NICE advice

Colli-Pee for first void urine collection

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Colli-Pee. It is intended to be used for first void urine collection.
- The **innovative aspects** are that Colli-Pee collects first void urine, without the person needing to interrupt the flow of urine and standardises the volume of urine collected.
- The intended **place in therapy** would be as an alternative to sterile urine collection containers for detecting human papillomavirus (HPV), sexually transmitted infections (STIs) or cancer biomarkers and for other sample collection methods such as cervical smear or self-sampling vaginal swabs in people presenting with symptoms. The experts note that the device might have particular benefits to specific groups of people, such as those who are less able to aim their urine or people with cognitive impairment.

- The **main points from the evidence** summarised in this briefing are from 1 randomised comparative study, 2 prospective cohort studies and 2 cross-sectional studies including a total of 984 people who were at high risk of HPV or STIs. They show that HPV or STI detection rates were similar using urine samples collected using Colli-Pee compared with other sampling methods including self-collected vaginal samples, home-collected urine samples (with Colli-Pee) and samples collected in a clinic. Sensitivity for cervical intraepithelial neoplasia grade 2+ (CIN2+) with the SPF10 assay system using samples by cervical smear, cervicovaginal brush and Colli-Pee was 100%, 100% and 95% respectively. Similar sensitivities were found for CIN2+ and CIN3+ using urine samples and vaginal samples.
- **Key uncertainty** is that that there is limited published evidence, and further comparative diagnostic studies on clinical accuracy compared with standard NHS practice would be useful.
- The **cost** of Colli-Pee depends on the variant (for example the volume of urine collection) with or without urine conservation medium (UCM). It ranges from £2.22 for 10 ml without UCM to £4.47 for 20 ml with UCM (excluding VAT). The cost of an HPV smear is estimated to be £6.00 and a swab for an STI is estimated to be £2.00. All stated costs do not include the reagent, the analysis and labour.

The technology

Colli-Pee (Novosanis) is a single-use urine collection device. It is designed to collect the first pass urine at any time of day, typically referring to the first 20 ml of urine flush because this can contain higher concentrations of DNA from human papillomavirus (HPV) and chlamydia compared with midstream urine (Pattyn et al. 2018; Wisniewski et al. 2008). It could also contain potential biomarkers for cancers such as cervical cancer and prostate cancer (Ducancelle et al. 2015; Theodorescu et al. 2008).

Colli-Pee consists of a housing, a floater within a tube, and a cap for final sealing of the tube. When collecting urine, the collator tube is screwed onto the Colli-Pee housing and the volume of urine needed is then collected. The device is then disconnected from the tube, which is then capped. The urine sample is sent to the lab. The collector tube can be prefilled with urine conservation medium, to allow preservation of DNA in urine. The company states that Colli-Pee has variants for collecting first void urine from 4 ml to 45 ml, and currently 2 variants to collect either 10 ml or 20 ml of urine are CE marked.

Innovations

There are a wide range of containers used for collecting urine. Unlike other available methods, the Colli-Pee device collects the exact volume of urine needed without the need to stop the stream of urine, because once the collection tube is full, the remainder of the stream will flow into the toilet. The device minimises the risk of spillage for the person when collecting urine and collects a standardised urine volume.

Current care pathway

Currently, urine testing is used to detect urinary tract infection and bacterial sexually transmitted infections (STIs). First void urine is collected for gonorrhoea and chlamydia testing in clinical practice. People are advised not to clean or wipe their genitals before passing urine. People are usually given a standard container to collect 10 ml or 20 ml of the first part of the urine stream (the first catch).

Cervical cancer can be caused by persistent infection with HPV. HPV detection in urine has recently been explored as an alternative means to identify people at increased risk of cervical cancer (Sargent et al. 2019).

Population, setting and intended user

Colli-Pee would be used for first void urine collection. The company states that the device could be used for any indication when first void of urine is needed for testing. Currently, the device is mainly used for collecting samples to test bacterial and viral STIs and HPV infections in people presenting with symptoms. It could be also used for sample collection for detecting cancer biomarkers such as prostate cancer and has been included in some testing kits.

Colli-Pee is intended to be used by people at home or in a clinic for urine collection. The urine sample is then sent to the laboratory for analysis. The company states that the Colli-Pee device could be sent as a letter through the post.

Costs

Technology costs

The costs of the Colli-Pee device are:

- €2.58 for a 10 ml Colli-Pee (equivalent to £2.22)
- €3.83 for a 10 ml Colli-Pee with urine conservation medium (UCM) preservative (equivalent to £3.30)
- €3.61 for a 20 ml Colli-Pee (equivalent to £3.11)
- €5.18 for a 20 ml Colli-Pee with UCM preservative (equivalent to £4.47).

The UCM is prefilled in the tube and this is to stabilise DNA in the urine sample.

Costs of standard care

A standard plain white universal container without an additional urine collection product costs between £0.05 and £0.09. The company states that the cost of a cervical smear for detecting HPV is estimated to be around £6.00, and the cost of a swab for STIs is estimated to be about £2.00.

All stated costs do not include the reagent, the analysis and labour.

Resource consequences

Colli-Pee has been launched in the UK but is not currently used in clinical practice. There are no anticipated practical difficulties or changes in facilities and infrastructure associated with adopting this technology.

Regulatory information

The Colli-Pee device both with and without urine conservation medium (UCM) is a CE-marked in vitro diagnostic medical device to collect 10 ml or 20 ml of first void urine.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Sexually transmitted infection (STI) risk is greatest in straight people aged 15 to 24; people from black ethnic minority groups; gay and bisexual men and other men who have sex with men. Age, race and sexual orientation are protected characteristics under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

The evidence from 1 randomised comparative study of 600 women in the UK, 2 cohort studies of 246 people in Belgium, and 2 cross-sectional studies of 113 people in Spain and 25 people in Belgium were included in the briefing.

Three abstracts were identified in the search. They were not included because:

- Castriciano and Martinelli (2019) compared the detection of human papillomavirus (HPV) using urine samples collected by Colli-Pee and UriSponge but no data for the detection rates was reported in the study.
- Donné et al. (2019) reported the development of Colli-Pee prototype and no clinical outcomes were reported in the study.
- Baetselier et al. (2017) was overlapped with Baetselier et al. (2019).

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

One UK single-centre comparative study (Cadman et al. 2021) compared a urine sample using Colli-Pee and 4 vaginal sampling devices, including wet and dry transport methods for HPV detection in 600 women who had a positive result after cervical screening. The study reported no differences in detection rates of high-risk HPV and sensitivity for detecting cervical intraepithelial neoplasia grade 2+ and cervical intraepithelial neoplasia grade 3+.

One single-centre study (Baetselier et al. 2019) included people at high risk of HIV and compared the molecular detection of sexually transmitted infections using home-collected urine samples and urine samples collected in a clinic. The agreements between 2 types of samples were over 95% for detecting chlamydia, gonorrhoea and *Mycoplasma genitalium*. The study also reported their experience using the Colli-Pee device.

Pattyn et al. (2019) included a small number of people who self-reported and had tested positive for HPV based on cervical samples (n=31). A total of 12 were found HPV positive based on their urine sample. The study analysis suggested that there was no significant effect of the timing of collection (morning compared with later during the day) on copies of HPV DNA detected. Colli-Pee collected urine samples show higher HPV concentrations than cup-collected samples. However, at high concentrations of HPV DNA, the benefit of Colli-Pee disappears.

Of 2 cross-sectional studies, Leeman et al. (2017) compared the sensitivity of detecting cervical intraepithelial neoplasia grade 2+ in self-collected urine samples, self-collected cervicovaginal samples and clinician-taken smears. The results were comparable. Téblick et al. (2021) compared the detection of human and viral outcomes using different volumes for the first urine samples, suggesting limited effects of collection volumes on human and HPV DNA endpoints.

Overall, there is limited published evidence on Colli-Pee. The evidence available is helpful to see the potential of the technology, particularly the sensitivity for detecting HPV reported in an abstract using samples by different methods. However, a well-done diagnostic study would be helpful to gain more certainty in terms of the diagnostic accuracy using Colli-Pee against standard reference methods used in the NHS and potential savings.

Cadman et al. (2021)

Study size, design and location

A randomised comparative study in 600 women who were referred to a colposcopy clinic after a positive cervical screening result in the UK.

Intervention and comparator

A stream urine sample was collected using the Colli-Pee collection kit, which collects a 20 ml sample, of which 7 ml is a prefilled urine conservation medium (UCM).

Vaginal samples were collected either as a wet sample or a dry sample (dry flocked swab [DF], Qvintip [QT] and HerSwab [HS]).

Key outcomes

The rates of detecting high-risk HPV positivity were 76.0% and 71.7% for urine samples (n=504) and wet samples (n=300) respectively. There was no statistically significant difference.

Similar sensitivities for cervical intraepithelial neoplasia grade 2+ and cervical intraepithelial neoplasia grade 3+ were seen for samples collected by a dry swab, a wet swab or a urine sample.

- The sensitivity for cervical intraepithelial neoplasia grade 3+ was 91.2% by wet sample, followed by 89.7% by a urine sample, 88.2% by DF, 81.8% by QT, and 77.4% by HS.
- The sensitivity for cervical intraepithelial neoplasia grade 2+ was 90.0% by wet sample, followed by 88.6% by DF, 87.0% by a urine sample, 82.5% by QT and 82.0% by HS, with a specificity of 34.2%, 33.8%, 27.4%, 34.3% and 39.5% respectively.

Results of a survey evaluating women's preference for sample methods, reported that 46% women (n=208) preferred one of the 2 non-urine (vaginal) devices, 32% preferred urine (collected using Colli-Pee; n=145), and 22% expressed no preference (n=101). Women found urine easiest to collect and were more confident they had taken the sample correctly compared with other vaginal samplings.

Strengths and limitations

This UK study included 600 women. It is a single-centre study. All women had urine samples. Women were randomised to collect vaginal samples as a wet sample or a dry sample. Time intervals between urine and vaginal samples were not reported in the study.

Téblick et al. (2021)

Study size, design and location

A cross-sectional study in 25 women who were diagnosed with high-risk HPV in Belgium.

Intervention and comparator

Home-collected first void urine samples using Colli-Pee with collector tubes that differ in volume (4 ml, 10 ml, 20 ml). Each collector tube was prefilled with UCM.

Key outcomes

There were no significant differences between the 3 first void urine collection volumes for detecting human endpoints including glyceraldehyde 3-phosphate dehydrogenase, beta-actin, and beta-globin. More high-risk HPV infections were detected using Colli-Pee for the collection of 10 ml compared with 4 ml and 20 ml, but the differences were not statistically significant.

Strengths and limitations

The study had a small sample size. The author noted that all participants self-reported to have a high-risk HPV infection in the previous 6 months, but this could not be verified by the study team.

Baetselier et al. (2019)

Study size, design and location

A single-centre prospective cohort study in 213 men who have sex with men at high risk of HIV in Belgium.

Intervention and comparator

People who agreed to take part in the study received a Colli-Pee device and a prepaid envelope. They were instructed to collect first void urine the next day at home using the Colli-Pee device (the home-based sample), to document the date and time of collection and to send the collector tube filled with urine back to the laboratory by regular post, using the prepaid envelope.

People also had urine samples collected during their visits to the clinic for testing for chlamydia, gonorrhoea, *Mycoplasma genitalium* and *Trichomonas vaginalis*.

Key outcomes

A total of 471 home-based samples from 213 people were received and included in the study. *Trichomonas vaginalis* was not detected. Percent agreement (Cohen's kappa coefficient) between home-based samples and clinical-based samples for chlamydia, gonorrhoea and *Mycoplasma genitalium* were 99.1% (0.75), 99.6% (0.87) and 98.3% (0.85) respectively.

A total of 164 people provided feedback about the use of the Colli-Pee device. Nearly 88% of people found that the Colli-Pee device was easy to use. Four people found the Colli-Pee difficult to use (2.4%) and another 4 people found it difficult to follow the instructions (2.4%). People liked Colli-Pee because it:

- is easy to use (54.9%)
- has no interruption of the urine flow (15.9%)
- is hygienic (11.6%)
- offers privacy of the home-based sample collection (11.0%).

People disliked the device because it:

- is not recyclable (14.6%)
- is not hygienic (10.4%)
- is too large (6.1%).

Strengths and limitations

This is a single-centre study. Most of the home-based samples (79.6%) were taken within 2 days after the clinical-based samples, and 3.8% were taken after 20 days. Not all people who used a Colli-Pee device completed the survey. The number of clinic and home-based samples received during the study decreased over time. The study was supported by Novosanis who provided the Colli-Pee devices and partially paid for the analyses done on the home-based samples.

Pattyn et al. (2019)

Study size, design and location

A prospective cohort study in 33 woman (aged 18 to 65 years) who had a previous HPV DNA-positive between July 2014 and February 2016 in Belgium.

Intervention and comparator

People who agreed to take part in the study received a package by postal mail containing 4 Colli-Pee devices. They also received standard urine cups to collect first void urine samples. They were asked to sample the very first void urine of the day (U1) and a first void urine sample later during the day (U2) for 4 consecutive days.

The Colli-Pee device captured a fixed volume of 13 ml (plus or minus 2 ml) first void urine and immediate mixing with 7 ml preservative [UCM]) leading to a final volume of 20 ml (plus or minus 2 ml). The standard urine cup collected a variable volume of first void urine and needed a manual transfer of 8 ml of urine to the 15 ml vial with 4 ml of UCM preservative by people in the study.

Key outcomes

A total of 258 urine samples from 31 people were collected and included in the analysis. A total of 12 of 33 people (61%) were detected as having high-risk HPV positivity during the study period.

The median human DNA yield in first volume urine was 7.14 (interquartile range [IQR]: 2.87 to 17.85) and 4.5 (IQR: 1.88 to 9.15) nanograms per microlitre DNA extract for the Colli-Pee device and urine cup, respectively. Colli-Pee collected samples had higher HPV DNA

concentrations than cup-collected samples at human DNA concentrations up to 12.18 nanograms per microlitre. At higher concentrations of human DNA (more concentrated samples), the benefit of the Colli-Pee disappeared.

Strengths and limitations

Sample size was small and included multiple samples from individuals. Study participants were self-reported to be HPV positive. The company provided the Colli-Pee device. Four study authors are co-founders and board members of the company.

Leeman et al. (2017)

Study size, design and location

A cross-sectional single-centre study in 113 people who were referred for colposcopy after an abnormal Pap smear in Spain.

Intervention and comparator

People were sent Colli-Pee to collect urine samples on the morning of colposcopy (U1). Urine samples later on (U2), brush-based cervicovaginal self-samples, and clinician-taken smears were also obtained from participants.

Key outcomes

All samples were tested for HPV DNA to detect cervical intraepithelial neoplasia grade 2+ (CIN2+) SPF10 assay and the clinically validated GP5+/6+ assay.

Samples from 91 of 113 people were analysed. Sensitivity for CIN2+ with the SPF10 system using samples by clinician-taken smears, self-collected samples, U1, and U2 was 100%, 100%, 95%, and 100% respectively. With the GP5+/6+ assay, sensitivity was 95% in all sample types.

Strengths and limitations

This is a single-centre study. Strengths and limitations have not been assessed because limited information was reported in the abstract.

Sustainability

The company states that this is a single-use device made of approximately 20 g unblended polymers that are well suited for recycling. There is no published evidence to support this claim.

One expert raised the issue about throw away plasticware because it is a single-use device. The expert noted that the plastic problem is not new in cervical screening because routine screening often uses a disposable plastic speculum (rather than a reusable one that must be sterilised between uses).

Recent and ongoing studies

There are studies on the device underway with further supporting evidence being generated.

- Urine HPV testing for cervical pre-cancer screening. Trial identifier: ISRCTN13132810. Status: recruiting. Indication: HPV infections. Country: UK.
- CASUS: Improved and quality assured collection of first void urine. Trial identifier: NCT04480866. Status: completed. Indication: cervical cancer. Devices: Colli-Pee. Country: Belgium.
- Evaluation of in vitro devices on self-collected vaginal swab and urine sample for testing of human papilloma virus (EU-VALHUDES). Trial identifier: NCT04312737. Status: recruiting (last update July 2020). Indication: human papillomavirus infections. Country: Italy.
- VALHUDES: A protocol for validation of human papillomavirus assays and collection devices for HPV testing on self-samples and urine samples.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three experts were familiar with or had used this technology before.

Level of innovation

All 3 experts agreed that Colli-Pee is an innovative approach to collect first void urine samples. One expert said that this is a minor variation on an existing procedure, and it would be a more hygienic collection rather than simply first catch into a universal container. Another expert thought that Colli-Pee is novel because it standardises the volume of urine collected and allows its immediate mixing with preservative. As a urine collection device, it is much easier for women to use than a standard sterile pot.

Potential patient impact

The main benefits identified by the experts are the potential of having a clean catch urine sample and improving cervical cancer screening. One expert explained that the device would be likely to be more acceptable to women. This could potentially improve access for cervical screening in some women, for instance those with a history of sexual violence for whom standard care is not acceptable or those from different ethnic groups who do not speak English. Two experts also considered that using Colli-Pee is a non-invasive way of collecting a urine sample for human papillomavirus (HPV) testing. The experts suggested that people who do not attend cervical cancer screening; and people who have difficulty catching the sample cleanly; or who have difficulties with vaginal speculums or examination because of menopause, previous abuse, altered anatomy or vaginismus; are most likely to benefit from the device.

Potential system impact

The device is currently only used in research and it is not in use in the NHS. The experts generally agreed that there may be potential for cost savings over routine cervical screening because of fewer GP or hospital visits needed and a reduction in resources needed such as staff.

General comments

One expert said that a liquid-based cervical sample for detecting HPV has been introduced in cervical screening. There is a move towards self-collection of a vaginal or urine sample, and there could be a change to the cervical screening pathway in coming years when Colli-Pee might be applied. But currently there is no convincing evidence to support that Colli-Pee offers advantages over sterile pot urine collection. Evidence is

needed to prove its clinical effectiveness comparing HPV detection using Colli-Pee urine collection with that of routine cervical screening (vaginal samples) and the sterile pot for urine collection. If Colli-Pee is shown to be superior to standard urine collection for infection detection such as STIs (sexually transmitted infections), it would have the potential to replace current standard care.

Expert commentators

The following clinicians contributed to this briefing:

- Emma Crosbie, professor of gynaecological oncology, University of Manchester. Professor Crosbie uses Colli-Pee devices in her research and the company donated 250 Colli-Pee devices for the work. The company is not involved in the analysis of the data, the decision to write it up for publication or how the results will be reported.
- Heather Cubie, honorary professor, Global Health Academy, University of Edinburgh. Registered with healthcare professional council. Did not declare any interests.
- Anna Parberry, nurse colposcopist, Barts Health NHS Trust. Did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement for medtech innovation briefings sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

Update information

Minor changes since publication

October 2021: Minor wording changes to update the definition of first pass urine and clarify costings.

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