reminder letter to a sample of women with a second sample being sent an unsolicited testing kit. The results (costs and numbers of completed tests) from the two sample groups would then be compared.</p>
3	<p>“the potential for a negative impact on usual responders had not been explored.”</p>	<p>Sexual health self-sampling services employ a range of techniques to control migration of patients from clinics to on-line services. These techniques include online triage (identifying specific cohorts of patients as eligible for self-sampling services), highly targeted promotion of on-line services and promotion of online clinic booking and appointment management via the self-sampling service (i.e. providing some of the convenience of online service to clinic patients).</p> <p>Similar techniques could be tested to discourage HPV clinic visitors from migrating to a self-sampling service, as could specific messages. For example, patients who visit a clinic have clearly made a positive decision that the potential inconvenience of doing so is outweighed by the health benefits. These patients may be very receptive to a simple message such as “clinic testing is safer.”</p>

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Friday 18<sup>th</sup> January 2019**.





UK National  
Screening Committee

UK National Screening Committee  
Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations

Consultation comments pro-forma

<b>Name:</b>	Clare Gilham & Julian Peto	<b>Email address:</b>	xxxx xxxx
<b>Organisation (if appropriate):</b>	London School of Hygiene & Tropical Medicine		
<b>Role:</b>	Assistant Professor (Gilham), Professor (Peto)		
<b>Do you consent to your name being published on the UK NSC website alongside your response?</b>			
Yes <input checked="" type="checkbox"/> No <input type="checkbox"/>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
1	An expanded, five year, screening interval for HPV negative women	This is a sensible suggestion. Data from the ARTISTIC trial show extremely low risk of CIN3+ within the 5 years following a negative HPV test.  Data (in press) regarding the 11 invasive cancers diagnosed within 5 years of baseline of the trial (10 prevalent, one 4 years later) show that two tested HC2 (Hybrid Capture 2)	

		<p>negative. Under a 5 year screening interval with primary HPV testing these two would have been missed. Reanalysis of the two baseline samples with a more sensitive PCR assay identified HPV16 in both. In addition, 4 of the further 7 cancers diagnosed 5-10 years after entry were HC2 negative at entry but only one was HPV negative by PCR. This raises the issue of primary HPV test sensitivity rather than safety of extending screening intervals, but it shows that 5 of the 6 cancers diagnosed within 10 years in HPV negative women were due to false negative tests rather than new HPV infections. HC2 is no longer commonly used in the NHSCSP, but the sensitivity of current tests needs to be reassessed in relation to prospective cancer risk instead of CIN3 risk.</p>
1	<p>Surveillance for HPV positive/cytology negative women</p> <p>Forthcoming work: "genotyping...is not being proposed as part of the primary screening strategy.."</p>	<p>We strongly suggest that HPV assays which can identify HPV genotypes 16 and 18 are used by the NHSCSP. Data from the ARTISTIC trial show that there is a large difference in risk following infection with HPV16/18 compared to the other 12 high risk types, so later recall of women with the other types, who are the majority of HPV positive women (eg at 1 year for HPV 16/18, 2 or 3 years for other types) would substantially reduce repeat testing with negligible increase in cancer risk. Women being tested by HPV for the first time will include many with long-standing persistence, but at subsequent rounds none will have been infected for over 5 years, and identification of cytology negative women with persistent infections with types other than HPV 16/18 can safely be delayed by 2 or even 3 years.</p> <p>We have also shown that women who clear an HPV infection and acquire a new HPV of a different type are at much lower risk than women with persisting type-specific HPV infection (data in press). Risk stratification based on HPV 16/18 versus other high-risk types could reduce repeat testing in HPV</p>

		positive/cytology negative women who do not have HPV16 or HPV18, but tests that identify all 14 high-risk types (or a national bank of LBC samples for case-control analysis of subsequent cervical cancers) would enable triage strategies based on type-specific persistence to be reconsidered in the future.
2	<p>Women aged 64 and over who are exiting the programme.</p> <p>HPV positive / cytology negative women should be recalled at 12 months and, if still HPV positive, be referred for colposcopy. If colposcopy is decisively negative this would prompt discharge from the programme</p>	<p>We do not think that this is a safe recommendation and would urge that these women are offered loop excision or continued screening.</p> <p>Evidence from modelling UK national data and from ARTISTIC shows that most cancers which arise after age 65 are due to infections contracted much earlier in life which have persisted for many years, often with normal cytology. In the era before HPV testing in the NHSCSP, women at high risk (i.e. normal cytology but HPV positive) were discharged from the programme at age 64. The majority of cancers at age 65-79 are in women who had been screened, and most of these were HPV+ with normal cytology when they were last screened. Evidence is lacking, but we believe that many, perhaps most, would have “decisively normal” colposcopy (whatever that means) at age 65.</p> <p>In women aged 65-79 35% of cancers arise in the 9% who have never been screened. Their cervical cancer risk is about 1 in 50. These women should be targeted, with an information sheet explaining that a single HPV test would identify those at high risk.</p>

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.



**UK National Screening Committee  
 Consultation on modifying the NHS Cervical Screening Programmes in the four UK nations**

**Consultation comments pro-forma**

<b>Name:</b>	Robert Music	<b>Email address:</b>	<a href="#">XXXX XXXX</a>
<b>Organisation (if appropriate):</b>	Jo's Cervical Cancer Trust		
<b>Role:</b>	Chief Executive		
<p><b>Do you consent to your name being published on the UK NSC website alongside your response?</b></p> <p align="center">Yes <input checked="" type="checkbox"/>      No <input type="checkbox"/></p>			
<b>Issue number (1, 2 or 3)</b>	<b>Document, page number and text to which comments relate (optional)</b>	<b>Comment</b>	
		<i>Please use a new row for each comment and add extra rows as required.</i>	
Issue 1	Overall response to issue 1	Jo's Cervical Cancer Trust is supportive of the move from three year screening to five yearly for HPV negative women based on the modelling outlined in document 3a, which shows: <ol style="list-style-type: none"> <li>1. Overall it is predicted there will be a reduction in cervical cancer incidence and mortality,</li> <li>2. It will reduce the number of primary screens (which is preferable for women)</li> </ol>	

		<p>3. It will increase identification of those with CIN2 or worse and  4. It has potential to reduce net health related costs by £35 million per annum.</p> <p>Despite there being a high degree of confidence in the findings, both documents 3 and 4 highlight limitations in the modelling and this must be carefully considered,.</p> <p>We could not currently support six or ten yearly screening intervals. The consultation documents state that there is not enough evidence for this proposal and the systematic review says they may result in life losses. This is clearly not acceptable.</p> <p>There is much emphasis on cost-saving benefits, however if incidence increases as a result then this should not be acceptable either. Furthermore consideration needs to be given to the significant cost of diagnosis to the individual, NHS and state (as our 2014 'Behind the Screen' report highlighted<sup>1</sup>).</p> <p>The focus of any programme change must be saving lives through reducing incidence and / or earlier diagnosis.</p> <p>Below are general comments that we believe are important and relevant to the discussion on issue 1.</p>
	Communicating changing intervals	We are already communicating a major change to screening with the move to HPV primary screening and are ensuring this is carefully managed to reduce the anxieties that we know exist. Another major change is being proposed through screening intervals changing meaning messaging and

<sup>1</sup> Jo's Cervical Cancer Trust 'Behind the Screen' <https://www.jostrust.org.uk/get-involved/behind-the-screen>

		communication must be carefully created, and not rushed, to ensure women fully understand that it is safe and backed by research. We know from those we support that any change in the programme will cause concern, lead to suspicion of cost-saving and could reduce trust and attendance.
	Document 4 page 13	We believe that for now 12 month recall is better than 24 months however, as stated in document 4 the evidence is contradictory between QUALY and Life Years gained and so an ongoing evidence review is needed.
	Document 4 page 4 - England v Scotland	<p>It is unclear which is the best approach to managing those who are HPV+ve and cytology negative after 24 months, out of the pathways in Scotland and England. Further evidence is needed to ascertain which is most effective and this should then be followed. It is worth noting that Wales who have already gone live with HPV primary screening are following the suggested English pathway.</p> <p>If there end up being two different pathways this could result in confusion and anxiety amongst women as to whether they are being offered the best option. Jo's Cervical Cancer Trust is already seeing a large increase in questions around HPV as a result of programme changes and we (and others) will be challenged to reassure women that their test is the best compared to what might be being offered in another country – ultimately that will be difficult to do.</p>
	Document 4 page 20 - True cost effectiveness	Document 4 highlighted that true cost effectiveness could not be ascertained by moving to 5 years screening intervals. As such there need to be ongoing reviews and close monitoring of women if there is to be such a change. We must be certain it is the right decision and safe.
	Consideration of non-attenders under 50	We believe consideration should be made to the possibility of non-attenders under 50 continuing to be invited every three years (as they are now) until

		<p>they attend screening. Then returning to five year cycle once back in the programme.</p> <p>However this will not be possible until a more sophisticated IT infrastructure is in place – as detailed at the end of this response.</p>
Issue 2 – women over 64	Document 4 page 14	<p>We are in principle supportive of the recommendations. However, as highlighted in document 4, there are no studies that provide evidence for differential strategies for women on exit. Nor is there any data outlining real benefits or risks on the recommended strategy versus alternative models.</p> <p>There is a clear need for ongoing clinical research to fully ascertain risk and benefits to identify the ideal pathway for those over 64. In addition focus group research with women of this age group is needed to understand what they would want.</p> <p>Until there is data to show the benefits of the recommended strategy we agree that a consensus statement as suggested in the consultation should be developed, but with a wide range of stakeholders beyond just clinicians.</p>
	Comment: An opportunity to review the last age of invitation for cervical screening	<p>It is surprising that there has been no consideration for a review to explore whether the current age of 64 for leaving the programme remains correct and urge this is taken forward.</p> <p>Women are on average living five years longer compared to when the programme was set up and sexual behaviours have also changed. The greatest number of new cases of sexually transmitted infections are in those aged over 50, who have not benefitted from the vaccine and we know HPV can also lie dormant for 20-30 years.</p>

		Released in 2018, our model <sup>2</sup> showed that incidence and mortality in the over 60s is predicted to significantly increase by 2040 and therefore the need to monitor for longer may well be necessary. Other countries such as Australia and the USA are already screening longer than the UK.
	How to offer a test to those who are HPV+ve and cytology negative at 64	For those post menopausal, it can be painful to undergo a speculum test and often difficult to find the transformation zone. Offering an HPV self test for this age group could address these issues and provide greater protection for a large cohort. This is becoming increasingly more important as we are seeing screening coverage among women in their 50s and 60s fall dramatically whilst in Wales, Scotland and England over 70% of cervical cancer mortality is from those aged fifty and above.
Issue 3 - Self sampling	Overall response to issue 3	<p>Jo's Cervical Cancer Trust fully supports a study into self sampling as a matter of urgency. We are seeing cervical screening coverage fall year on year, at a ten year low in Scotland and an all time low in England while incidence in parts of the UK is on the increase.</p> <p>Self sampling could reverse this, saving lives and costs to the NHS, state and public. Many countries around the world have already introduced self-testing whilst Denmark has just announced that from January 2020 it will be offering the option for women to ask for a home self testing kit after their second reminder.</p> <p>In terms of getting a self sampling project underway quickly we could look to Scotland as they have a well developed IT infrastructure.</p>

<sup>2</sup> <https://www.jostrust.org.uk/about-us/our-research-and-policy-work/our-research/projected-incidence-and-mortality-cervical-cancer>



	Evidence for self-sampling	<p>Many pieces of our own research have shown that high percentages of women, regardless of whether they currently attend or not, would prefer to self test. This includes a survey<sup>3</sup> in 2018 which showed that 80%, from a UK wide sample of over 2,000 women would prefer to self sample. Among non-attenders alone this increased to 86%.</p> <p>Certain groups where attendance is lower will significantly benefit including those with a physical disability, those who experience pain and survivors of sexual violence. It is estimated that one in five women will experience sexual violence in their life and our research has shown that close to three-quarters of survivors of sexual violence<sup>45</sup> feel unable to go for a smear test.</p>
	New evidence	<p>Overall the rapid review (document 5) was positive in its support for self sampling. There were a few uncertainties compared to cytology such as sensitivity and specificity, however, there has been new data since the launch of this consultation which further supports introduction of self sampling. Most recently a paper presented by Arbyn <sup>6</sup>at EUROGIN 2018 on updated meta analysis of self sampling projects which showed results similar to clinician samples in terms of sensitivity.</p> <p>And the Copenhagen Screening initiative (CSi) has shown positive results<sup>789</sup>, including 20% of non-attenders who were invited to self sample</p>

<sup>3</sup> <https://www.jostrust.org.uk/node/1074459>

<sup>4</sup> [https://www.jostrust.org.uk/sites/default/files/jcct\\_rc\\_information\\_and\\_support\\_needs\\_-\\_survivors\\_of\\_sexual\\_violence.pdf](https://www.jostrust.org.uk/sites/default/files/jcct_rc_information_and_support_needs_-_survivors_of_sexual_violence.pdf)

<sup>5</sup> <https://www.jostrust.org.uk/node/1075195>

<sup>6</sup> <https://www.bmj.com/content/363/bmj.k4823.full>

<sup>7</sup> <https://www.nature.com/articles/bjc2017371>

<sup>8</sup> <https://jcm.asm.org/content/55/10/2913>

<sup>9</sup> <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5516138/>

		<p>taking up the offer with another 10% choosing to book a GP based test. 40% of self samples returned were from those who had delayed for over ten years which is very significant. Additionally self samples had higher numbers with CIN3 or cancer compared to those that were clinician taken, again highlighting the benefits of this test.</p>
	Without investment in a new IT system self sampling isn't achievable	<p>To ensure a self sampling programme can be as efficient and cost effective as possible and focusses on the needs of the woman it will require investment in new IT. The current and 'not fit for purpose' cervical screening IT infrastructure in England does not have the ability to manage such a programme.</p> <p>Sexual health service settings have been successfully running self sampling programmes for many years and we should look to them for expertise and evidence. This includes use of IT, turnaround times, full automation, online ordering, development of kits and being able to deal with large volumes.</p>
	Costs	<p>The cost/benefits of self sampling must of course be carefully reviewed, but any analysis must also include costs saved through numbers of reduced cancers and the impact on the NHS, state and the woman.</p> <p>Our research 'Behind the Screen'<sup>10</sup> showed savings of a minimum of £10 million a year through reduced initial cervical cancer treatment costs. This figure will be significantly more millions based on the ongoing costs of cancer care beyond initial diagnosis and treatment. There are also reduced benefits costs and patient costs such as fewer numbers affected by long term consequences of treatment or loss of work.</p>

---

<sup>10</sup> <https://www.jostrust.org.uk/get-involved/behind-the-screen>

	Eligibility	<p>The rapid review strongly highlights benefits in offering self sampling to non-attenders to improve coverage. Further studies such as the Copenhagen research backs that up.</p> <p>However if it is proven to be a more acceptable test, in terms of equity, the screening programmes may at some stage have to consider offering it as the first test for all women. Otherwise it could result in women being aware of the self test option and choosing to ignore their screening invitation hoping for a self test invitation to follow.</p>
	Best way to offer the test	<p>Meta analysis shows that participation in self testing studies is higher than clinical sampling and that a self testing kit sent to a woman's home will see the best results. Additionally being sent a kit can act as a prompt with around 10% of those mailed a pack choosing to book a test at their GP.</p> <p>Any pilot should consider all options including mailing a kit directly (unsolicited), offering a kit being mailed and the opportunity to pick up a kit at a GP practice.</p>
	UK needs to be a leader in eliminating cervical cancer	<p>Elimination of cervical cancer is achievable and that is a fantastic opportunity. However, other countries are far ahead of the UK in achieving this goal as they already offer self sampling, HPV primary screening and HPV vaccination for boys and girls. Australia is currently the best example.</p> <p>The lack of speed that the UK has taken in moving forward with any innovation is resulting in an inequity compared to other countries. We do not have the best service available to women. If self testing is supported then ensuring a pilot takes place quickly is essential and, assuming the results are positive, we need to be agile and ready to make it part of the programme as soon as possible.</p>

		<p>We do not want to be falling behind other countries in terms of women's health and self sampling could be the catalyst to turn around ongoing falls in coverage. Ten years ago as a result of Jade Goody's battle with cervical cancer an extra 400,000 women went for their test. To reach the current coverage target of 80% it is estimated we need an extra 1.2 million women, which shows the size of the task and why self sampling could be so vitally important.</p>
<p>Comments on the issues outside the scope of the consultation but which should be considered</p>		<p>The current cervical screening IT system in England is preventing several of the innovations above from happening. It was called 'not fit for purpose' in 2011 and continues to be a cause of great concern despite England being so close to HPV primary screening going live. Further information regarding this critical issue can be found in our recent report.<sup>11</sup></p> <p>A new system would provide the ability to target women at variable times based on their screening and vaccination history. This would mean that different cohorts can be targeted in the best way, and will ensure the programme is as agile, efficient and cost effective as possible.</p>

Please return to the UK NSC Evidence Team at [screening.evidence@nhs.net](mailto:screening.evidence@nhs.net) by **Monday 18<sup>th</sup> January 2019**.

---

<sup>11</sup> [www.jostrust.org.uk/access](http://www.jostrust.org.uk/access)

## Response to consultation on primary HPV cervical screening on behalf of ACCS and Primary HPV Pilot Steering Group

### Issue 1: Screening and surveillance intervals

#### \* Expand screening intervals to five years.

We agree that the evidence from controlled trials and other high quality studies indicate that the greater sensitivity of high risk human papillomavirus(HR-HPV) compared with cytology, and the duration of its negative predictive value, support extension of the three year screening interval for women aged 25-49 to five years. Women aged 50-64 already have a five year screening interval. Data from extended follow up in the ARTISTIC trial, indicated that the incidence of high grade cervical intraepithelial neoplasia(CIN) six years following a negative HPV screen was similar to that three years following a negative cytology screen (Eur J Cancer; 47, 864-871, 2011). Furthermore the Primary HPV Screening Pilot Study has revealed that three years following a negative baseline HR-HPV screen, the detected incidence of CIN grade 3 or worse was just 0.1%(21/40944) with no screen detected cancers, compared with 0.4%(365/93,608) for women with a negative baseline cytology screen, and 15 screen detected cancers (BMJ in press). The most recently updated analysis with larger numbers showed again showed zero screen detected cancers among women screened with baseline HR-HPV, and 37 screen detected cancers amongst those screened with baseline cytology. These data confirm the safety of extending the interval from three to five years for primary HPV screening.

#### \* A 12 months surveillance interval for HPV positive/cytology negative women.

We agree that this is the correct strategy, as it allows natural viral clearance to occur in around 40% of cases by 12 months, thus avoiding large numbers of unnecessary colposcopy. The strategy does however require adherence to early recall for affected women, and the evidence from the pilot study is that over 80% of these women attend early recall, and if colposcopy referral is indicated because of abnormal cytology, over 90% attend. This is important evidence of the feasibility of this approach. In the pilot around 20% of all high grade CIN detected was found at 12 months early recall, which confirms the additional sensitivity of primary HPV. Around 10% of the screen detected cancers in the entirety of the baseline round of the pilot, were detected at the 12 months early recall.

\* Surveillance of persistently HPV positive/cytology negative women should be continued to a further early recall at 24 months. We agree with this strategy, which allows further natural clearance to occur, and again in the pilot, over 80% of women adhered to this. Referral to colposcopy of women with persistent HR-HPV yielded 5% of the total detection of high grade CIN(with zero screen detected cancers) in the baseline round, and while the positive predictive value for colposcopic detection of high grade CIN is reduced by the inclusion of women with negative cytology, this proved manageable and provides reassurance that annual surveillance can be safely discontinued for those with persistent HR-HPV.

### Issue 2: Women aged 64 and over exiting the programme.

#### \* HPV positive/cytology positive should be managed in the same way as other groups.

We agree.

\* HPV positive/cytology negative women should be recalled at 12 months, and if still HPV positive referred for colposcopy. We agree.

i) If colposcopy were decisively negative this would prompt discharge from the programme. We agree.

ii) If colposcopy were decisively positive this would prompt the offer of loop excision. We agree, with the proviso that if cancer, rather than CIN were suspected, an appropriate biopsy should be taken, and the management would depend of the histological findings.

iii) If colposcopy were indecisive, this would prompt the the offer of loop excision or recall after a further 12 months. We agree, however the offer would be based on the woman's informed choice. If

when the women had been recalled to colposcopy 12 months later, and this was again indecisive with persistently positive HR-HPV and negative cytology, then the choice would be between loop excision or, based on three negative cytology samples over 24 months, discharge from the programme.

\* we agree that there is a lack of informative data regarding the management of this new class of results in women exiting the programme. Longer term follow up data from the pilot could be informative. In the meantime, professional consensus will be important to develop clinical guidance which will help to standardise practice.

Issue 3: Self sampling as a strategy to address non-attendance for screening.

We agree that self sampling warrants further study prior to implementation. Women who do not attend for screening are a 'hard to reach' group, and studies that have been performed to address this challenge, have found that uptake of self sampling amongst non-attenders is variable but generally low. Offering a sample kit if they opt in for it, is not as effective as sending a kit to all, and in the STRATEGIC trial, many who did respond, did so by attending for a cervical sample rather than self sampling( NIHR HTA; Vol 20, 2016). The ACCS has heard the argument, and would concur, that if women in this group were screened in a study, then this should be recorded as a screen, thus incentivising primary care and indeed the women, to participate.

It is undoubtedly the case that self sampling technology would be seen by many women as a more convenient means of obtaining a sample than attendance at a clinic.

Sampling has been sufficiently developed methodologically, to warrant a large pilot study.

Other comments.

1. The advent of abnormal results which incorporate negative cytology, is the principal management challenge when compared with primary cytology. This requires some thinking about the threshold for colposcopy referral based on the positive predictive value(PPV) in terms of detection of CIN grade 2 or worse. With primary cytology, this threshold was around the PPV of 16/17% for HPV positive low grade cytology. The recommendation around colposcopy for women at 24 months recall for example requires a lower threshold in terms of PPV, and there is a balance between maximising cost effectiveness, achieving maximum sensitivity and reassuring HR-HPV persistently positive women. Opinions regarding notional thresholds naturally vary from country to country, and we feel it would be useful to convene a multidisciplinary meeting within the English system to discuss this. The increasing sensitivity of the programme, combined with the advent of the HPV vaccinated cohort into the programme will see a trend tend towards lower PPV as the underlying quantum of disease lessens.

2. There is a good case to be made for a cost effectiveness study based on one of the existing models and the large pilot dataset, and we would like the case for this to be considered.

3. We wish to reaffirm our view that an IT system capable of supporting not only the new programme, but also linking HPV vaccination status with cervical screening is crucial.

Henry Kitchener

Chair of the ACCS and the Primary HPV Cervical Screening Pilot Steering Group.