DOI:10.31557/APJCP.2023.24.10.3429
Cervical Cancer Screening, Uterine Cervix, Histologically Proven

RESEARCH ARTICLE

Editorial Process: Submission:03/29/2023 Acceptance:10/22/2023

Factors Affecting Non-Histologically Proven Invasive Cancer of the Uterine Cervix that Had an Abnormal Pap Smear: Results of the CCS Program

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Abstract

Background: Cervical cancer (CC) ranks fourth among cancers diagnosed around the world, but early detection and treatment can reduce invasive cervical cancer and mortality. Screening programs (CCSP), such as the one covering Thailand's 75 provinces, use histology to confirm cases. The study determined the incidence rate (IR) and investigated the factors associated with non-histologically proven invasive cancer of the uterine cervix (non-HPICUC) with an abnormal pap smear from the CCSP at Mahasarakham Hospital, Thailand. **Methods:** The CCSP was used to analyse a retrospective cohort of 288 women between 30 and 60 years of age. All abnormal pap smears were followed up until April 30, 2022. We estimated the IR and assessed the relationship between various independent variables and non-HPICUC using the generalised linear model (GLM) for testing association data. We reported the adjusted RR and 95% confidence intervals (95%CI). **Results:** 260 non-HPICUC cases had abnormal CCSP pap smears for an overall IR of 90.0 (95% CI: 86.3 - 93.2). After adjusting the model for all variables, age at recruitment and pregnancy had a statistically significant association with non-HPICUC (p-value < 0.05). We found that the risk of non-HPICUC increased 1.02 times for every 20-year increment in age compared to below that age (adjusted RR=1.02, 95% CI: 1.01 - 1.04). Pregnancy at risk for non-HPICUC was 0.89 times compared to non-pregnancy (adjusted RR=0.89, 95% CI: 0.80 - 0.99). Pathological vaginal discharge (PVD) did not have a statistically significant association with non-HPICUC (p-value = 0.094); notwithstanding, women with PVD had 1.08 times the risk of non-HPICUC compared to women without PVD (adjusted RR=1.08, 95% CI: 0.97 - 1.20). **Conclusions:** Based on an abnormal pap smear from the CCS Program at Mahasarakham Hospital Thailand, age and pregnancy are associated with an increased risk of non-HPICUC. High-risk groups with abnormal pap smears should be targeted for CC campaigns.

Keywords: Cervical cancer screening- uterine cervix- histologically proven

Asian Pac J Cancer Prev, **24 (10)**, 3429-3436

Introduction

Cervical cancer (CC) is the fourth most commonly diagnosed cancer among women worldwide and remains a significant public health problem, especially in developing countries that lack resources. Additionally, infection with human papillomaviruses (HPV), commonly transmitted by sexual contact, can cause CC (World Health Organization, 2020). In 2020, there were 604,127 new cases and 341,831 deaths from CC worldwide. The incidence rate of CC (Age Standardized Rate, ASR) was 13.3 per 100,000 (Globocan, 2020). The International Agency for Research on Cancer (IARC) estimates that 7.6 million deaths occur annually from all types of cancer and approximately 13 million new cases of all types of cancer. By 2030, the cause of deaths from cancer will have increased to 13 million, with new cancer cases rising to 21.3 million. The IARC also reported increasing trends in CC (IARC, 2008). The World Health Organization (WHO) reported that the implementation of screening every five years was associated with an improvement in CC survival to ~70.0% and that mortality had been reduced by 55.0% (WHO, 2002). The WHO proposes that if 90.0% of women were screened annually, CC mortality rates could be reduced even further. The monograph on cancer incidence from Cancer in Thailand (Vol. VI-X) used data from a population-based cancer

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registry throughout the country between 2004 and 2006. The ASR for CC was 17.7 per 100,000, third after liver and bile duct and breast cancers (Khuhaprema et al., 2012). Between 2007 and 2009, CC had the second-highest incidence rate (ASR = 16.7 per 100,000) after breast cancer (Khuhaprema et al., 2013), and between 2010 and 2012, the second-highest incidence rate (ASR = 14.4 per 100,000) after breast cancer (Imsamran et al., 2015), and between 2013 and 2015, the third-highest incidence rate (ASR = 11.7 per 100,000) after breast, liver, and bile duct cancers (Imsamran et al., 2018). In the latest version, between 2016 and 2018, CC had the fifth highest incidence rate (ASR = 11.1 per 100,000) after breast, colorectal, liver and bile duct, and lung cancers. The respective number of new cases of CC between 1990 and 2018 was 5,593, 5,462, 6,268, 9,999, and 5,422 (Rojanamatin et al., 2021).

Based on the high incidence of CC cases, the National Cancer Control Program (NCCP) in Thailand established the Cervical Cancer Screening Program (CCSP) in the 75 provinces to screen women between 30 and 60 years of age using standard Pap smears. Women are recruited for free cervical cancer screening every 5 years at one of Thailand's 10,000 local Tambon Health Promoting Hospitals. The CCSP aims to screen not less than 80.0% of women between 30 and 60 years of age to reduce invasive cervical cancer and mortality. However, between 2015 and 2019, the cumulative CC screening rate was less than 80.0% of the high-risk group.

Currently, there are three main methods of cervical cancer screening available in Thailand, including (1) HPV testing, (2) cervical cytology, and (3) visual inspection with acetic acid (VIA) together with cryosurgery (Laowahutanont et al., 2018). The incidence of CC can be reduced after organised screening (OS) by (1) inviting the high-risk group to CC screening every 1 to 2 years, (2) having an appropriate frequency of cervical cancer screening, (3) and, most importantly, providing a referral to effective treatment after having an abnormal result or histologically-proven diagnosis (National Cancer Institute., 2018). According to the Regional Health Promotion Center 7 (covering Kalasin, Khon Kaen, Mahasarakham, and Roi Et provinces), the rate of cervical cancer screening by Pap smear in the last 5 years among women aged 30 to 60 years was 44.3% of all target groups, which is lower than the 80% target set by the Ministry of Public Health (Health Data Center, 2021). Data on cervical cancer screening at Mahasarakham Hospital, Thailand, showed that the CC screening rate was 28.1% (i.e., 33,584 high-risk women between 30 and 60 years of age divided by the target group of 119,788). Furthermore, the CCSP result revealed that pap smear testing as >+ASC-US (indicating abnormal CC) was 372, 300, 235, 112, and 119 cases annually between 2015 and 2019, respectively (Mahasarakham Hospital, 2021). If not confirmed in a timely manner, early cancer can become advanced late-stage cancer and be difficult to treat (National Cancer Institute, 2018).

There have been no large-scale studies on the non-confirmation of pathologic findings in CC screening abnormalities, so too little is known about them. However, the benefit of early detection and treatment has been a reduction in the incidence rate of invasive CC and mortality because an abnormal Pap smear from CCSP must be histologically-confirmed as invasive uterine cervix cancer. Information collected from the current study will strengthen the screening policy to help prevent and/or diagnose CC in the early stages. In addition, public information campaigns are needed to alert high-risk groups—those who have an abnormal test from CC screening results—to confirm whether they have a histologically-confirmed CC. The current study aimed to determine the incidence rate (IR) and factors affecting non-histologically confirmed invasive cancer of the uterine cervix (non-HPICUC). However, it had an abnormal pap smear from the CCSP, Mahasarakham Hospital, Thailand.

Materials and Methods

Study design

Using the CCSP dataset, a retrospective cohort analysis was conducted on women between 30 and 60. We thus recruited participants from the data set between 2015 and 2019. All participants with an abnormal pap smear were followed up until 30 April 2022.

Sample size calculation

The sample size for multiple analyses was estimated to be 288. This was adapted based on a method of estimating sample sizes in a prospective cohort study with variance inflation factor adjustment (Hsieh et al., 1998). According to previous findings, we assumed p0=0.361 and p1=0.564 (Sonkong K, 2021). We assumed a level of significance of $\alpha = 0.05$ ($Z\alpha/2=1.96$) and a power of the test of $\beta = 0.1$ for 80% power ($Z\beta=0.842$). After adjusting the variance inflation factor (VIF), the partial correlation coefficient = 0.4. The total sample size was 288, as multiple models.

Eligibility criteria and operational definitions

Participants were women (a) between 30 and 60 years of age who came for CCSP at Mahasarakham Hospital, Mahasarakham Province, under the National Health Security Office (NHSO) fiscal years 2015 to 2019; (b) who underwent Pap smear CC screening and had a cervical cytologic abnormality; and, (c) whose hometowns were in Muang district, Mahasarakham province, for at least 6 months during the study period between October 1, 2015, and September 30, 2019.

Data Collection

A trained research assistant conducted face-to-face interviews in the Muang subdistrict, Mahasarakham province. The responses were recorded in a standard questionnaire. It took 10 to 15 minutes for each interview. In addition, we collected data (including details on an abnormal Pap smear, biopsy, and colposcopy) from the CXS2012 program from the Outpatient Department (OPD) of the Department of Obstetrics and Gynecology and the Pathology Unit at Mahasarakham Hospital up to April 2022 (Figure 1).

Statistical methods

Descriptive statistics

Patient characteristics, patient knowledge of CC, and whether the CC was histologically-proven were summarised using descriptive statistics for continuous variables, means (standard deviations, SDs), medians (minimum and maximum), and frequency counts and percentages for categorical variables.

Inferential statistics

Incidence rate (IR) of histologically proven CC

We calculated the incidence rate (IR) and the 95% confidence interval for histologically-confirmed cases.

Crude analysis

A crude analysis determined the associations between various independent variables and non-HPIUC without controlling for confounding variables. The crude relative risk (crude RR) and its 95% confidence intervals (95%CI) were calculated by bivariate analysis. Generalised linear models (GLM), binomial family distribution, linking functions, and linear models (log) were used for the analyses (Hardin and Hilbe, 2012).

Multivariable analysis

Multivariable analysis was used to compute the adjusted relative risk (adjusted RR) and their 95% confidence intervals (95% CI) to investigate the various factors on non-HPICUC while controlling for the effects of confounding variables such as demographics variables (Kleinbaum et al., 2005).

Model fitting

Candidate variables for the multivariable analysis were selected according to two criteria: first, variables in the crude analysis with a p-value < 0.25, and second, variables—from a literature review associated with non-HPICUC. Backward stepwise elimination was used for the model-fitting strategy. Finally, Akaike's Information Criterion (AIC) was performed to assess the best model (Akaike, 1973).

All test statistics were two-sided; a p-value < 0.05 was considered significant. All analyses used Stata version 10.0 (Stata Corp., 2007).

Ethical considerations

The Human Research and Ethics Committee of Khon Kaen University (HE642300) and Mahasarakham Hospital (MSKH_REC 65-02-033) reviewed and approved this project.

Results

Descriptive epidemiology and baseline characteristics

The number of women with an abnormal pap smear who attended the CCSP at Mahasarakham Hospital between 2015 and 2019 was 288. The mean age was 48.1 years (SD=7.6 years), with a median of 49.0 years (min-max: 32 - 63 years). The most common marital status was married (n=230, 79.9%), while separated was the lowest (n=6, 2.1%). The most common level of education was elementary school (n=151, 52.4%), while the least common was a bachelor's degree or higher (n=39, 13.5%). The most common occupation was agriculture (n=134, 46.5%), while the least common was unemployed (n=11, 3.8%). The average family income was 12,332.6 baht (SD=17935.6 baht), with a median of 6,000 baht (Min = 600 baht: Max = 100,000 baht).

Reproductive characteristics

According to reproductive statistics, 263 of the 288 women with an abnormal Pap smear were pregnant (91.3%). The average number of abortions was 2 (n=5, 1.7%). The highest number of pregnancies was 5 (n=6, 2.1%). Most had two living children (n=148, 51.4%), while one had 7 children (n=1, 0.4%). The average age at the first pregnancy was 24.3 years. (SD=4.4 years), the median was 26.0 years (min-max: 16 - 37 years). Due to contraceptive use (n=236, 81.9%), the most commonly used contraceptive was tablets (n=191, 77.0%), followed by sterilisation (n=59, 23.8%) and injections (n=43, 17.3%).

Some had a family history of CC (n=5, 1.7%). After an abnormal Pap smear, pathology revealed pathological vaginal discharge (PVD) (n=34, 11.8%), postcoital bleeding (n=15; 5.2%), and postmenopausal bleeding (n=19, 6.6%). Annual health examinations are the most common reason for screening (n=204, 70.8%), followed by fear of CC (n=199, 69.1%), responding to a screening campaign (n=117, 40.6%), a doctor appointment (n=54, 18.8%), and having abnormal CC symptoms (n=38, 13.2%). The most common reason for non-HPICUC after an abnormal pap smear (n = 269) was fear of the doctor (embarrassment) (n = 157, 58.4 %), fear of pain (n = 137, 50.9), lack of time (n = 100, 37.2%), fear of cancer detection (n = 61, 22.7%), and lack of transport (n = 40, 14.9%) (Table 1).

Incidence of non-HPICUC

The incidence rate of non-HPICUC among women with abnormal pap smears, according to the CCSP at Mahasarakham Hospital, was 90.3 per 100 person-years (95% CI: 86.3 - 93.2). The highest incidence rate of those 50-54 years of age was 94.2 per 100 person-years (95% CI: 86.6 – 97.6), while the lowest incidence was for those 30-34 years of age at 66.7 per 100 person-years (95% CI: 37.2 – 87.1). The most common educational attainment was secondary at 95.5 per 100 person-years (95% CI: 70.4 – 99.5), while the lowest was for high school at 88.2 per 100 person-years (95% CI: 78.5 - 93.8). As for marital status, the most common incidence was married at 88.7 per 100 person-years (95% CI: 83.8 - 92.2), while the lowest was for separated at 83.3 per 100 person-years (95% CI: 18.6 - 99.1). Based on knowledge of CC, the highest incidence of non-PHICUC was a low level of 100.0 per 100 person-years (Table 2).

Factors affecting non-HPICUC that had an abnormal pap smear from CCSP, Mahasarakham Hospital (Multivariable analysis)

The results of the current study showed that age and pregnancy have a statistically significant association

Table 1. Characteristics of Women who have an Abnormal Pap Smear According to the CCSP at Mahasarakham Hospital (n = 288).

Characteristic	Number (n = 288)	Percentage (%)
1. Age at recruitment		
30-34	15	5.2
35-39	28	9.7
40-44	47	16.3
45-49	58	20.1
50-54	86	29.9
55-59	31	10.8
60+	23	8
Mean (standard deviation)	48.1 (7.6)	
Median (minimum: maximum)	49.0 (32:63)	
2. Marital status		
Single	13	4.5
Married	230	79.9
Widowed	26	9
Divorced	13	4.5
Separated	6	2.1
3. Education attainment		
Not educated	-	-
Primary	151	52.4
Secondary	22	7.6
High School	76	26.4
Bachelor Degrees	39	13.5
4. Occupation		
Unemployed	11	3.8
Housewife	15	5.2
Farmer	134	46.5
Employed	73	25.4
Merchant	23	8
Civil servant	32	11.1
5. Family Income (Bath)		
Mean (standard deviation)	12,332.6 (17,935.6)	
Median (minimum: maximum)	6,000 (600 : 100,000)	
6. Pregnancy		
No	25	8.7
Yes	263	91.3
7. Abortions (Times)		
1	21	7.3
2	5	1.7
Did not answer	262	91
8. Gravida		
1	52	18.1
2	144	50
3	30	10.4
4	5	1.7
5	6	2.1
Did not answers	51	17.7
9. Number of living children		
1	60	20.8
2	148	51.4

Table 1. Continued

Characteristic	Number (n = 288)	Percentage (%)
9. Number of living children		
3	36	12.5
4	5	1.7
5	2	0.7
7	1	0.4
Did not answers	36	12.5
10. Age at first pregnancy		
Mean (standard deviation)	24.3(4.4)	
Median (minimum: maximum)	26.0 (16:37)	
11. Contraception		
No	52	18.1
Yes	236	81.9
12. Type of contraceptive (n=248)		
Oral contraceptive pills	191	77
Female sterilization	59	23.8
Injectable contraception	43	17.3
Intrauterine device	34	13.7
Condom	15	6.1
Implant contraception	1	0.4
13. Family history of cervical cancer		
No	283	98.3
Yes	5	1.7
14. Pathologic vaginal discharge		
No	254	88.2
Yes	34	11.8
15. Postcoital bleeding		
No	273	94.8
Yes	15	5.2
16. Postmenopausal bleeding		
No	269	93.4
Yes	19	6.6
17. Reasons for Screening Test		
Annual health check-ups	204	70.8
Fear of cervical cancer	199	69.1
Have a campaign	117	40.6
A doctor's appointment	54	18.8
Have abnormal symptoms of cervical cancer	38	13.2
others (Friend advice)	4	1.4
18. The reason for non-HPICUC after abnormality pap smear (n = 269)		
Embarrassment	157	58.4
Fear of pain	137	50.9
Busy and didn't have time	100	37.2
Fear of cancer detection	61	22.7
Inconvenience transportation	40	14.9
No information about place and time	13	4.9
Have no money to pay for transportation	10	3.7
Fear of infection	7	2.6
Other	14	5.2

Table 2. Incidence Rate of Non-Histologically Confirmed among Women with an Abnormal Pap Smear in the CCSP (n=288).

Characteristic	non-histologically proven (n=260)	Incidence (per 100 person-years)	95%CI
Overall Incidence rate	260	90.3	86.3 - 93.2
1. Age at recruitment			
30-34	10	66.7	37.2 - 87.1
35-39	24	85.7	66.0 - 94.9
40-44	42	89.4	76.2 - 95.7
45-49	47	94	84.7 - 98.4
50-54	62	94.2	86.6 - 97.6
55-59	25	87.1	68.9 - 95.4
60 +	50	91.3	68.6 - 98.1
2. Education attainment			
Not educated	-	-	-
Primary	136	90.1	84.1 - 93.9
Secondary	21	95.5	70.4 - 99.5
High School	67	88.2	78.5 - 93.8
Bachelor Degrees	36	92.3	77.8 - 97.6
3. Marital status			
Single	13	100	-
Married	204	88.7	83.8 - 92.2
Widowed	26	100	-
Divorced	12	92.3	53.1 - 99.2
Separated	5	83.3	18.6 - 99.1
4. Educational level of Cervical cancer knowledge			
Low (0-5 score)	16	100	-
Moderate (6-7 score)	63	98.4	89.2 - 99.8
High (8-10 score)	181	87.1	81.9 - 91.0

with non-HPICUC (p-value < 0.05) after adjusting for all variables in the model. For every 20-year increase in age, women with an abnormal CCSP pap smear had 1.02 times the risk of having non-HPICUC compared to those under 20 years of age (adjusted RR=1.02, 95% CI: 1.01 - 1.04). Pregnant women had 0.89 times the risk of having non-HPICUC compared to non-pregnant women (adjusted RR=0.89, 95% CI: 0.80 - 0.99).

However, pathologic vaginal discharge (PVD) had no statistically significant association with non-HPICUC (p-value = 0.094). Women with PVD had a 1.08 times risk of having non-HPICUC compared to women without PDV (Adjusted RR=1.08, 95% CI: 0.97 - 1.20) (Table 3).

Discussion

The primary aim of the current study was to investigate the factors associated with non-HPICUC among women 30-60 years of age with abnormal pap smears from cervical cancer screening within the CCSP

Table 3. Multivariable Analyses Identified Associations between Variables and non-HPICUC among Women with an Abnormal Pap Smear within the CCSP (n=288).

Variable	Non-Histologically Proven		Histologically Proven		Crude RR	Adjusted RR	95%CI	P-value
	Number	Percentage (%)	Number	Percentage (%)				
1. Age at recruitment								0.018
Every 20 years increased					1.02	1.02	1.01 - 1.04	
2. pregnancy								0.036
No	24	96	1	4	1	1	-	
Yes	236	89.7	27	10.3	0.98	0.89	0.80 - 0.99	
3. Pathologic vaginal discharge								0.094
No	228	89.8	2	10.2	1	1	-	
Yes	32	94.1	26	5.9	1.02	1.08	0.97 - 1.20	

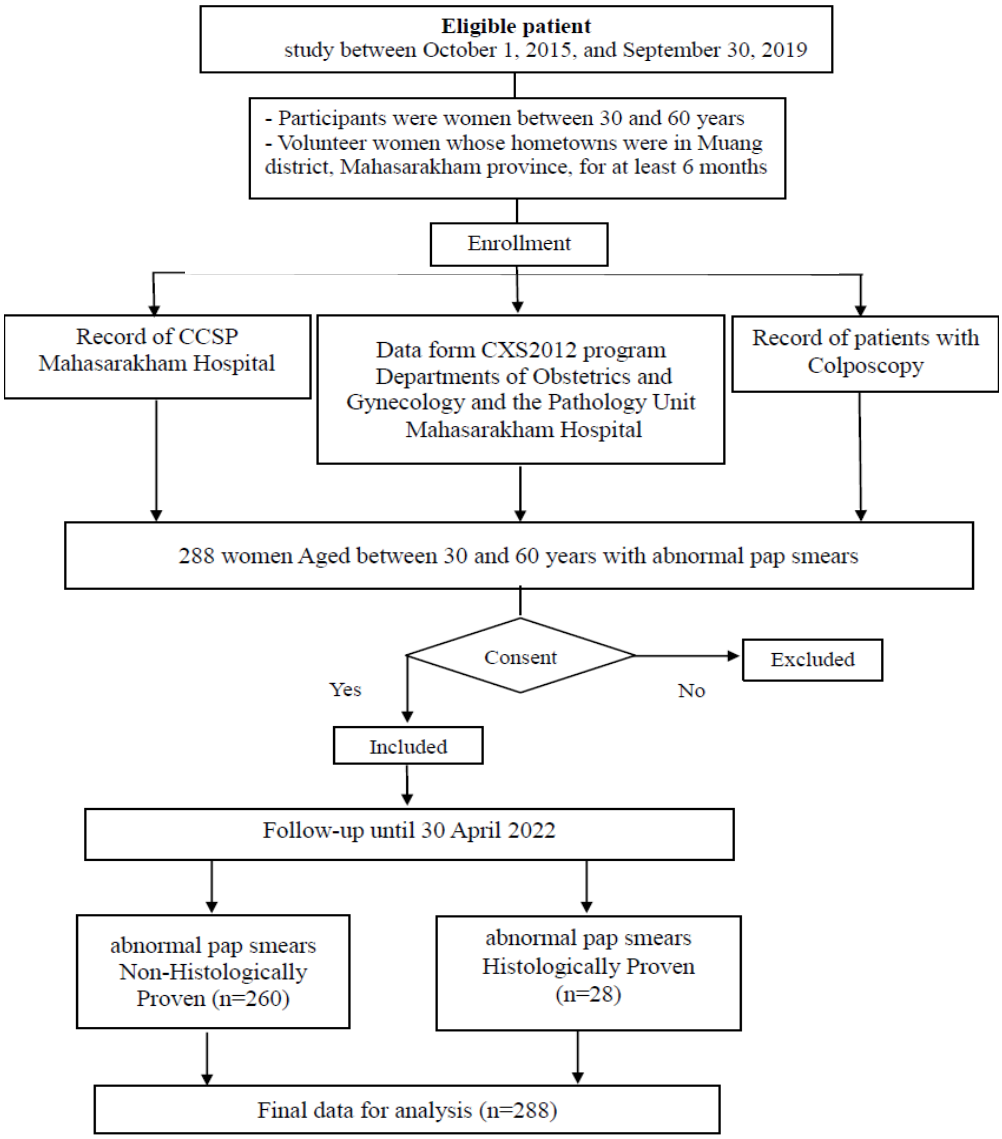

Figure 1. Flowchart of Eligibility Criteria: Data Sources and Screening Results

at Mahasarakham Hospital. The findings demonstrated that age and pregnancy were significantly associated with non-HPICUC (p-value < 0.05), while PVD was not (p-value =0.094).

Age

Age was significantly associated with non-HPICUC among women between 30 and 60 with an abnormal pap smear from the cervical cancer screening (adjusted RR=1.02, 95% CI: 1.01 - 1.04, p-value=0.018). This finding is consistent with a previous study investigating the factors that affect cervical cancer screening among at-risk women in Nakhorn-Chum, Nakhon Thai district, Phitsanulok province. In addition, age was significantly associated with cervical cancer screening among the risk group of women (adjusted OR = 1.07, 95%CI: 1.02 - 1.12, p-value = 0.009) (Wangwonsin et al., 2021).

However, in the study by (Summutte and Pinitsoontorn, 2015, Sonkong, 2021, and Wongwatcharanukul et al., 2014), age had no significant association with women's willingness to participate in cervical cancer screening services (p-value > 0.05). Among those ≤ 44 years of age, women were 1.04 times more likely to have received cervical cancer screening services compared to those ≥ 45 years (Crude OR = 1.04, 95%CI: 0.59-1.81, p-value= 0.893) (Summutte and Pinitsoontorn, 2015).

A study of factors associated with cervical cancer screening among women aged 30-60 years found that age 50-60 years was associated with a 1.33- fold chance of coming for cervical cancer screening compared to 30- 39 years (Crude OR = 1.33, 95%CI: 0.71-2.49, p value = 0.368) (Sonkong, 2021). Furthermore, in a study of factors that affect the acceptance of cervical cancer screening by Hmong Hilltribe women in Thailand, age did not significantly affect cervical cancer screening (p-value = 0.391). After adjusting for all variables in the model, the group ≥ 50 years who received cervical cancer screening services of age was than those of age (compared to the age group < 50 years old (Adjusted OR = 0.82, 95%CI: 0.52-1.29, p-value = 0.391) (Wongwatcharanukul et al., 2014). In the study, to determine colposcopy non-attendance studied, the potential factors associated with

and described non-attendance reasons in a population-based screening study. Age was not significantly associated with colposcopy attendance among all women referred (Liang et al., 2022).

The current study found a significant association between different age groups and levels of knowledge about cervical cancer and its being histologically proven (p-value = 0.031). Moreover, education attainment and knowledge regarding cervical cancer are risk factors for cervical cancer screening (Sonkong, 2021, Nantachai et al., 2016).

Pregnancy

The current study found that pregnancy was significantly associated with non-HPICUC among women 30-60 with abnormal pap smears from the CCSP (p-value = 0.036). In addition, pregnant volunteers were at 0.89 times the risk of being non-histologically proven compared to non-pregnant (adjusted RR=0.89, 95%CI: 0.80 - 0.99). This is consistent with a previous study that determined the factors associated with cervical cancer screening and found that the first pregnancy was significantly associated with coming for cervical cancer screening (p-value=0.005) after adjusting for all variables in the model. In addition, it was found that women the age of first pregnancy > 20 years were 2.22 times more likely to be screened for cervical cancer compared to women with the age of first pregnancy ≤ 20 years (adjusted OR=2.22, 95%CI: 1.27 - 3.86) (Sonkong, 2021).

The current study found that knowledge of cervical cancer and histologically-proven was significantly associated with contraceptive methods (p-value < 0.001). The implication is that women who have used contraceptives for a long time may be at increased risk for cervical cancer; so, such women were enthusiastic about confirming their diagnosis histologically after getting an abnormal pap smear from the CCSP.

Pathologic vaginal discharge (PVD)

In the current study, PVD was not significantly associated with non-HPICUC among women aged 30-60 with abnormal CCSP pap smears (p-value = 0.094). However, for women with PVD, there was a 1.08 times risk of having non-histologically proven compared to non-PVD (adjusted RR=1.08, 95%CI: 0.97 - 1.20). This finding is consistent with a previous study that found no significant association between PVD and attending cervical cancer screening (crude OR=1.20, 95%CI: 0.51 - 2.81, p-value = 0.679) (Sonkong., 2021).

Significant causes of CC include signs and symptoms such as bleeding after sex and irregular bleeding before or after menopause (American Cancer Society., 2020). Importantly, data from the current study revealed the reason for non-HPICUC among women aged 30-60 years with abnormal CCSP pap smears, and the reasons include shyness (n=157, 58.4%), fear of pain (n=137, 50.9%), and did not have time (n=100, 37.2%). Consequently, despite having abnormal pap smears, women with PVD did not come to the hospital to get a histologically-confirmed diagnosis.

In summary, the findings show that age at recruitment and pregnancy are associated with an increased risk of non-HPICUC with an abnormal pap smear from the CCS Program at Mahasarakham Hospital, Thailand. High-risk groups with abnormal pap smears should be targeted for CC campaigns.

Author Contribution Statement

KT was the principal investigator and provided project management supervision. SK provided advice on study design and statistical analyses. WM provided and supervised the interviewers and assisted in assessing data quality. WT was involved in exploratory analysis and data quality. MDHH—a highly experienced obstetrician gynaecologist—oversaw data quality.

Acknowledgements

The authors thank (a) the Anti-Cancer Foundation, Faculty of Medicine, Khon Kaen University, that provides research funding, (b) the staff of Mahasarakham Hospital for data collection and management, and (c) Mr. Bryan Roderick Hamman—under the aegis of the Publication Clinic, Khon Kaen University—for assistance with the English-language presentation of the manuscript.

Advantages and Disadvantages of the study
Advantages

The advantage of the study is the information regarding early cancer detection and cervical cancer diagnosis. Furthermore, the study provides additional evidence to support public information campaigns to encourage high-risk groups to undergo cervical cancer screening to reduce the incidence and mortality of CC. Targeting high-risk groups is essential because these women have abnormal CCSP pap smears. Unfortunately, they often do not come to the hospital for histological confirmation because they are self-conscious, fear pain from the procedure, or lack time: issues that can be addressed with education.

Disadvantages

The study had some limitations. Firstly, some volunteers were lost to follow-up, introducing information bias. Secondly, there was a lack of follow-up data for women with abnormal pap smears from CC screening.

Statement conflict of interest

The authors declare that they have no conflicts of interest.

References

Akaike H (1973). Information Theory and an Extension of the Maximum Likelihood Principle. In 2nd International Symposium on Information Theory. B.N. Petrov and F.Csaki, eds. *Akademiai Kiado Budapest*, pp 267-81.

American Cancer Society (2020). Signs and Symptoms of Cervical Cancer. Available: https://www.cancer.org/cancer/cervical-cancer/detection-diagnosis-staging/signs-symptoms.html. Accessed November 20, 2022.

Global Cancer Observatory. (2020). Cervix uteri. Available from:

https://gco.iarc.fr/today/data/factsheets/cancers/23-Cervix-uteri-fact-sheet.pdf. Accessed November 20, 2021.
Hardin JW, Hilbe J (2012). Generalized Linear Models and Extensions, 3rd Edition, Stata Press books, StataCorp LP.
Health Data Center (2021). Ministry of Public Health, Available from: https://hdcservice.moph.go.th/ hdc/main/index.php. Accessed November 20, 2021.
Hsieh FY, Bloch DA, Larsen MD (1998). A simple method of sample size calculation for linear and logistic regression. *Statis Med*, **17**, 1623-34.
Imsamran W, Chaiwerawattana A, Wiangnon S, et al (2015). Cancer in Thailand Vol. VIII, 2010-2012. Bangkok, National Cancer Institute, Thailand.
Imsamran W, Pattatang A, Supattagorn P, et al (2018). Cancer in Thailand: Vol. IX, 2013-2015. Bangkok, National Cancer Institute, Thailand.
International Agency for Research on Cancer (IARC). IARC launches the definitive cancer statistics resource GLOBOCAN 2008. Available from: https://www.iarc.who.int/wp-content/uploads /2018/07/pr201_E.pdf Accessed November 20, 2021.
Khuhaprema T, Attasara P, Sriplung H, et al (2012). Cancer in Thailand Volume VI, 2004-2006. Bangkok, National Cancer Institute, Thailand.
Khuhaprema T, Attasara P, Sriplung H, Wiangnon S, Sangrajrang S (2013). Cancer in Thailand Vol. VII, 2007-2009. Bangkok, National Cancer Institute. Thailand.
Kleinbaum DG, Klein M (2005) Survival Analysis: A Self-Learning Text. 3rd ed. New York, NY: Springer New York (Statistics for Biology and Health). doi: 10.1007/0-387-29150-4. Accessed Accessed January 12, 2023.
Laowahutanont P, Imsamran W (2018). Clinical Guidelines for screening Diagnosis and treatment Cervical cancer. National Cancer Institute, Thailand. Available: https://www.nci.go.th/th/cpg/Cervical_Cancer.pdf.
Liang LA, Zeissig SR, Schauberger G, et al (2022). Colposcopy non-attendance following an abnormal cervical cancer screening result: A prospective population-based cohort study. *BMC Womens Health*, **22**, 285.
Mahasarakham Hospital (2021). Health Data Center. Available from: https://www.mkh.go.th. Accessed November 20, 2021.
Nantachai K, Jirapornkul C, Tungsrithong N, Mingsiricharoen P (2016). Factors associated with not receiving cervical cancer screening among the Akha hilltribe women in Muang District, Chiangrai Province. *Srinagarind Med J*, **31**, 192-201.
National Cancer Institute. National Cancer Control Programme (2018-2022). Available from: https://www.nci.go.th/th/File_download/D_index. Accessed November 20, 2021.
Rojanamatin J, Ukranun W, Supaattagorn P, et al (2021). Cancer in Thailand Volume X, 2016-2018. Bangkok, National Cancer Institute, Thailand.
Sonkong K (2021). Factors associated with cervical cancer screening among women aged 30-60 years in the Taktok sub-district health promotion hospital in Tak Province. *J Med Health Sci*, **3**, 61-74.
StataCorp (2007). Stata Statistical Software: Release 10. Texas, USA: StataCorp LP. Available: http://www.stata.com, Accessed February 15, 2021.
Summutte U, Pinitsoontorn S (2015). The intention to cervical cancer screening utilization among 30-60 year old women at Banprow Health Promotion Hospital, Mueang District, Nong Bua Lam Phu Province. *Commun Health Develop Quarterl Khon Kaen Univ*, **3**, 529-46.
Wangwonsin A, Jaruk M (2021). Factors Effected to Cervical Cancer Screening Among Risk Group of Women in Nakhorn Chum, Nakhon Thai District, Phitsanulok Province. *BCNUT J Nurs*, **13**, 100-13.
Wongwatcharanukul L, Promthet S, Bradshaw P, Jirapornkul C, Tungsrithong N (2014). Factors Affecting Cervical Cancer Screening Uptake by Hmong Hilltribe Women in Thailand. *Asian Pac J Cancer Prev*, **15**, 3753-56.
World Health Organization.(2020). Cervical cancer. Available from: https://www.who.int/health-topics/cervical-cancer#tab=ta. Accessed January 12, 2021.
World Health Organization.(2002). National cancer control programmes : policies and managerial guidelines, 2nd ed. Available from: https://apps.who.int iris/handle/10665/42494 Accessed January 12, 2018.