First-void urine self-sampling for primary HPV cervical cancer screening: an implementation tool for US healthcare professionals

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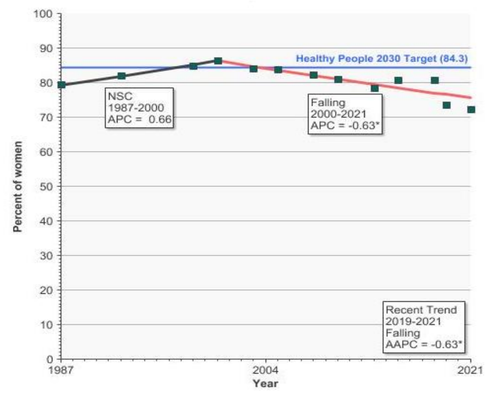
Background

Cervical cancer screening in the US

- In the US, the American Cancer Society (ACS) recommends cervical cancer screening for all women aged 21–65[1].
- Screening is available as part of private health insurance provision and free of charge through publicly funded prevention programmes (e.g. National Breast and Cervical Cancer Early Detection Program) for women without insurance[2].
- The national coverage of cervical cancer screening is falling (Figure 1), with about 1 in 4 women not up-to-date with screening[3].
- Under-screened women bear the greatest burden of disease; 60-64% of American women diagnosed with cervical cancer are unscreened[4-6].
- Cervical cancer diagnoses and mortality vary by ethnic group. Hispanic women are the most likely to develop cervical cancer, while Black women are the most likely to die from cervical cancer[7]. Compared to non-Hispanic white women, Black women were 30% more likely to develop cervical cancer, and 50% more likely to die from it[7].
- There is an urgent need to explore alternative screening approaches to improve access to screening in underserved groups.

Figure 1: Trend over time in cervical cancer screening uptake in the US



Source: National Cancer Institute[3]
Footnote: The self-reported screening uptake may be overestimated since the proportion of women up-to-date with cervical cancer screening is lower when calculated using direct measures[11]

Self-collection for cervical screening

- Globally, women in some cervical cancer screening programs are now offered the choice of sample self-collection[4-6] using a swab or brush[8].
- Evidence supports self-collection as an acceptable, safe and reliable[9] modality for sample collection which has the potential to remove individual and systemic barriers associated with clinician-collected sampling.
- Pilot studies confirm the feasibility and accurate clinical performance of using self-collected first-void urine (FVU) for HPV screening[10]. The VALHUDES protocol can be leveraged to validate different HPV assays on FVU samples for use in HPV primary screening[11].
- Using FVU provides some advantages over other sample types, since it is non-invasive and easy to collect using a urine collection device such as Colli-Pee™ FVU collection device for standardized, volumetric collection[12]. (See our definition of 'What is first-void urine?').
- Healthcare professionals (HCPs) and providers who want to evaluate and promote the use of self-sampling for screening in their patient population can face barriers to introducing self-collection.

Aim

We aimed to develop an implementation tool (framework) to enable healthcare professionals and providers to become active stakeholders in improving access to HPV screening by identifying opportunities for FVU self-sampling within their patient population.

Methods

The implementation tool was developed using a phased approach:

- Phase 1: Defining the purpose, users, and clinical context.
- Phase 2: Collating ideas and defining themes informed by a targeted literature review.
- Phase 3: Consolidating themes and developing the tool's content.
- Phase 4: Piloting the tool to refine and validate it using input from screening experts and potential users.

Three subject matter experts from different professions related to cervical cancer and HPV screening and different regions in the US were interviewed. During the (virtual) semi-structured interviews, the tool was piloted by asking each interviewee the questions from the tool. The experts were then asked to reflect on the contents of the tool and indicate where improvements could be made. Each interview was recorded. Insights were used to improve and finalise the tool.

What is first-void urine?

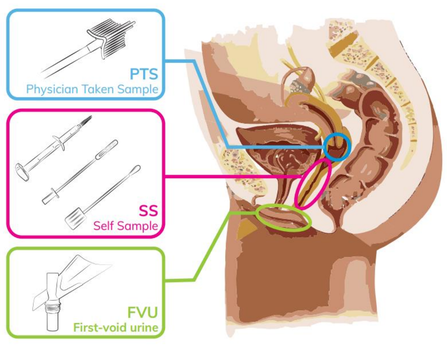
First-void urine (FVU) is **the first part of the urine stream, collected at any time of the day**[12-14].

It is sometimes referred to as 'first-catch' or 'first-pass' urine and does not need to be the first or 'first-morning' urine of the day.

FVU contains washed away mucus and debris from the exfoliated superficial cell layers of the cervix carcinoma which accumulate between the labia minora and around the urethra (Figure 2)[15]. It contains higher concentrations of HPV DNA than subsequent void fractions and is therefore optimal for HPV screening[14].

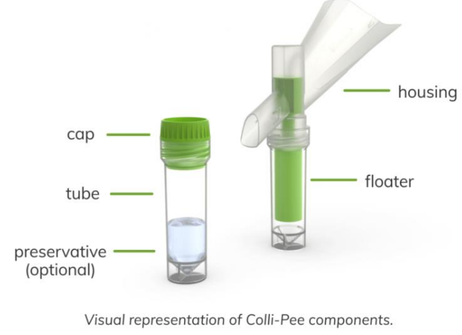
Colli-Pee™ (Figure 3) is a collection device that allows for standardised, volumetric collection of 4mL, 10mL or 20mL FVU. It provides an optional format in which the collection tube is prefilled with a non-toxic urine preservative solution (UCM) to allow for safe storage, transportation and handling of the sample[12]. HPV DNA remains stable in the UCM preservative solution, from 7 days at room temperature to 90 days at -20°C[16].

Figure 2: Source of collection for different sample types



Source: Laeremans *et al* (2019) [15]

Figure 3: Colli-Pee™ FVU collection device



Visual representation of Colli-Pee components.

Source: Novosanis website[12]

Results

The implementation tool guides the user through a series of 22 questions within five key themes:

Theme 1. The value of self-sampling
Theme 2. Existing healthcare structures
Theme 3. Key stakeholders
Theme 4. Evidence available
Theme 5. Barriers and facilitators to implementing urine-based self-sampling

Example questions from the tool:

- What evidence is available already about urine self-sampling for HPV primary-based cervical cancer screening including acceptability, safety, accuracy, clinical benefit, cost-effectiveness, etc.?
- Are there data on cervical cancer rates or cervical screening coverage in my area that help us understand where there is an unmet need and what are the underserved groups?
- What individuals or groups would be affected by the introduction of self-sampling? How will they be affected?

In answering the series of questions, the tool prompts the user to consider what evidence they have, who the key population groups are that will benefit from the implementation of self-sampling and who the key stakeholders are in their area.

Insights from piloting the tool resulted in some changes including:

- Renaming the 'implementation framework' as an 'implementation tool'.
- Including a definition of FVU at the start of the tool.
- Introducing the tool by including a summary of its purpose.
- Changing to a numbering system for questions to avoid repetition and promote usability.
- Including additional questions for laboratory professionals, a key stakeholder group.

The final implementation tool can be accessed by scanning the QR code.

A summary of the answers from the three pilot interviews can be found below:

Use Case 1

- Patient population: young women in California.
- Under-screened and un-insured women, particularly immigrants, were identified as a target population with unmet need.

Use Case 2

- Patient population: underserved women in North Carolina.
- Uninsured women were identified as those who would benefit the most from self-sampling

Use Case 3

- Interviewee stated that while most of the unscreened population do not have insurance, there is a lack of education on screening, we need to expand beyond the underserved population and offer all women the same screening options.

Key themes

- Socioeconomic status and lack of insurance are key characteristics associated with reduced screening.
- Other barriers include cultural differences, lack of education on available services and the importance of screening, proximity of free clinics, needing childcare to attend appointments and medical distrust.
- Lack of screening registry data means it is difficult to identify women who are under screened.
- While many women have shown a preference for urine-based sampling, there may be difficulties in implementing and getting buy-in from other stakeholders.
- Laboratories are an important stakeholder. Urine specimens require specific processing steps which may introduce new operational challenges to maintaining efficient loading and testing of samples on HPV platforms.
- Non-profit and community groups are also important in raising awareness, educating and encourage women to screen.
- Understanding the benefits of FVU is a current barrier in the field. Many HCPs are not aware of urine-based self-sampling and will not have the same understanding of the definition of "first-void".
- More evidence and education is needed on urine self-sampling, including its performance and cost-effectiveness. Having guidelines and policymakers recommend it will increase buy-in from key stakeholders.
- Responses to the tool questions will vary by state (e.g. availability of free screening services and data on screening coverage).

Conclusion

- FVU self-sampling for primary HPV cervical cancer has the potential to address unmet need in under-screened women.
- This implementation tool guides HCPs through a list of questions that helps them identify opportunities for FVU self-sampling within their patient population and better understand potential barriers.
- Barriers to implementation include a lack of awareness of FVU-based self-sampling and a lack of a standard definition for "first-void urine". HCPs want more evidence on its cost-effectiveness and the performance compared to traditional sampling methods, as well as guidance on how to implement it.
- More education is needed on the benefits of self-sampling to address unmet need in cervical cancer screening. A clear definition of "first-void urine" will reduce confusion.

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