Evaluate the Agreement of High-risk Human Papillomavirus Type Between Self-collected Vaginal Discharge Sample Using "HygeiaTouch Self Sampling Kit for Woman" and Physician Collected Sample From the Cervix

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Statistical Analysis Plan

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Study purpose

"HygeiaTouch Self Sampling Kit for Women " was developed and commissioned by Hygeia Touch Inc. This kit contains a self-sampling swab, designed for oriental women, made of non-toxic and non-allergenic materials, and can be used for self-collection sufficient vaginal exfoliated cells for HPV testing. This product is a single use product, which is easy to operate and allows women to take specimens freely and comfortably. The collected samples can be sent to a professional laboratory at room temperature for high-risk HPV typing test . Providing women with cervical screening an alternative will increase cervical screening rates nationwide and further reduce the incidence of cervical cancer.

In order to verify the consistency of the high-risk HPV test results between the samples collected by women using this kit and the samples collected by doctors from the cervix , 1,200 women will be included in this experiment, and they will undergo self- collection and doctor -collected inspections respectively. The test results of the samples collected by doctors will be used as the standard to evaluate the consistency of HPV typing results between the samples obtained by using the self- collection kit group and the samples collected by doctors . This product has been classified by the Food and Drug Administration of the Ministry of Health and Welfare, and it has been judged as a class 2 medical device. If the test results show a high degree of consistency between the self- collection and the doctor's test , it will be used to apply to the Ministry of Health and Welfare that this set can be used as a second-level medical device inspection registration for women's self- collection for high-risk HPV typing .

A. The main purpose of the test primary objective:
   For the test group, the consistency (agreement) of whether there is high-risk HPV detected by using the samples obtained by the self-collection kit and the samples collected by the doctor . Consistency definitions are described in Section 6.3.

B. Secondary objectives of the test :
   1. Evaluate whether women can complete effective self-specimen sampling by following the instructions or videos.
   2. Safety assessment of sampling, including physician and self - examination
   3. collection success rate, consistency evaluation and comparison of each group
   4. the correlation between the HPV test results of physician's test /self- test and the results of smear and histopathological diagnosis
   5. Self -test satisfaction assessment

Inclusion criterias

Participants must meet the following three conditions:

A. Women over 21 years old (inclusive) and under 65 years old (inclusive), who have never received total hysterectomy and never received radiation therapy for the uterus / cervix
B. Understand the content of the experiment and sign the subject's consent form
C. meet one of the following 5 conditions :

1. No history of abnormal smear or cervical lesions
2. There have been mild smears or pathological abnormalities within 3-12 months, and those who need to receive Pap smear follow-up

   Mild smear abnormalities include atypical squamous cell of undetermined significance, first-degree cervical intraepithelial neoplasia grade 1 , or atypical glandular cell .
3. Those who have had moderate to severe smear or pathological abnormalities or cervical cancer, have undergone conical surgery , and are currently receiving follow-up

   Including atypical squamous cells favor high-grade squamous intraepithelial lesion in smear, cytopathic lesion cannot exclude high -grade squamous intraepithelial lesion, smear or histopathology is cervical intraepithelial neoplasia of the second degree lasia grade 2, cervical intraepithelial neoplasia grade 3, cervical carcinoma in situ , squamous cell carcinoma of the cervix, or atypical glandular cells favor neoplasm, adenocarcinoma in situ of the cervix, or Cervical adenocarcinoma patients.
4. Mild smear or pathological tissue abnormalities within 3 months without treatment

   Mild smear abnormalities include atypical squamous cell of undetermined significance, first-degree cervical intraepithelial neoplasia grade 1 , or atypical glandular cell .
5. Moderate or severe abnormalities in smear or pathological tissue or cervical cancer found within 3 months, and those who have not received treatment

   Including atypical squamous cells favor high-grade squamous intraepithelial lesion in smear, cytopathic lesion cannot exclude high -grade squamous intraepithelial lesion, smear or histopathology is cervical intraepithelial neoplasia of the second degree lasia grade 2, cervical intraepithelial neoplasia grade 3, cervical carcinoma in situ , squamous cell carcinoma of the cervix, or atypical glandular cells favor neoplasm, adenocarcinoma in situ of the cervix, or Cervical adenocarcinoma patients.

   stratification of the statistical analysis of this experiment .

Exclusions criterias

Subjects who meet any of the following conditions cannot participate in this trial:

A. Those who have undergone total hysterectomy (those who have undergone subtotal hysterectomy and still retain the cervix do not need to be excluded)
B. pregnant
C. with cervicitis who must be treated
D. Those who have received treatment for cervical lesions within 90 days
E. who have received or are receiving uterine / cervix or vaginal radiation therapy
F. Women under the age of 21 or over the age of 65
G. 4 8 hours before having sex without a condom
H. Excessive vaginal secretions, such as excessive transparent mucus during ovulation
I. Those who are receiving local treatment for vaginitis and have drugs in the vagina
J. Menstrual period, the menstruation has not ended

Outcome measures

Primary evaluation indicators:

A. HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and other 14 types are high-risk cancer-causing types. Therefore, the main purpose of the agreement is whether there is high-risk HPV detected in the samples collected by doctors and self - sampled . Consistency is defined as follows:

B. The high-risk HPV test results are consistent (agree) , and the test results show that both of them have any of the above-mentioned high-risk HPV or neither of them has high-risk HPV .

C. The test results of high-risk HPV are inconsistent (disagree). One of the samples collected by doctors and self- collected samples does not have any of the above-mentioned high-risk HPV types , and the other has any of the above-mentioned high-risk types.

D. The consistency between the test results of the samples collected by the physician and the test results of the subjects' self- collected samples will be evaluated by Cohen 's kappa coefficient or compared with related tests.

Secondary evaluation indicators:

A. The success rate (proportion of effective specimens) of HPV typing in physician - collected and self-collected specimens of all detectable HPV types.

B. The incidence of adverse reactions was used as the safety evaluation index to evaluate whether there would be adverse reactions caused by doctors' self-examination of vaginal secretions or self-examination of vaginal secretions. The test process was recorded according to the grading standard of CTCAE version 5.0 .

C. Evaluate whether women can complete effective self-specimen sampling by following the instructions or videos. The beta-globin of the test results will be used as an evaluation index for valid specimens, and the reliability of the explanatory files will be evaluated by the results of the questionnaire survey.

D. -collection success rate (proportion of effective specimens) and consistency evaluation of each group under the test group .

E. The correlation between the HPV test results collected by physicians , the HPV test results of self-collected samples, and the results of Pap smear and histopathological diagnosis at the same time . Taking the most serious pathological diagnosis as the standard, calculate

    1. Predict the sensitivity, specificity, positive predictive value and negative predictive value of cervical lesions based on the HPV test results of the samples taken by doctors

    2. Predict the sensitivity, specificity, positive predictive value and negative predictive value of cervical lesions based on the test results of self- collected samples

F. The questionnaire was used to evaluate the satisfaction of the subjects' self-testing .

Statistical considerations

Statistical design, methods and analysis procedures

A. This study is a multi-center clinical trial in Taiwan to test the blindness of operators . It mainly explores the consistency between self- testing of products and doctor -testing . In this experiment, the test results of samples collected by doctors will be used as the standard, and compared with the results of HPV type test of samples collected by the same subject to verify the consistency of HPV types in samples collected by doctors and self- sampled samples.

B. The experimental design uses the status of cervical precancerous lesions as a stratification variable, and the 5 groups of test groups are divided into the following proportions:

5 groups of subjects included in the subjects	**Inclusion ratio**
1. No history of abnormal smear or cervical lesions	10%
2. There have been mild smears or pathological abnormalities within 3-12 months, and those who need to receive Pap smear follow-up	15%
3. Those who have had moderate to severe smear or pathological abnormalities or cervical cancer, have received conical surgery , and are currently receiving follow-up	20 %
4. Mild smears or pathological tissue abnormalities within 3 months, who have not yet been treated	20 %
5. Moderate and severe abnormalities in smear or pathological tissue or cervical cancer found within 3 months, and those who have not received treatment	35%

According to relevant literature research, it is estimated that the positive probability of HPV in the five groups is (1) 10% , (2) 70% , (3) 50%, (4) 70% , (5) 90%, depending on the experimental design Under the stratum recruitment ratio , the overall HPV positive rate is expected to be about 67% , as shown in the table below .

Stratification	**Al location rate**	**S tratified HPV positive prob.**
1. No history of abnormal smear or cervical lesions	0.1	0.1
2. There have been mild smears or pathological abnormalities within 3-12 months, and those who need to receive Pap smear follow-up	0.15	0.7

3. Those who have had moderate to severe smear or pathological abnormalities or cervical cancer, have received conical surgery , and are currently receiving follow-up	0.20	0.5
4. Mild smears or pathological tissue abnormalities within 3 months, who have not yet been treated	0.20	0.7
5. Moderate and severe abnormalities in smear or pathological tissue or cervical cancer found within 3 months, and those who have not received treatment	0.35	0.9
Total _	**0.67 _**	

C. Subjects who meet the admission requirements will be included in one of the 5 stratified groups according to their pathological conditions. All test institutions will accept cases through competition. After the stratified groups reach the predetermined acceptance ratio, no subjects from this group will be recruited.

D. In this experiment, each subject will provide two specimens, one from a doctor's examination and one from a self- examination . In order to maintain the scientific nature of the consistency assessment, the tester will be blinded , that is, the tester cannot know the samples corresponding to the two collection methods of any subject.

E. This study intends to achieve the blindness requirement by means of coding, that is, the sample number collected by the doctor is the number of the subject of this study (the number is given according to the order of admission), and the self- collected sample of the same subject is based on the sample number collected by the doctor, and the number obtained by random garbled operation makes it impossible to directly correspond to the sample collected by the doctor .

F. According to the main evaluation indicators of the test, the consistency of this study is defined as : for 14 high-risk types such as HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, the main purpose is to list the consistency (agreement) of the detection in the doctor's inspection and self- sampling samples . Consistency is defined as follows:

(1) The high-risk HPV test results are consistent (agree) , and the test results show that both of them have any of the above-mentioned high-risk HPV or neither of them has high-risk HPV . .
(2) The test results of high-risk HPV are inconsistent (disagree). One of the samples collected by doctors and self- collected samples does not have any of the above-mentioned high-risk HPV types , and the other has any of the above-mentioned high-risk types .

According to the definition of the test result, a contingency table can be obtained as follows, the K appa statistic $K = (P_0 - P_c)/(1- P_c)$ for statistical verification, where $P_0 =(a+d)/(a+b+c+d)$ is the observed agreement (observed agreement), and $P_c = \left(\frac{cm_1 \times rm_1}{n}\right) + \left(\frac{cm_2 \times rm_2}{n}\right)/n$ is the theoretical expected

agreement (chance agreement). The standard error of the K appa statistic is based on Fleiss, Cohen, and Everitt (1969) as S E (K) = S D (K) /$\sqrt{N}$, where S D (K) = $\sqrt{P_0(1-P_0)/(1-P_c)^2}$. The 100(1-α)% interval estimate of the K appa statistic is K. $\pm z_{\alpha/2} SE(K)$_

		Physician check _		
		High-risk HPV detected	No high-risk HPV detected	sum
self - test	High-risk HPV detected	**a**	**b**	***rm 1***
	No high-risk HPV detected	**c**	**d**	***r m 2***
	sum	***cm 1***	***cm 2***	***no***

For each HPV type (type-specific) , the consistency between the test results of the samples collected by the physician and the samples collected by the subjects will be evaluated by Cohen 's kappa coefficient or compared with related tests.

G. Consistency assessment will take valid samples as the analysis group, that is, the same subject's verification physician and self- sampling samples are all valid samples.

H. A valid sample is defined as a positive test for the β-globin gene in the internal control group of Jingyu Human Papillomavirus Genotyping Detection Kit . The intent-to-treat group (ITT) was used as the analysis group for safety, self- collection success rate, and satisfaction evaluation.

Test Hypothesis and Verification

Null hypothesis (H 0): The high-risk HPV test results of the samples collected by physicians and those collected by subjects themselves were consistent with Cohen 's kappa coefficient k ≤ 0.66.

Alternative Hypothesis (H 1): The high-risk HPV test results of the samples collected by the physician and the samples collected by the subjects themselves are consistent with Cohen 's kappa coefficient k > 0.66.

If the test results show that the opposite hypothesis is established, the expected goal of the test is achieved.

Sample size calculation

The above-mentioned kappa value is preset to be 0.72, under the condition that the test power is 80% and the significance level is 0.05, according to the proportion of subjects included in each group, the required samples are 1,049 cases . Considering that there are up to 10% of invalid samples and patients requesting to withdraw from the trial, the trial is expected to recruit 1,200 subjects , and the number of subjects assigned to each group is as follows according to the original test group ratio.

5 groups of subjects included in the subjects	**Inclusion ratio**	**Estimated number of people included**
1. No history of abnormal smear or cervical lesions	10%	120 people
2. There have been mild smears or pathological abnormalities within 3-12 months, and those who need to receive Pap smear follow-up	15%	180 people
3. Those who have had moderate to severe smear or pathological abnormalities or cervical cancer, have received conical surgery , and are currently receiving follow-up	20 %	240 people
4. Mild smears or pathological tissue abnormalities within 3 months, who have not yet been treated	20 %	240 people
5. Moderate and severe abnormalities in smear or pathological tissue or cervical cancer found within 3 months, and those who have not received treatment	35%	420 people
The total number of subjects expected to be included		1,200 people

Interim analysis

This trial had no interim analysis

Secondary evaluation indicators to be analyzed

A. Evaluation of the success rate (proportion of effective specimens) of HPV typing by doctors ' samples and self- collected samples of all detectable HPV types.

B. Consistency assessment will take valid samples as the analysis group, that is, the same subject's verification physician and self- sampling samples are all valid samples. A valid sample is defined as a positive test for the β-globin gene in the internal control group of Jingyu Human Papillomavirus Genotyping Detection Kit . The intent-to-treat group (ITT) was used as the analysis group for safety, self-collection success rate, and satisfaction evaluation.

C. used as a safety evaluation index to evaluate whether there will be adverse reactions (such as psychological discomfort or other physical discomforts) in the self - examination of vaginal secretions by doctors or by women .

D. Evaluate whether women can complete effective self-specimen sampling by following the instructions or videos. The beta-globin of the test results will be used as an evaluation index for valid specimens, and the reliability of the explanatory files will be evaluated by the results of the questionnaire survey.

E. -collection success rate (proportion of effective specimens) and consistency evaluation of each group under the test group .

F. The correlation between the HPV test results collected by physicians , the HPV test results of self-collected samples, and the results of Pap smear and histopathological diagnosis at the same time . Taking the most serious pathological diagnosis as the standard, calculate :
   1. the sensitivity, specificity, positive predictive value and negative predictive value of cervical lesions based on the HPV test results of the samples taken by doctors
   2. the sensitivity, specificity, positive predictive value and negative predictive value of cervical lesions based on the test results of self- collected samples

G. Use the subject questionnaire in the case report form to collect the survey data of the subject's self- test satisfaction survey, and conduct related evaluations.

Procedures for incorporating all data into the analysis

the Investigator (Investigator) , the test personnel are responsible for data collection and file management. All original documents and inspection reports must be reviewed by the research team and data entry personnel for correctness and completeness. Unexpected events and adverse events must be reviewed by the investigator or designee. The designated institution (Chang Gung Hospital Clinical Trial Center Biostatistics Group) is responsible for data management, confirmation, statistical analysis and output reports, and uses the data analysis software SAS for data collection and analysis.

In multi-center clinical trials, the minimum and maximum number of subjects included in each trial institution

A. This trial adopts a competitive type of case acceptance, and the case will stop after the expected number of trial subjects is included.

B. each test institution will allocate 10 test work bags that meet the conditions of the subjects . According to the acceptance speed of each test institution, when the test work bags are estimated to be used up, an application should be submitted to the test commissioner to supplement the next batch of test work bags to make the test run smoothly.

C. Based on the above, in this trial, each trial institution will include a minimum of 50 subjects, but there is no standard for the maximum number of subjects.

Except for the analysis of the main evaluation indicators and secondary evaluation indicators in this trial, the rest of the data analysis is exploratory analysis.

All data included in the output table of the analysis

Figure 1. Test flow chart

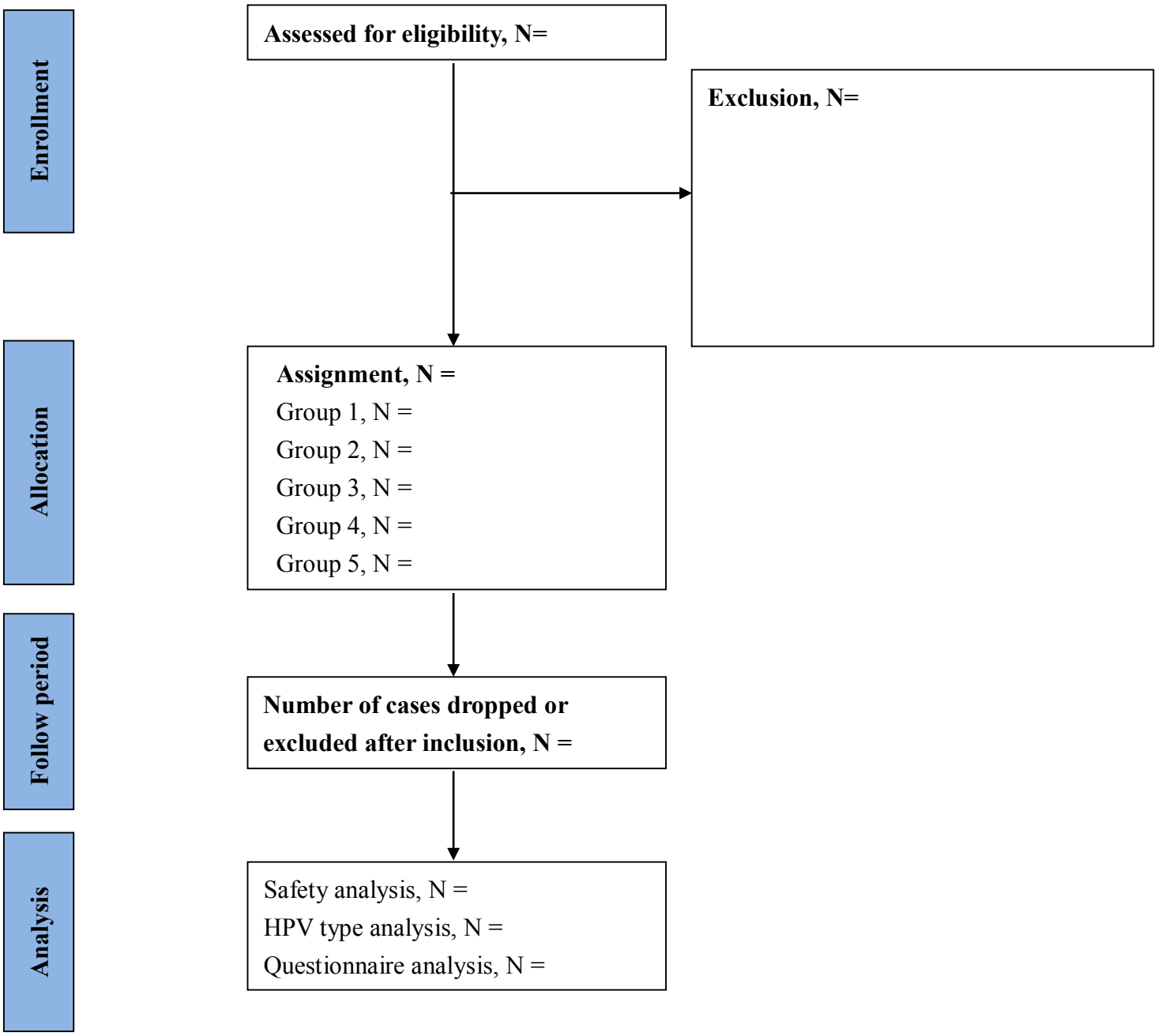

Table 1 Basic information of subjects

	Total (N=)		Group 1 (N=)		Group 2 (N=)		Group 3 (N=)		Group 4 (N=)		Group 5 (N=)	
Characteristics	N	%	N	%	N	%	N	%	N	%	N	%
Age (year)												
Mean ± SD												
Median, range												
Colposcopy												
Yes												
No												
Finding												
Normal												
Punctation												
Mosaicism												
Atypical vessels												
Condyloma accuminata												
Leukoplakia												
Invasive carcinoma suspected												
Others												
Past history of cervical histology*												
CIN1												
CIN2												
CIN3												
LSIL												
HSIL												

Squamous cell carcinoma	
Adenocarcinoma	
Others	
None	
Menopaused	
No	
Yes	
Histological results	
SM-C-	
SM+	
atypical	
CIN1	
CIN2	
CIN3	
SCC	
AIS	
Adca	
clearCC	
No biopsy taken	

*Histological diagnosis preferred

ASCUS, atypical squamous cell of undetermined significance

ASCH, atypical squamous cells favor high-grade squamous intraepithelial lesion

CIN, cervical intraepithelial neoplasia

HSIL, high-grade squamous intraepithelial lesion

LSIL, low-grade squamous intraepithelial lesion

Table 2 Smear examination results before inclusion in the trial (90 days ago)

	Total (N=)		Group 1 (N=)		Group 2 (N=)		Group 3 (N=)		Group 4 (N=)		Group 5 (N=)	
Cytology	N	%	N	%	N	%	N	%	N	%	N	%
No Pap smear taken												
Within normal limit												
Reactive changes: Inflammation, repair, radiation, and others												
Atrophy with inflammation												
Atypical squamous cells (ASCUS)												
Atypical glandular cells												
Mild dysplasia (CIN1) with koilocytes												
Mild dysplasia (CIN1) without koilocytes												
Moderate dysplasia (CIN2)												
Severe dysplasia (CIN3)												
Carcinoma in situ (CIN3)												
Squamous cell carcinoma												
Adenocarcinoma												
Other malignant neoplasm												
Other												
Atypical glandular cells favor neoplasm												
Atypical squamous cells cannot exclude HSIL												
Dysplasia cannot exclude HSIL												
Endocervical adenocarcinoma in situ												

Table 3 Smear examination results when included in the trial (within 90 days)

	Total (N=)		Group 1 (N=)		Group 2 (N=)		Group 3 (N=)		Group 4 (N=)		Group 5 (N=)	
Cytology	N	%	N	%	N	%	N	%	N	%	N	%
No Pap smear taken												
Within normal limit												
Reactive changes: Inflammation, repair, radiation, and others												
Atrophy with inflammation												
Atypical squamous cells (ASCUS)												
Atypical glandular cells												
Mild dysplasia (CIN1) with koilocytes												
Mild dysplasia (CIN1) without koilocytes												
Moderate dysplasia (CIN2)												
Severe dysplasia (CIN3)												
Carcinoma in situ (CIN3)												
Squamous cell carcinoma												
Adenocarcinoma												
Other malignant neoplasm												
Other												
Atypical glandular cells favor neoplasm												
Atypical squamous cells cannot exclude HSIL												
Dysplasia cannot exclude HSIL												
Endocervical adenocarcinoma in situ												

Table 4 Consistency of high-risk HPV detection in all cases

	Physician-collected				
Self-collected	Positive	Negative	Kappa statistic (95% CI)	*p* value	Overall Agreement
Positive					
Negative					

High-risk HPV types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and other 14 types. The definition of consistency is as follows: high-risk HPV test results are concordant (concordant), the test results of the subject's physician -collected sample and self- collected sample both have any of the above-mentioned high-risk HPV (high-risk HPV positive) or both have no high-risk HPV (high-risk HPV negative); high-risk HPV test results are inconsistent (discordant), the test results of the subject's doctor-collected sample and self-collected sample, one does not have any high-risk HPV, and the other has any of the above- mentioned high -risk types .

Table 5 Consistency of high-risk HPV types detected in each group

	Physician-collected				
Self-collected	Positive	Negative	Kappa statistic (95% CI)	*p* value	Overall Agreement
Group 1					
Positive					
Negative					
Group 2					
Positive					
Negative					
Group 3					
Positive					
Negative					
Group 4					
Positive					
Negative					
Group 5					
Positive					
Negative					

High-risk HPV types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68 and other 14 types. The definition of consistency is as follows: high-risk HPV test results are concordant (concordant), the test results of the subject's physician -collected sample and self- collected sample both have any of the above-mentioned high-risk HPV (high-risk HPV positive) or both have no high-risk HPV (high-risk HPV negative); high-risk HPV test results are inconsistent (discordant), the test results of the subject's doctor-collected sample and self-collected sample, one does not have any high-risk HPV, and the other has any of the above- mentioned high -risk types .

Table 6 Consistency of detecting any type of virus in all cases

	Physician-collected				
Self-collected	Positive	Negative	Kappa statistic (95% CI)	*p* value	Overall Agreement
Positive					
Negative					

27 HPV types: HPV6, 11, 16, 18, 31, 33, 35, 39, 45, 51, 52, 53, 54, 56, 58, 59, 61, 62, 66, 68, 69, 70, 72, 73, 81, 82, 84. Consistency is defined as follows: HPV test results are concordant, the test results of the subject's physician-collected sample and self-collected sample both have any of the above-mentioned HPV types (HPV-positive) or neither of the above-mentioned types (HPV-negative); HPV test results are inconsistent (discordant), the test results of the subject's physician-collected sample and self-collected sample, one does not have any of the above-mentioned HPV types, and the other has any of the above-mentioned HPV types.

Table 7 Consistency of HPV16, HPV18, HPV16 or 18, non-16/18 high-risk HPV and low-risk HPV detected in all cases

	Physician-collected				
Self-collected	Positive	Negative	Kappa statistic (95% CI)	*p* value	Overall Agreement
HPV 16[a]					
Positive					
Negative					
HPV 18[b]					
Positive					
Negative					
HPV 16/18[c]					
Positive					
Negative					
hrHPV non-16/18[d]					
Positive					
Negative					
Non-hrHPV[e]					
Positive					
Negative					

[a] HPV 16: HPV 16 present only and/or co-infections with other types; [b] HPV 18: HPV 18 present only and/or co-infections with other types; [c] HPV 16/18: HPV16 and/or HPV18 present and/ or co-infections with other types; [d] HPV31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 excluding HPV16 and HPV18 ; [e] HPV 6, 11, 53, 54, 61, 62, 69, 70, 72, 73, 81, 82 and 84 excluding HPV16, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68.

Table 8 Distribution of all measurable HPV types in medical samples and self- collected samples of each group

	Total (N=)		**Group 1** (N=)		**Group 2** (N=)		**Group 3** (N=)		**Group 4** (N=)		**Group 5** (N=)	
HPV	Physician	Self	Physician	Self	Physician	Self	Physician	Self	Physician	Self	Physician	Self
6												
11												
16												
18												
31												
33												
35												
39												
45												
51												
52												
53												
54												
56												
58												
59												
61												
62												
66												
68												
69												
70												
72												
73												
81												
82												
84												
Negative												

Figure 2. Distribution of HPV types on physician-collected and self-collected specimens

Figure 3. Distribution of HPV types in Physician-collected and Self-collected specimens without precancerous lesions or cervical cancer (N =)

Figure 4. The distribution of HPV types on physician-collected and self-collected specimens of participants with cervical intraepithelial neoplasia grade 1

Figure 5. The distribution of HPV types on physician-collected and self-collected specimens of participants with cervical intraepithelial neoplasia grade 2 (N =)

Figure 6. The distribution of HPV types on physician-collected and self-collected specimens of participants with cervical intraepithelial neoplasia grade 3 (N =)

Table 9 Sensitivity, specificity, PPV and NPV between medically collected and self- collected HPV test results and cervical histopathology

	self- collected specimen		Physician check _		Relative accuracy	
cervical histopathology _	n/N	(95% CI)	n/N	(95% CI)	(95% CI)	p value
CIN1+						
Sensitivity						
Specificity						
Positive predictive value						
Negative predictive value						
CIN2+						
Sensitivity						
Specificity						
Positive predictive value						
Negative predictive value						
CIN3+						
Sensitivity						
Specificity						
Positive predictive value						
Negative predictive value						

*No histological diagnosis is calculated as Negative

Table 10 Analysis of Satisfaction Questionnaires Included in Total Cases (N = , ITT)

	very low		Low		high		very high	
satisfaction survey	N	%	N	%	N	%	N	%
1. Do you like the appearance design of this product?								
2. Do you find it easy to use this product ?								
3. Using self -testing to screen for HPV will increase your willingness to do HPV screening regularly ?								
4. Would you like to use this product again next time ?								
5. Would you like to recommend relatives and friends to use this product ?								
6. May I ask you, is the process of putting this product into the vagina for sampling easy ?								
7. Do you think the process of using this product for inspection is safe ?								
8. Do you feel comfortable after using this product ?								
9. Is the instruction manual of this product easy to understand ?								

Table 11 Self -sampling Illustrative Video Questionnaire (N = , ITT)

	yes		no	
Self- Sampling Instructions Video Questionnaire	N	%	N	%
1. Can I use the self -testing stick to take samples during the menstrual period?				
sampling stick to sample when there is a lot of mucus secretion during the ovulation period?				

Table 12 Adverse events related to experimental medical materials (N = , ITT)

Patient	Adverse Events	Grade	Onset Time	Duration	Related SAE