

RESEARCH ARTICLE

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Experience of Cervical Cytology and High-Risk HPV Testing (Physician vs Self-Collected) for Primary Cervical Cancer Screening in an Urban Hospital of Thailand

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Abstract

Objective: To explore the experience of conventional Pap smear (CPS), physician-collected HPV (pHPV) and self-collected HPV test (sHPV) for cervical cancer (CC) screening in the general population in the north-eastern region of Thailand. **Methods:** A retrospective study was conducted among women who visited the gynecology and colposcopy clinic in Kuchinarai Crown Prince Hospital for CC screening between January 2020 and December 2023. Participants received counselling before choosing between CPS, pHPV, and sHPV testing. Data reviewed from medical records included age, parity, CC screening results, colposcopy results, and treatment. **Results:** A total of 5,984 women were enrolled in the study. There were 1,727, 2,962 and 1,295 cases in the CPS, pHPV, and sHPV, respectively. The average age of participants was 40.6, 49.5 and 47.6 years old in the CPS, pHPV, and sHPV, respectively. Percentage of multiparous participants were 86.3, 94.4 and 93.8 in CPS, pHPV and sHPV, respectively. Positive test results from the CPS, pHPV, and sHPV were 1.4, 5.7, and 6.8 percent, respectively with statistical significance. Return to colposcopy of CPS (62.5%) was highest and followed by pHPV (35.3%) and sHPV (18.2%) groups with statistical significance. Detection rate of CIN2+/CIN 3+ were 0.1/0.1, 0.5/0.4 and 0.2/0.2 percent from CPS, sHPV, and sHPV groups, respectively with statistical significance. **Conclusion:** Primary HPV and CPS testing had comparable reliability and acceptability for CC screening among Thai women. High missing rate for reflexed cytology or colposcopy of sHPV was a major issue.

Keywords: Pap smear- HPV- self-collected- physician-collected- cervical cancer

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Introduction

Cervical cancer (CC) is the fourth most common cancer among women globally. In 2022, there was an estimate of 662,301 new cases and 348,874 deaths. Almost 90 percent of the cases and deaths occurred in low-and middle-income countries [1]. In Thailand, CC is the second most common cancer among women aged between 15 and 44 years old [2]. Currently, the incidence rate of CC is declining since it is one of the most preventable and treatable types of cancer [1]. The human papillomavirus (HPV) is the most common pathogen responsible for precancerous and cancerous cervical lesions. Over 100 HPV types have been identified, but only up to 15 anogenital types may be referred to as oncogenic with HPV 16 and 18 being known as the high-risk types (hrHPV) most associated with CC [3]. Therefore, screening is key to early detection and diagnosis of the disease.

Nowadays, CC screening tools consist of cervical

cytology, HPV testing, and combined testing methods. Over 90 years ago, conventional Pap smear (CPS), a cervical cytology-based screening tool, was first introduced and became widely used for screening and early detection of precancerous cervical lesions. Later in the 1990s, liquid-based cytology testing was developed. Rather than smearing the sample onto a slide as in CPS, the liquid-based method involves transferring the sample into a liquid medium. This filter out blood and debris and increases cellular yield, which was then automatical processed. In 2003, a combination of hrHPV testing with cytology testing was approved, increasing sensitivity to 100 percent and allowing for longer intervals between screenings [4].

In 2020, the American Society of Colposcopy and Cervical Pathology (ASCCP) issued a risk-based management guideline and recommendations for primary HPV screening [5]. In 2021, the World Health Organization (WHO) strongly recommended the use of

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HPV DNA detection as the primary CC screening test rather than CPS. Due to its high quality, good detection rate for high-grade cervical intraepithelial neoplasia (CIN) 2 and CIN3 lesions, and longer intervals between screenings, HPV-based testing has become the screening tool of choice [6].

The WHO Global Strategy aims to eliminate CC as a public health problem. In 2018, the goal was to reduce incidence of CC to below 4 per 100,000 women-years by 2030. The target follows the 90-70-90 strategy: 90% of girls vaccinated with the HPV vaccine by age 15, 70 percent of women screened with a high-quality test by ages 35 and 45, and 90 percent of women with cervical disease receiving treatment [6]. To achieve such goals, increasing access to screening tools and participation of at-risk women is crucial. Thus, self-collection (sHPV) of either urine or cervical samples for hrHPV testing has become an option. Both types of specimens showed high sensitivity and accuracy for detection of CIN2+ lesions [7]. Previous studies had also shown high concordance between sHPV tests and physician-collected HPV tests (pHPV), with higher participation and acceptability in sHPV testing among Thai women [8, 9]. However, these sHPV tests were done in scheduled gynecologic examination or colposcopy clinic. Therefore, the sample was not representative of the real population.

In Thailand, primary HPV testing was recommended by The Royal Thai College of Obstetricians and Gynaecologists (RTCOCG) in 2021 and by the National health security office (NHSO) of Thailand [10]. The Ministry of Public Health of Thailand (MoPH) offered a CC screening program with primary HPV testing and cytology for all Thai women aged between 30 and 60 years at 5-year intervals.

The aim of this study is to explore the experience of CPS, pHPV and sHPV for CC screening in the general population in the north-eastern region of Thailand.

Materials and Methods

This retrospective study was performed at a gynaecology and colposcopy clinic in Kuchinarai Crown Prince Hospital, Kalasin, Thailand. This study was approved by the Kalasin Provincial Public Health Office Research Ethics Committee in 2024. Women who visited the gynecology clinic between January 2020 and December 2023 for CC screening were recruited. Participants received counselling from healthcare personnel before choosing between CPS, pHPV, and sHPV testing. Those with abnormal results was counselled to undergo colposcopic-directed biopsy. Women with prior history or prior treatment for CIN or CC and those with incomplete medical data were excluded from this study. The pHPV screening test was performed by using the Cobas 4800 HPV test (Roche Diagnostic GmbH, Mannheim, Germany), which is a qualitative test for detection of HPV DNA. While the sHPV group received HPV self-sampling kits from a government healthcare facility and were instructed by gynecologic nurses. The specimens were sent to Kalasin Hospital to run the HPV automated detection test using the STARlet-AIOS

(Seegene, South Korea).

A positive test result in the CPS group is defined as abnormal cytology. In the pHPV and sHPV groups, positive test results are defined as detection of hrHPV. Women with any of the following indications are counselled and referred for colposcopy: abnormal cytology results, positive for HPV 16/18 from pHPV or sHPV testing, and hrHPV non 16/18 with abnormal cytology results. Abnormal cytology results are defined atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cell cannot exclude HSIL (ASC-H), atypical glandular cells (AGC), or high-grade squamous intraepithelial lesion (HSIL).

Data reviewed from medical records included age, parity, CC screening results, colposcopy results, and treatment. Statistical analysis was done by SPSS version 29 (SPSS Inc, Chicago, IL, USA). Data were analysed using descriptive statistics. Median, mean, and standard deviation (SD) were used for continuous data. Chi-squared test or Fisher exact test were used for categorical data. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 5,984 sexually active women were enrolled in the study. The participants were divided into three groups. There were 1,727, 2,962, and 1,295 in the CPS, pHPV, and sHPV groups, respectively as shown in Figure 1. The baseline characteristics of participants enrolled in the study were presented in Table 1. The average age of participants was 40.6, 49.5 and 47.6 years old in the CPS, pHPV, and sHPV groups, respectively. Participants in the CPS group were the youngest among the three, with participants from the pHPV group being statistically older than the sHPV group.

Of the 1,727 women in the CPS group, 1,491 women (86.3%) were multiparous, compared to approximately 94 percent of the women in both the pHPV (2,795/2,962) and sHPV (1,215/1,295). Multiparity was significantly lower in the CPS group than in the other two groups ($p < 0.001$), without significant difference observed between the pHPV and sHPV groups. Positive test results from the CPS, pHPV, and sHPV groups were 1.4, 5.7, and 6.8 percent, respectively. Positive results from the pHPV and sHPV were comparable and significantly higher than positive CPS test results.

Among those with indication for colposcopy, more participants from the CPS groups returned for colposcopy (62.5%) than the HPV groups. The missing rate of CPS, pHPV and sHPV were 33.3, 22.9 and 65.9 percent, respectively. A statistically higher number of women from the pHPV group (35.3%) came back for colposcopy than from the sHPV group (18.2%). Detection rate of CIN2+ were 0.1, 0.5, and 0.2 percent and CIN3+ 0.1, 0.4, 0.2 percent from the CPS, sHPV, and pHPV groups, respectively. The detection rate of CIN2+ and CIN3+ lesions were not statistically different across all groups.

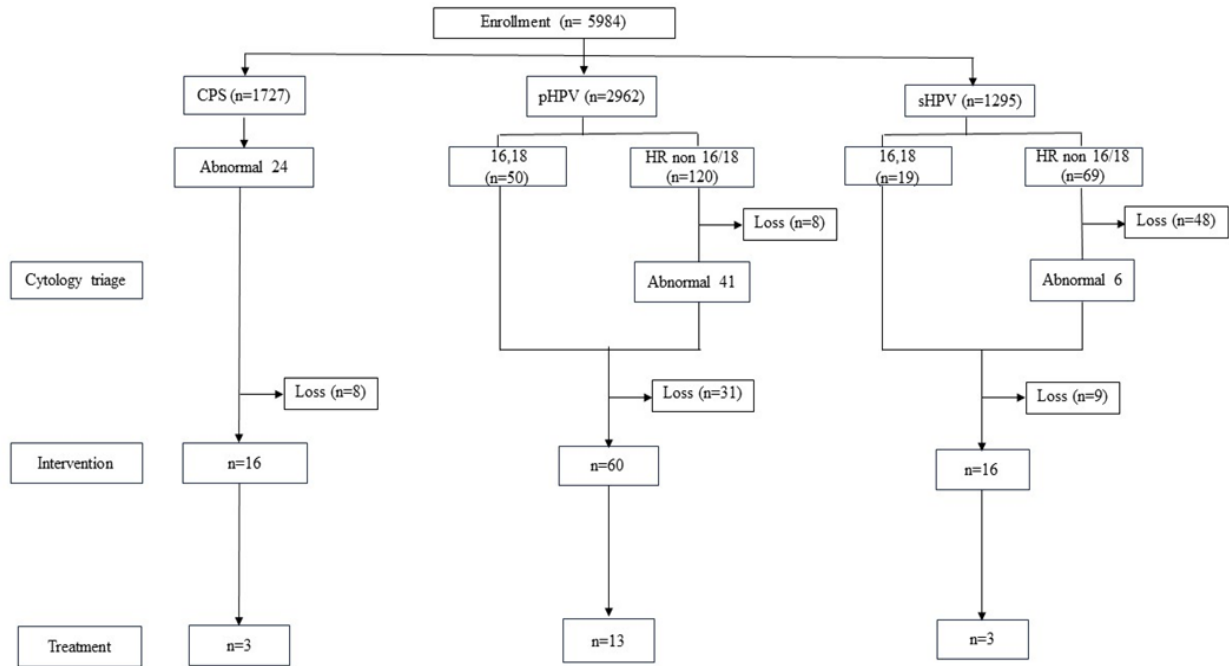


Figure 1. CONSORT Flowchart for Cervical Cancer Screening in the Study. CPS, conventional cervical cytology; pHPV, physician collected human papillomavirus; sHPV, self-sampling human papillomavirus; HPV, human papillomavirus; HR, high risk

Table 1. Baseline Characteristics of Participants

	CPS	pHPV	sHPV	P1	P2	P3
Case (n)	1727	2962	1295			
Age (years)*	40.62±14.0	49.46±6.9	47.62±7.5	<0.001	<0.001	<0.001
Multiparity**	1491 (86.3)	2795 (94.4)	1215 (93.8)	<0.001	<0.001	0.488
Positive test**	24 (1.4)	170 (5.7)	88 (6.8)	<0.001	<0.001	0.184
CDB**	16 (62.5)	60 (35.3)	16 (18.2)	<0.001	<0.001	<0.001
CIN2+	2 (0.1)	14 (0.5)	3 (0.2)	0.987	0.328	0.162
CIN3+	2 (0.1)	13 (0.4)	3 (0.2)	0.913	0.328	0.205
Missing (%)**	8 (33.3)	39 (22.9)	58 (65.9)	0.583	<0.004	<0.001

*mean ± standard deviation (SD); **n(%); CPS, conventional Pap smear; HPV, human papillomavirus; pHPV, physician collected human papillomavirus; sHPV, self-sampling human papilloma virus; CDB, colposcopic directed biopsy; CIN, Cervical intraepithelial neoplasia; P1, p-value of CPS with pHPV; P2, p-value of CPS with sHPV; P3, p-value of pHPV with sHPV

Discussion

In order to achieve the WHO Global Strategy, set in 2018, at least 70 percent of women should be screened for CC. However, factors such as inconvenience, fear, and embarrassment are still preventing Thai women from undergoing cervical cancer screening [8]. Primary

HPV testing was introduced as the screening tool of choice in 2020 in Thailand by MoPH and sHPV testing were introduced in 2022 to address the challenges. Both sHPV and pHPV tests had high reliability with higher participation and acceptability in sHPV testing among Thai women [8, 9].

In the present study, the average age of participants

Table 2. Comparison of Adherence to Triage among Women with HPV-Positive Self-Collection in Various Studies

	Year	Country	Age*	LOCT**	LOT**	CIN2+**
Rossi	2015	Italy	N/A	36	30	0.2
Francesca	2020	Nicaragua	40.8	45	46.8	N/A
Paolino	2020	Argentina	41.7	60	40	0.5
Olthof	2024	Netherland	N/A	7	4.3	N/A
Present	2024	Thailand	47.6	69	36	0.2

*mean; **%; CIN, cervical intraepithelial neoplasia; LOCT, loss of cytology triage; LOT, loss of treatment; N/A, not applicable

in the sHPV and pHPV were significantly older than those in the CPS group. In terms of multiparity, more participants in the sHPV (93%) and pHPV (94%) were multiparous compared to the CPS group (86%). This demonstrated that older and multiparous women were more accepting of primary HPV testing, which could be explained by being more experienced with gynecologic examination and could have received CPS testing done before, resulting in less fear and embarrassment than younger, nulliparous women. Older women in both HPV groups may also have more knowledge on the various methods of screening while younger participants in the CPS group may only know of Pap smear. Nevertheless, sample collection by a physician was still preferred than self-collection. Table 2 displayed the demographics of participants from other studies who were younger at 40 to 41 years old. This indicates higher acceptability and easier access to sHPV testing which could be explained by better knowledge and support from the healthcare sector compared to Thailand.

Positive test results in sHPV (6.8%) and pHPV (5.7%) were comparable with both being higher than in CPS group (1.4%) due to high sensitivity of HPV testing [3]. While the detection rate of CIN2+ and CIN3+ were similar across all three groups. The total missing rate, which included loss to follow up for either cytology testing or colposcopy, of the sHPV group was the highest (65.9%). This could be that CPS (33.3%) and pHPV (22.9%) participants were required to visit the clinic for test results and therefore were able to discuss further management plans with a gynaecologist, while sHPV participants did not receive the same amount of counselling and encouragement for follow-up appointments. This further highlights the importance of counselling and physician-patient relationship. Supposing that more participants were to come for follow-up appointments, HPV testing could have better detection rate for CIN2+ and CIN3+ lesions than CPS.

Similar missing rates of sHPV participants from different countries were also found in studies done by Francesca and Paolino in middle income countries including Argentina and Nicaragua [11, 12]. The missing rate was found to be 45%, and 60% in the cytology triage phase and 46%, and 40% during the colposcopy phase, respectively (Table 2). All of which were consistent with the missing rate of our study. A study done in a high-income country such as Italy had a missing rate of 36% in the cytology triage phase and 30% were lost to colposcopy treatment, which was similar to our study done in a middle-income country like Thailand [13]. This could be because self-collection sampling was just introduced in Italy at the time and therefore the screening rates were similar since sHPV testing was recently introduced in Thailand as well. However, a recent study done in 2024 in the Netherlands, which is a high-income country, had a loss rate of 7 and 4% in the cytology triage and colposcopy treatment phase, respectively [14]. This was significantly lower than studies done in low-middle income countries. It was likely due to better healthcare systems and access to information and knowledge on CC, leading to widespread awareness in preventing precancerous diseases.

Compared to other studies, the detection rates for CIN2+ and CIN3+ of our study were similar but this could be due to the high missing rate. This could be explained by the lack of knowledge and need for counselling by a healthcare provider in low-to-middle income countries. Difficult access to healthcare in certain regions, as well as travel and accommodation expenses, also play roles in the high missing rate and are obstacles in CC prevention.

Strengths of this study included a large sample size and the rural area setting that adequately represents the Thai population, allowing us to evaluate problems realistically. Limitations being a retrospective study with a high missing rate and thus cannot differentiate the detection rate of CIN2+ between CPS, pHPV, and sHPV groups. Further study on the reasons for loss rate could help tackle the problem and improve participation rates, reducing the incidence of CC in the future.

In conclusion, primary HPV testing and CPS testing have comparable reliability and acceptability for CC screening among Thai women. Despite HPV testing giving more positive results than CPS, both types of screening tests had similar CIN2+ and CIN3+ detection rates. A major issue in sHPV testing was the high missing rate for cytology triage and/or colposcopy. Once more participants return for follow up, the detection rate for CIN2+ and CIN3+ lesions could improve in the HPV groups.

Author Contribution Statement

AW and KS conceptualized and designed the study; AW collected the data, analysed, and interpreted the results; AW, ST and KP prepared the initial manuscripts. All authors reviewed the results and approved the final version of the manuscript.

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Availability of data

All data relevant to this study has been presented in the manuscript. More data requirement was controlled by the institution board according to request.

Conflict of interest

The authors declare that there is no conflict of interest.

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