REVIEW

Editorial Process: Submission:07/21/2022 Acceptance:07/03/2023

A Comprehensive Review of Cervical Cancer Screening Devices: The Pros and the Cons

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Abstract

Objective: The low screening coverage and reluctance of women in participation lead to low uptake in cervical screening tests. Hence the majority of cervical cancer patients visiting the hospitals are diagnosed at advanced stage, often leading to poor survival rate. This paper aims to review and compile available cancer screening devices so that more people in this field will adopt suitable devices in cervical cancer screening routine depending on requirements which may encourage the uptake in cervical screening tests. **Methods:** This paper reviews devices invented for different cervical cancer screening methods, which are Pap smear test, visual inspection with acetic acid (VIA) or Lugol's iodine (VILI), and HPV (human papillomavirus)-DNA (deoxyribonucleic acid) self-test in terms of functionality, performance in solving the limitations of screening procedure and additionally where applicable, the cervical cell collection efficacy and abnormality detection accuracy. The devices are either available in the market, published in research articles or published in international patent databases. **Result:** The reviewed devices either simplified the screening procedure to improve the clinical efficiency and accuracy in screening, reduced the pain and discomfort experienced by women during screening procedures, or achieved both outcomes. **Conclusion:** Many devices have been invented to improve the screening procedures which may potentially improve the uptake in cervical screening tests and encourage the organization of screening campaigns to reduce cervical cancer incidence.

Keywords: Cervical cancer screening- cervical cancer prevention- Pap smear test- VIA/VILI- HPV DNA test

Asian Pac J Cancer Prev, **24 (7)**, 2207-2215

Introduction

According to World Health Organization, cervical cancer is ranked as the fourth most common cancer among women, where there were approximately 570,000 diagnosed cases and 311,000 deaths in 2018 (World Health Organization, 2020). Majority of the diagnosed cases and deaths are from developing countries, where there are lack of screening programs and treatment plans for cervical cancer. In developed countries, early intervention such as early-stage screening and treatment programs has successfully reduced cervical cancer incidence and death rate. The difference in incidence rate between developed and developing country is huge, whereby the highest age standardized incidence rate is seen in Swaziland at 75.3 per 100,000 women whereas the incidence rate for European regions is between 6.8 to 9 per 100,000 only in 2018 (World Cancer Research Fund, 2018). In Southeast Asia, cervical cancer incidence rate is 17.2 per 100,000.

The main cause of cervical cancer is HPV, which is the most common sexually transmitted disease. Vaccines produced by Merck, known as Gardasil 9 protects against 9 subtypes of HPV types 6, 11, 16, 18, 31, 33, 45, 52, and 58 whereas Cervarix is effective against HPV type 16 and 18 (National Cancer Institute, 2015) However, these vaccines can only give maximum protection for women who never had exposure to HPV, such as prepubescent and teenagers. Even so, women who had received the vaccine before will still need to undergo cervical cancer screening in later age to prevent cervical cancer caused from other strains of HPV not covered by vaccine. Also, many developing countries could not afford to vaccinate their children, causing them to be highly exposed to HPV in adulthood. Thus, cervical cancer screening program is very crucial to reducing cancer incidence and mortality.

There are a few cervical screening methods, which are conventional Pap smear test, liquid-based Pap smear test, HPV DNA test, and visual inspection with acetic acid (VIA) or visual inspection with Lugol's iodine (VILI) where their information is shown in Table 1. A good test

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will have a balance between sensitivity and specificity to prevent late or unnecessary treatment. For all the methods above, the initial procedure is the same, where clinicians will first insert a speculum which separates the vaginal walls for external visualization of cervix. Then, a medical assistant or nurse will shine a light source into the cervix for the clinician to have a clear view of the cervix or by using wall mounted examination light. For both Pap smear tests and HPV DNA test, clinicians will use sampling tools such as Ayre's spatula, cytobrush or cytobroom to scrape cervical cells by rotating the sampling tools around the cervix. The sample will be collected from three cervical regions known as ectocervix, endocervix and transformation zone.

For conventional Pap smear test, the sample will be smeared onto a glass slide, where Pap stain and fixative will be applied for sample preservation. The slide will be sent to a pathologist for microscopic evaluation based on The Bethesda System (TBS) to identify cervical cell abnormality. As for liquid-based Pap smear test and HPV DNA test, the samples are preserved in a liquid preservative in a bottle and sent to a laboratory to identify cervical cell abnormality and DNA of HPV, especially HPV-16 and HPV-18 which are present in 70 % of cervical cancer patients worldwide (World Health Organization, 2020). In rural areas where the methods above are not accessible or unaffordable, VIA or VILI will be applied, which is an alternative method suitable for low resource settings due to low cost and technology requirements. 3 to 5 % of acetic acid or Lugol's iodine will first be applied on the cervical region using cotton ball. Then, visual inspection on cervix will be done via naked eye. For VIA, precancerous lesion will turn white whereas for VILI, precancerous lesions will remain colourless or become yellow while the remaining epithelium cells will turn brownish black.

According to Table 1, conventional Pap smear test has the lowest sensitivity in detecting abnormalities as the discarded sampling tools may contain some abnormal cells that are not smeared to the slide while the slide contains obstructive blood and mucus (Koliopoulos et al., 2017). Liquid-based Pap smear test have improved sensitivity because the liquid sample processing will filter out obstructive blood and mucus before microscopic analysis. Also, the same liquid sample can be used for HPV DNA test. HPV DNA test have the highest sensitivity among all other methods. However, the cost of HPV DNA is also the highest (Horizon Scanning, 2019). In long term, HPV DNA is more cost effective because having negative HPV with normal Pap test results allows five years break before follow-up test, whereas normal Pap test without HPV DNA testing needs three yearly follow-up tests. The biggest advantage of VIA/VILI method is the immediate availability of results, thus making screening and treatment on-site possible. However, this method has high number of false positives (Huy et al., 2018). It is also difficult to perform visual inspection on postmenopausal women due to receding of endocervical region. Moreover, visual inspection is subjective, therefore VIA provider needs to understand cervical anatomy and undergo proper training to correctly identify precancerous lesion of cervix.

For all the methods mentioned, Pap smear test is still the most common cervical screening method used around the world as it is very cost effective with acceptable accuracy (Karimi-Zarchi et al., 2013). The test is often paired with HPV DNA test and VIA/VILI to prevent overdiagnosis and unnecessary colposcopy due to its high specificity (Darus et al., 2011). Although there are different cervical cancer screening methods available, the uptake of test among the women is still very low especially in developing countries due to low screening coverage and reluctance of women to undergo cervical screening tests (Adamson et al., 2015). Reasons given by reluctant women are fear of pain during speculum insertion, shyness especially in countries with conservative cultures, fear of undesirable test outcome, poor health care accessibility in rural regions, inability to afford the cost, and lack of time (Sumarmi et al., 2021). This situation causes late intervention of cervical cancer, where majority of cervical cancer patients visiting the hospitals are diagnosed at advanced stage, often leading to poor recovery rate (Mesafint et al., 2018).

There are two main issues to solve to increase cervical screening uptake, which is to increase screening coverage via organized screening campaigns nationwide and to improve the willingness of women to undertake the screening test. Various devices have been invented to aid

Table 1. Comparison of Different Cervical Cancer Screening Methods

	Conventional Pap smear test	Liquid-based Pap smear test	HPV DNA test	VIA/VILI
Sensitivity (%)	62.5[a]	72.9[a]	89.9[a]	79.2/89.2[b]
Specificity (%)	96.6[a]	90.3[a]	89.9[a]	84.7[b]
Cost (MYR)	40[c]	80[c]	250[c]	13.52[d]
Cost (USD)	9.09	18.17	56.69	3.07
Results duration	Few days	Few days	Few days	Immediate
Personnel skills	Minimal skills for smear takers, high skills for cytologists.	Minimal skills for smear takers, high skills for cytologists.	Minimal skills for smear takers, high skills for cytologists.	High skills for observers.
Results reliability	Moderate as it tends to produce false negative.	More reliable than conventional method.	High reliability.	Low because it is highly subjective and dependent on training of observer.
Equipment required	Many	Many	Many	Minimal

†, Data are from (Koliopoulos et al., 2017); [a], (Darus et al., 2011); [b], (Horizon Scanning, 2019); [c], (Devine et al., 2021); [d], The cost conversion is based on 1 USD = 4.4 MYR.

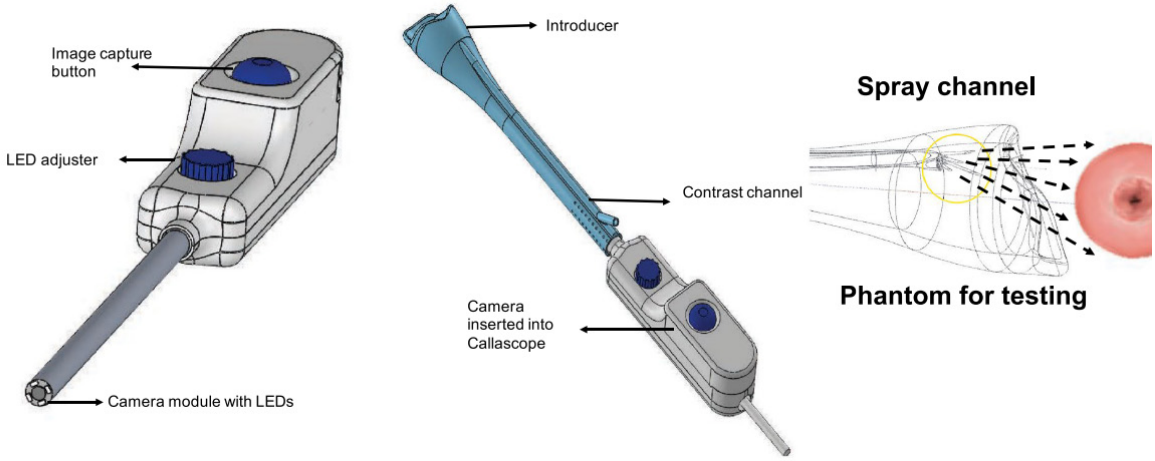

Figure 1. A Speculum-Free Imaging Device for VIA/VILI Screening Test (Asiedu et al., 2020). [*Note to editors: License is CC BY 4.0]

the clinicians in improving the efficiency of screening procedure and to increase the comfort of women during the procedure. This paper aims to review these devices which are either patented or available in the market for Pap smear test, VIA/VILI and self-sampling test.

Pap smear test devices

There have been various inventions that help improve the efficiency of Pap smear procedure in terms of improved visualization of cervix and automation of cervical cell collection. Some of the inventions can eliminate the usage of speculum, which may increase women's comfort during the Pap procedure. With these improvements, Pap smear procedure will be more efficient.

One of the ways in improving visualization of cervix is by using an illuminated speculum which eliminates the need for a wall-mounted light or an assistant holding a torchlight. An old, yet effective design for an illuminated speculum is created by attaching a chemiluminescence light source such as chemical light sticks onto the inner blade of speculum (Lonky, 1993). This idea is more advantageous in clear plastic speculum, whereby the light can be transmitted throughout the whole vaginal cavity. The attachment of light sticks is made possible by creating insertion tab on inner speculum blade, which also means the standard speculum needs to be redesigned. The benefits of such speculum are its cost effectiveness, design simplicity and it does not pose much disposal issues to the environment which makes it suitable for low-resource countries. Besides, the inventors reported that this device successfully reduced the false negative rate by 10 % due to higher accuracy in sampling the cervix, while there was no significant difference in false positive rate in their study on 600 samples. However, users will need to activate the light sticks and insert it into the speculum prior to usage.

Speculums utilizing light-emitting diode (LED) are emerging due to the low heat produced and the low power consumption. One of the most common designs is the placement of LED unit at the handle of the speculum. In this design, light travels from the lower dilator blade throughout the cavity of vagina. In the market, LED speculums are disposed after single-use, which produces high cost and wastage issues although it is very convenient because it is ready to use. Illuminated speculums are usually used for performing procedures such as artificial insemination, cervical biopsy, endometrial biopsy and so on, where the duration of activity is longer which makes the cost of illuminated speculum more worthwhile. As for Pap smear test, it is usually a quick examination which takes within three minutes to complete. Hence, it is wasteful if disposable illuminated speculums are used in large scale campaigns. Therefore, a patent discloses a design whereby the LED and battery unit acting as a handle, is detachable from the speculum (Bonenfant et

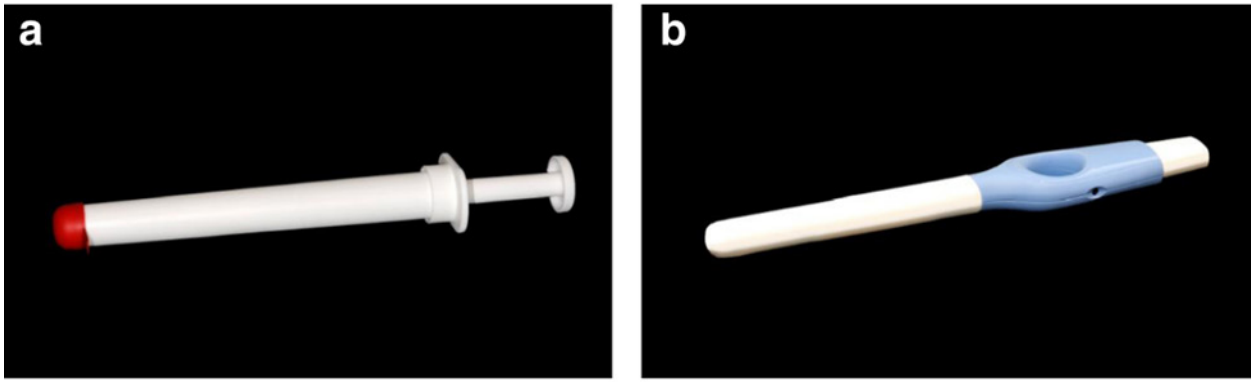

Figure 2. (a) First version of Delphi screener. (b) Second version of Delphi screener (Verhoef et al., 2013). [*Note to editors: License is CC BY 2.0]

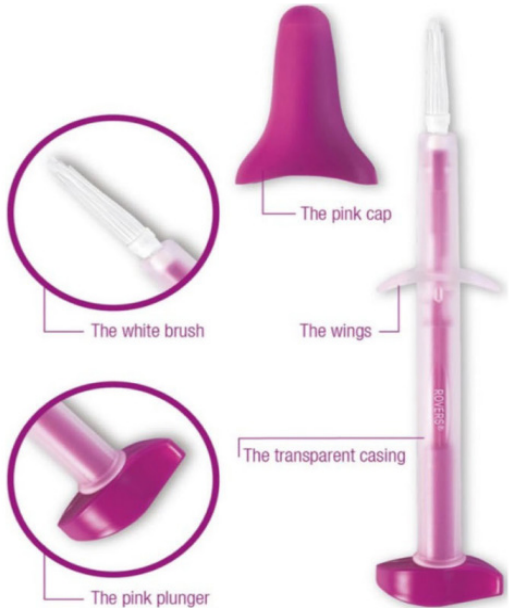

Figure 3. Rovers® Self-Sampling Device, Commercially Known as Evalyn brush (Manguro et al., 2019). [*Note to editors: License is CC BY 4.0]

al., 2016). The LED and battery unit can be recharged by attaching it to a charger dock which ultimately reduces battery wastage and long-term cost. This design is suitable for high-resource countries where the budget is sufficient in manufacturing this technology. There is also a simple design where a detachable small LED tube is fitted onto an aperture created on upper dilator blade at the observation window of disposable speculum which allows the portable LED tube to be reused many times (Paul, 2012). The disadvantage of this design is the placement of LED is inside the observer window, which may cause glaring and may reduce the effectiveness of the examination.

Besides illuminated speculum, there are devices that opt out speculums and visualize the vaginal cavity using thin vaginal inserters that works like an endoscope to improve women's comfort, but with additional function to allow the sampling of cervical cells. One such device is a cylindrical hollow cover acting as a vagina expander, which allows a separate camera and LED wrapped in plastic sheet to be inserted into the cover to obtain live recording of cervical examination findings (Jawaid and Alexis, 2015) . The top of the cover also contains a hole to allow various sampling tools to be pushed through to collect cervical cells. This device lacks integration between cover, visualization device and the sampling tools as each part is separately operated. Besides, the entire cover is a uniform cylinder, without any curvature at the insertion end which may cause pain and discomfort for women during insertion. Other speculum-free devices have better ergonomics, where they are shaped like a gun for improved handling (Jay and Clifford, 2010; Sefi, 2020) These two devices are similar where they utilize inflatable vaginal inserter with a hollow longitudinal tube in the middle to allow insertion of sampling tools to collect cervical cells. The inserter is disposable and can be attached or detached from the reusable handle. The difference is that the former uses fibre optic lens that allows direct cervix visualization which is suitable for low-resource settings whereas the latter uses a video recorder that requires extra computer resources for indirect cervix visualization.

There had been attempts in improving the efficiency by automating the cell collection step in cervix. One such design is an automatic electrical cervical sampler that works like an electric drill (Huang, 2020). Clinicians will first secure a sampling tool into the rotary sleeve of the electric sampler. Once the sampling tool is positioned at cervical orifice, a push of a button will cause the sampling tool to rotate twenty times around cervix automatically. Besides ease of use, the electric sampler is reusable and has good ergonomics such that it is shaped like a gun for good grip. This device was used to sample large population of women efficiently while identifying HPV-positive women. However, the inventors found a low positive rate of 3.7 % out of 14.2 % from high-risk population using liquid-based cytology. The high missed rate could be due to the low sensitivity of Pap smear test itself, and thus it was recommended to pair the test with HPV DNA test or VIA/VILI. The device is recommended for countries with high prevalence rates for cervical cancer such as China and India so that large populations can be sampled efficiently.

Next, a syringe device using fine needle aspiration concept was invented to screen for cervical cancer, where it utilizes a cannula with tiny holes perforated at the tip to aspirate cervical cells into the tube when the plunger is pulled externally, then released onto the glass slide (Cagnes, 2015). The small cannula can be inserted deep into endocervix without the risk of injuring endocervix. It is beneficial in situations where endocervix recedes and cannot be sampled using cytobrush. However, as yet there are no studies which evaluated the utility of this concept for routine cervical cancer screening, but merely for diagnosis of cervical cancer. A study performed on women with cervical cancer found that fine needle aspiration method has a sensitivity and specificity of 71 % and 86 %, whereas another study found that aspirated samples were all satisfactory and accurately diagnosed cervical cancer in small population of patients (Cendrowski et al., 2003; Alele et al., 2020). This cytology method is especially suitable for low-resource countries with high incidence rate where histology method for diagnosis is not amenable due to the lack of qualified histologists versus the low skill requirement for this simple low-cost device. Nonetheless, more field studies are needed to assess this device's practicality for mass screening.

VIA/VILI devices

VIA/VILI is very subjective and dependent on the skills of observer. A cotton ball will be immersed in acetic acid or iodine, which will be used to dye cervical region using forceps. The results will not be accurate if the observer miss the best observation period during the dyeing procedure. If the cervical region is not dyed sufficiently, some region with abnormal cells can be missed. Besides, the results cannot be saved which means it cannot be validated by other clinicians. Therefore, there are devices invented to improve VIA/VILI technique to

reduce human error mentioned.

To improve the reliability and validity of VIA/VILI results, the entire cervix dyeing procedure needs to be recorded to be reviewed by clinicians. There is a small circular portable device known as digital electronic colposcope that can be attached to the observation window of a standard speculum (Huang, 2020). The colposcope contains light source and video recorder, which will automatically record the illuminated images of cervical changes throughout the whole process of VIA/VILI and send the video to a cloud database that can be reviewed by clinicians again, improving the results reliability and validity. When utilized on a large-scale state campaign, this device successfully found 40.5 % of women with different gynaecological diseases, and 4.5 % of the population were found to have precancer or cervical cancer. Combining this device with the electronic sampler for HPV DNA and Pap smear test had successfully identified 81.47 % of women with negative results. This device is suitable for countries with high technological resources to implement the entire database system and large medical team to validate the results.

In terms of procedure simplification, there is a sponge stick stamping device that can dye the cervical and surrounding vaginal region in simple steps (He et al., 2016). This device is a rod handle that is attached to a disposable cervical cup which consist of donut-shaped sponge mimicking cervical orifice. The inside of the rod is used to store the dye liquid bag. When the circular cervical cup is pressed against the cervical region, the needle in the rod handle will rupture the bag and inject the liquid to the absorbent sponge in cervical cup, dyeing the cervical and vaginal region uniformly which may effectively reduce missed diagnostic rate compared to manually staining with a cotton ball. This rapid stamping device greatly simplifies and saves time for dyeing process which allows ample time for observation of cervical changes. This device is recommended for low-resource countries with high cervical incidence rate that practice VIA/VILI due to the simplicity of the device and low skill requirement on clinicians compared to conventional VIA/VILI.

Additionally, there exists automatic dye sprayer device equipped with light source and camera, where the cervix can be stained by pressing a button, then observed directly (Yi and Zhang, 2019). This automatic sprayer consists of a long flexible sleeve that is thin enough to be inserted into endocervical canal, allowing dye solutions to be sprayed inside the endocervical canal and observed via captured photos, which is usually difficult to do so. Hence, this device is beneficial especially in situations where the endocervix had receded and cannot be observed via naked eye. Another version of automatic dye sprayer is also available, where it eliminates the usage of speculum via a detachable introducer that protects the light source and camera while having spray channel to store and deliver dye solutions as shown in Figure 1 (Asiedu et al., 2020). This device has successfully visualized 83 % of the overall test patients' cervix while significantly reduced the pain experience by women during the procedure compared to speculum usage. However, the camera module and LED tip needs to undergo 8 minutes of hydrogen peroxide disinfection after every patient, which is very time-consuming and not practical for large scale-campaigns and low-resource settings. Hence, both these devices are more suitable for high-resource countries due to the additional electronic resources requirement such as a computer for cervix visualization.

Self-sampling devices

Due to embarrassment and discomfort of getting screened by a clinician, many inventors had investigated self-sampling devices. Self-sampling devices allow patients to scrape cervical samples by themselves. The samples will then be collected and sent to the laboratory to analyse the results. Many studies have shown that women are more comfortable and willing to perform self-sampling than to have clinicians sampling their cervix (Othman and Zaki, 2014). There are several types of self-sampler known as Dacron swab, flocked swab, tampon self-sampler, vaginal lavage, and brush self-sampler. HPV DNA test is performed for self-samples most of the time as the self-samples consist mainly of vaginal cells and some shed cervical cells (Schmeink et al., 2011).

The Dacron swab is a long stick with winded fibres wrapped around the tip. It performs poorly as it tends to trap cervical cells and unable to release the cells onto glass slide (Hughes et al., 1993). To improve on Dacron swab, flocked swabs are designed where nylon strands are flocked onto the swab tip using electrostatic force, which allows much greater absorption and release of cells by capillary action. A self-sampling study has proven that flocked swabs have significantly higher cervical cell efficacy collection and HPV detection rate than Dacron swab (Viviano et al., 2018). Another study where cervical cells are collected by clinicians has also shown that HPV detection rate is higher for flocked swabs, although the cervical cell efficacy is similar (Krech et al., 2009). Hence, the design of flocked swabs is more suitable for self-sampling due to better results although the price is higher than traditional Dacron swab. The swabs can be stored as dry samples in a plastic bag or in liquid preservative samples, where dry samples are preferred due to ease of transportation especially in rural regions. Besides, dry swab does not compromise sample integrity and the sensitivity for CIN (Cervical intra-epithelial neoplasia) 1 and above are similar between two transportation methods (Eperon et al., 2013).

To perform self-sampling, women must carefully insert the swab into their vagina while avoiding contact with external genitalia. Upon feeling a resistance, women will stop pushing and start rotating the swab for five times before removal from vagina. The design for swab lacks user-friendliness because women do not know how deep to insert the swabs to reach the cervix, which may also create risks of self-injury such as injury to the vaginal walls or cervix. Hence, FLOQSwabs® developed by Copan Diagnostics have red mark guide or a disc-shaped stopper guide on the shaft to prevent over insertion of swab into the vagina. Besides, these soft flocked swabs are shaped to fit and have full contact with endocervical canal and ectocervix for a complete cervical sampling. The sensitivity and specificity of high-risk HPV using

FLOQSwabs® for dry samples are 93.8 % and 87.5 %, whereas for wet samples are 96.3 % and 97.5 % (Kwan et al., 2016). This study proved that flocked swabs can be a great alternative for HPV DNA self-test.

Another self-sampling tool is tampon, which is a very low-cost self-sampling method. Usually, tampons with light absorbance are used, where women will insert the tampon deep inside vagina (Adamson et al., 2015). Upon removal, the tampon will be preserved in liquid fixative to prevent the collected samples from drying out before mailing the tampon to the laboratory. One study collecting self-samples using tampons from women infected with HIV in South Africa found that the HPV DNA results from tampons are in good agreement with clinician performed cytology test results, where the sensitivity and specificity are 77.4 % and 77.8 % (Adamson et al., 2015). Another study in South Africa which studies normal women population found that tampon self-sampling HPV DNA results have high negative predictive value, where it accurately predicts negative HPV for normal cytology results, and has comparable sensitivity as cytology (Mnisi et al., 2013). However, another self-sampling study in Bolivia that compared between cotton swab and tampon found that cotton swab has a higher HPV DNA detection rate than tampons (Surriabre et al., 2017). For the first two studies, tampons were inserted inside the vagina for one to two hours whereas for the last study, the tampons were inserted for 30 seconds only which may not be sufficient in collecting the cell samples.

Tampons are a great alternative for self-sampling as it is widely available in the market. However, if women in a certain population are not familiar with tampon usage, they may not know how to insert it properly which may affect the sensitivity of test results. Increasing the duration of tampon insertion may also decrease the acceptability of women towards self-sampling due to decreased comfort. Besides, tampons are found to mainly contain squamous epithelial cells with little cervical cells as it is mainly in contact with vaginal walls (Schmeink et al., 2011). To allow sampling close to cervical region, there is an invention where the tampon is encased inside a hollow cardboard cylinder with a handle that acts as a guide (Arthur, 2002). After insertion of the cardboard inside the vagina, women will press the handle to extend the tampon distally towards the cervical region, then rotate the tampon around the vagina and cervix region with the handle. Subsequently, the tampon is retracted into the casing and immersed inside a container with liquid preservative. This invention is inexpensive, easy to manufacture and use which is suitable for mass testing especially in low-resource countries with high cervical cancer incidence. Nevertheless, the usage of tampons for self-collection was only applied for HPV DNA molecular assays, and in none of these studies were the collected cells subjected to cytology tests for observing cellular changes or pre-cancer lesions. It is worth stressing the HPV positivity does not equate to presence of pre-cancerous lesions or of cancer. A subsequent cervical cytology smear has to be conducted to detect any cell transformation using routine gynaecologist administered sampling to rule out or confirm any cancerous changes. Hence, the utility of such tampon devices needs more consideration.

Another self-sampling tool used widely in Japan, and later tested in Thailand and Malaysia, is the Kato (or Katou) self-sampling tool, which is a self-inserter with sponge tip. Sancharisuriya et al found that a larger proportion of women with higher level of education believed the screening procedures undertaken by a doctor to be more accurate in achieving a valid result than the Kato device, whereas number of female villagers who favoured the Kato device over the medical doctor was half-half (Sanchaisuriya et al., 2004). Latiff and coworkers compared the efficacy of the Kato self-sampling over gynaecologist sampling and found 100% agreement between self-sampling and gynaecologist sampling for measuring specimen adequacy and cytology interpretation of the cell abnormality (Latiff et al., 2015). Nonetheless, they also found that for endocervical cells/transformation zone (EC/TZ) cells, 68% of samples from Kato device were absent of EC/TZ but present in gynaecologist sampling, indicating a potential weakness of the device.

Another low-cost self-testing method is vaginal lavage, where saline solution is injected into the vagina to collect vaginal and cervical cells. The saline solution will be removed almost immediately after rinsing the cervical region. The advantage of this method is that it uses materials and apparatus that are easily available in a health facility which is a urethra probe attached to a syringe filled with saline solution. Women will self-insert the probe deep into vagina until a resistance is felt, inject the saline solution, then recollect the saline solution filled with vaginal and cervical cells. The limitation of this method is the leakage of fluid out of vagina, which results in partial loss in sample and discomfort of women. Besides, a study in Brazil found that self-collected lavage sensitivity for CIN 2+ cytology and HPV DNA results are only 33.3 % and 50 %, which is much lower than cytology samples obtained by clinicians (Kuil et al., 2017). A similar results for CIN 2+ sensitivity was reported at 42 %, but with higher sensitivity for HPV DNA tests at 81 % (Nobbenhuis et al., 2002)

To solve the issues mentioned, Rovers® Medical Devices came up with a vaginal lavage device known as Delphi screener as shown in Figure 2. Both devices are pre-filled with saline solution at 5 ml and 3 ml to save sampling time while reducing leakage. After insertion in vagina, women will press the button plunger, compressing the spring while injecting the saline solution into the cervical region. After three seconds, women will release the button plunger, causing the spring to recoil while aspirating the saline solution back into the device. It also can be observed that the second version of Delphi screener has improved ergonomics, where the grip position is more comfortable.

Although the first and second versions of Delphi screeners store different volumes of saline solution, a study found that both devices gave similar concentration of DNA and high risk HPV positivity rate without significant differences (Verhoef et al., 2013). When compared to highly reliable brush self-sampler such as Evalyn brush, a study found that the second version of Delphi screener performed equally good, where the high-risk

HPV genotypes, CIN 2 and 3 detection rates are similar (Bosgraaf et al., 2015). These devices have a high level of acceptability among women, with most of the women citing high ease of use and comfort when taking the sample (Karjalainen et al., 2016). Hence, it can be concluded that lavage is an accurate and reliable technique for self-sampling provided that a good ergonomic device such as Delphi screener is used, where the liquid is injected and collected efficiently without spilling. However, a consideration is that the device would likely collect mostly shed cells as it does not scrape the cervix directly, hence its utility is more towards HPV DNA molecular testing rather than cytology.

Lastly, brush self-samplers have bristles at the end of the shaft to collect cervical cells. The most popular brush self-sampler is Evalyn® brush as shown in Figure 3, where the soft flexible bristles are made from low-density polyethylene (LDPE). Evalyn brush is more expensive than other self-sampling tools mentioned. Therefore, another cheaper option is Viba-brush®, where the shaft holds the same sampling head bristles as Evalyn® brush, but without the ergonomic vaginal inserter and stopper guide. Many studies have found that brush-self samplers have similar performance compared to clinician collected samples. In Netherlands, studies comparing between self-collected cervical samples using Viba-brush and clinician collected samples found that the sensitivity for CIN 2+, specificity and high-risk HPV genotype concordance are in close agreement (Dijkstra et al., 2012; Gök et al., 2012). Similar results were obtained using Evalyn® brush when compared against clinician collected samples (Polman et al., 2019). Besides, dry Evalyn brush sample is as reliable as clinician samples stored in liquid-preservative (Van Baars et al., 2012).

Evalyn® brush works by self-inserting the device into the vagina until the wings acting as a stopper guide touches the labia. Then, the plunger will be pushed to extend the brush head and rotated five times, with each rotation signalled by a 'click' sound. After the sample collection, the plunger is pulled back to retract the brush into the cover. The benefit of this device is the stopper guide, where it prevents women from over-inserting the device into the vagina for safety purposes. Also, this device is highly accepted by women due to ease of use and comfort (Van Baars et al., 2012). Another brush self-sampling device that works similarly to Evalyn® brush can automatically extend and rotate the sampling brush inside vagina when the plunger is pushed, then retract into the inserter cover when the plunger is released using spring inside the barrel and spiral thread design (Aghdam, 2018). This newer device is more time saving and easier to use compared to Evalyn® brush.

Besides, there exists another sampling tool that has similar automatic rotation mechanism. However, it is made from two separate parts, a sampling tool connected to a plunger syringe via a flexible tube (Omar, 2019). The benefit of this device is the tip of the sampling tool is covered by a curved rounded cap which allows comfortable insertion into the vagina, and the cap will open to expose the extending sampling brush when force is transmitted from the syringe plunger via the flexible tube. Besides maintaining sterility, such design ensures that the sampling brush is not exposed to vulva during insertion. The limitation of this device is its bulkiness as it is made from two components which limits its portability compared to the other devices.

Although these brush self-sampling devices are very effective in capturing abnormalities and have high acceptance among women especially the non-attendees for routine screening, the costs are very high which may be the reason why the studies are mostly conducted in countries with strong economic backgrounds such as countries in Europe. Hence, brush-self sampling devices are recommended for high-resource countries with low cervical cancer incidence rate to perform routine screening. Many developing countries will not be able to afford these brush self-samplers and will use simpler and cheaper devices such as tampons, Dacron swabs, and lavage self-sampler.

In conclusion, This paper had reviewed various devices catered for cervical cancer screening in terms of Pap smear test, VIA/VILI and HPV DNA self-sampling test. Some devices for Pap smear test and VIA/VILI solved women's discomfort by eliminating the speculum while maintaining visualization of cervix, whereas others increased the efficiency of screening methods by simplifying the procedure. With a variety of devices available ranging from low to high technological requirements, clinicians can choose suitable devices based on their budget, requirement, and settings. Besides, self-sampling devices encourage the participation of women in routine cancer screening programme as they collect vaginal and cervical samples with privacy easily. However, the devices are designed based on average women's anatomy, which may be difficult for obese women to self-insert the device into their vagina (Othman and Zaki, 2014). Hence, different sizes of self-sampling device need to be designed to cater for women of all sizes. With many advanced and portable devices available, it is hoped that more cervical screening campaigns will be organized especially in rural regions with low resources, and more women will be willing to take up cervical screening tests routinely to reduce cervical cancer incidence.

Author Contribution Statement

Hui Juen Hon is the main author who is responsible for researching and writing the paper. Pei Pei Chong is the corresponding author who conceptualized the research topic and edited the paper. Hui Leng Choo is the co-author who is responsible for researching and editing the paper. Pwint Phyu Khine is the co-author who is responsible in providing the gynecologist's expert views and editing the paper.

Acknowledgements

General

The authors would like to acknowledge Malaysia's Ministry of Higher Education for the Prototype Development Research Grant, with the project code of PRGS/2/2019/SKK05/TAYLOR/01/1 that fully supports

this project. The authors would also like to acknowledge Taylor's University through its TAYLOR'S RESEARCH SCHOLARSHIP Programme.

Funding Statement

The project was funded under Malaysia's Ministry of Higher Education Prototype Development Research Grant, with the project code of PRGS/2/2019/SKK05/TAYLOR/01/1. This work was supported by Taylor's University through its TAYLOR'S RESEARCH SCHOLARSHIP Programme.

Ethical Declaration

There is no ethical declaration made as no humans or animals are involved in this review study.

Study Registration

The study is not registered in any registering dataset.

Conflict of Interest

The authors declare no conflict of interest.

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