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Dry Storage and Transport of a Cervicovaginal Self-Sample by Use of the Evalyn Brush, Providing Reliable Human Papillomavirus Detection Combined with Comfort for Women

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Primary screening using high-risk human papillomavirus (hrHPV) detection has been suggested as a way of improving cervical cancer prevention. Women currently not attending screening (nonresponders) are more likely to participate when given the opportunity of self-sampling for hrHPV testing. The Evalyn Brush is a new cervicovaginal self-sampling device, developed specifically to meet women's demands, which is user-friendly and easy to use. The aims of this study were to investigate agreement of hrHPV detection by two PCR methods between the Evalyn Brush and physician-obtained samples and to study women's acceptance of this self-sampling device. Each of 134 women visiting the gynecology outpatient clinic collected a self-obtained sample (self-sample) and completed a questionnaire. The brush was stored dry. After self-sampling, a trained physician obtained a conventional cervical cytology specimen in ThinPrep medium. HrHPV detection was performed using the SPF_{10}-DEIA-$LiPA_{25}$ and GP5+/6+-LQ-test. The overall agreement for hrHPV detection using SPF_{10}-DEIA-$LiPA_{25}$ between the self-sample and the physician-taken sample was 85.8% (kappa value, 0.715; 95% confidence interval [CI], 0.597 to 0.843; $P = 1.000$). The overall agreement for hrHPV detection using GP5+/6+-LQ between the self-sample and the physician-taken sample was 86.6% (kappa value, 0.725; 95% CI, 0.607 to 0.843; $P = 0.815$). Ninety-eight percent of the women rated their experience as good to excellent. Moreover, 95% of women preferred self-sampling to physician sampling. Self-sampling using the dry Evalyn Brush system is as good as a physician-taken sample for hrHPV detection and is highly acceptable to women. To validate this self-sampling device for clinical use, a large screening cohort should be studied.

Cervical cytology screening programs have significantly decreased the incidence and mortality of cervical cancer. Primary screening using high-risk human papillomavirus (hrHPV) detection has been found to be more sensitive than conventional cervical cytology for detecting cervical precancer (11, 34, 41, 42). All data argue for the implementation of hrHPV testing as a primary test in cervical cancer screening, and the Health Council in the Netherlands has advised the Minister of Health to implement primary screening with hrHPV detection as a way of improving cervical cancer prevention (24).

Cervical cancer incidence is higher among women who do not respond (nonresponders) or have no access to cervical screening programs than in screened women. A substantial number of nonresponders participate in screening when given the opportunity of self-sampling for hrHPV testing (1, 19). Self-sampling for hrHPV therefore has the potential to reduce cervical cancer incidence, especially among nonresponders (5).

Cervicovaginal self-collected samples (self-samples) have proved to be as reliable as physician-obtained cervical samples for the detection of hrHPV (9, 22, 37–39, 44–45, 50). Studies on HPV self-sampling have used a great variety of collection devices, such as tampons, swabs, cervicovaginal brushes, and cervicovaginal lavage. Women are more familiar and comfortable with tampons than with other self-sampling methods, and the use of tampons is an attractive self-sampling method for women (15, 22, 23). However, tampons need more extensive processing than swabs and brushes for performance of HPV analysis (21). Furthermore, studies that used a brush or lavage (7–9, 43) for self-collection have demonstrated a higher sensitivity for cervical intraepithelial neoplasia grade two or worse (CIN2+) than studies that used a Dacron or cotton swab (2, 6, 48, 51).

Although cervicovaginal lavage is the most studied self-sampling technique (1, 3, 9, 20, 31, 37), the main disadvantage is that liquid specimens are not convenient to send by mail. This might be an obstacle in national screening programs (32). Brushes, on the other hand, may be used for dry transport and storage (47). Richman et al. (40) showed that the majority of women who were offered the choice between the Qiagen cervical brush, the Fournier cervical self-sampling device, and the Pantarhei cervicovaginal lavage preferred the brush. Brushes are flexible and easy to use, can be processed in the same way as physician-obtained smears, and are suitable for sending by mail (32, 44, 45). Although self-sampling for HPV testing is very acceptable to women, they are still concerned about performing the self-sampling procedure properly (4, 14, 16, 22, 37, 49).

To improve women's confidence and the convenience of performing self-sampling, a new cervicovaginal self-sampling device, the Evalyn Brush, was developed. This device is more understand-

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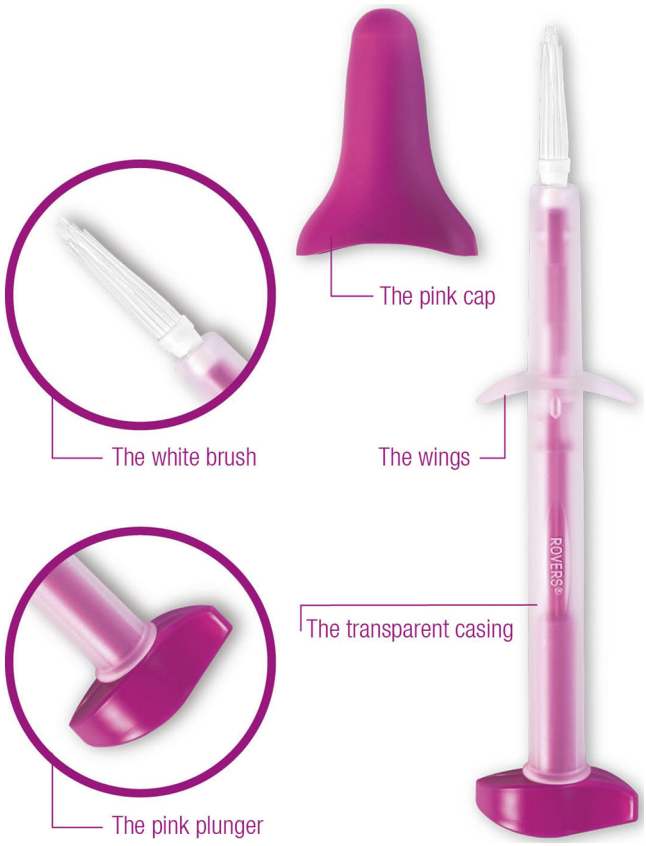

FIG 1 The Evalyn Brush. The Evalyn Brush is about 20 cm in length and consists of a transparent case with wings. Within the casing is a pink stick with a pink plunger at one end and a white brush at the other. You can push the white brush out of the case by pushing the pink plunger toward the transparent casing. After self-sampling, you can pull the brush back in, and a cap can be clicked onto the case before transport.

able and user-friendly to women, as it indicates a standard depth of insertion and the number of rotations (Fig. 1). The depth of insertion is controlled by the wings. The brush needs to be rotated five times, and at each rotation, there is an audible click indicating the number of rotations. After self-sampling, the cap can be clicked onto the case and the brush can be sent by mail as is. The FTA cartridge, another previously reported dry storage system (13, 32), has the disadvantage that the DNA from the brush can be only partly transferred to the cartridge.

We conducted the present study to investigate clinical applicability of the Evalyn Brush as a dry transport system compared to concurrently physician-obtained samples for the detection of hrHPV. We also investigated the acceptability of self-sampling using this device and women's preferences for self-sampling or physician sampling.

MATERIALS AND METHODS

Clinical specimen collection. Clinical specimens were collected between September 2010 and May 2011 from 134 women aged 18 years and above visiting the gynecological outpatient clinics of the Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, and of the Reinier de Graaf Hospital, Voorburg, Netherlands, for colposcopic evaluation due to an abnormal Pap smear or for a follow-up visit after an abnormal Pap smear. Women self-collected a cervicovaginal sample with the Evalyn Brush (Rovers Medical Devices B.V., Oss, Netherlands) after they had received verbal and written instructions with illustrations and consented to the study. After the specimen was obtained, a cap was clicked onto the case, and it was stored dry in the original state. After self-sampling, a trained physician obtained a liquid-based cytology sample using a Rovers Cervex-Brush (Rovers Medical Devices B.V., Oss, Netherlands). The Cervex-Brush was rinsed in ThinPrep medium (Hologic, Marlborough, MA) at Radboud University Nijmegen Medical Centre and in SurePath medium (Klinipath BV, Duiven, Netherlands) at Reinier de Graaf Hospital. Cytological examination and classification were performed at the local laboratory according to the CISOE-A (composition, inflammation, squamous epithelium, other and endometrium, endocervical columnar epithelium, and adequacy of the smear) classification, which can easily be translated into the Bethesda 2001 classification (10). All samples were stored and transported at room temperature to DDL Diagnostic Laboratory, Voorburg, Netherlands, for molecular testing. All samples were assigned an anonymous, unique patient code.

Questionnaires. To investigate the acceptability of using the Evalyn Brush, all women were asked to fill out a short questionnaire using a 5-point ordinal scale to record their general experience, their response to the instructions, and their assessment of the convenience of using the Evalyn Brush. Participants were also asked whether they preferred self-sampling or physician sampling.

Specimen preparation. The dry Evalyn Brush was resuspended in 1 ml of ThinPrep. The vials were vortexed for 3 × 15 s, stored overnight at 4°C, and again vortexed for 2 × 15 s. From each resuspended dry Evalyn brush specimen and from each cervical cytological specimen in liquid-based medium, 250 μl was used to obtain 100 μl of eluate with the QIAamp MinElute Virus Spin kit (Qiagen Inc., Valencia, CA) as described by the manufacturer. The mean interval between obtaining the specimen and HPV DNA isolation was 2 months, with a range of 2 weeks to 6 months. Each DNA isolation and PCR test run contained HPV-positive and -negative controls. All self-collected and physician-obtained samples were tested for HPV with both the analytically sensitive SPF_{10}-PCR system (29, 30) and the clinically validated GP5+/6+-PCR-based test (25, 35).

HPV detection and genotyping. (i) SPF_{10} PCR-DEIA-$LiPA_{25}$ system. Broad-spectrum HPV DNA amplification was performed using a short-PCR-fragment assay (HPV SPF_{10}-$LiPA_{25}$, version 1; Labo Bio-medical Products B.V., Rijswijk, Netherlands). This assay amplifies a 65-bp fragment of the L1 open reading frame of HPV genotypes, as described by Kleter et al. (29, 30). HPV detection of at least 54 anogenital HPV genotypes was performed using a cocktail of 9 conservative probes in a microtiter hybridization assay, the DNA enzyme immunoassay (DEIA) (30, 36). The samples positive for HPV by DEIA were then analyzed with the line probe assay ($LiPA_{25}$) by reverse hybridization with type-specific probes for HPV 6, 11, 16, 18, 31, 33, 34, 35, 39, 40, 42, 43, 44, 45, 51, 52, 53, 54, 56, 58, 59, 66, 68/73, 70, and 74 (29). The LiPA strips were visually inspected and interpreted following the standardized reference guide.

(ii) GP5+/6+-EIA-LQ HPV amplification and detection. The samples were also tested with the clinically validated hrHPV GP5+/6+ primer-mediated PCR assay (Diassay, Rijswijk, Netherlands). With this, detection of DNA from 14 hrHPV genotypes, i.e., HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, can be determined (46). Briefly, 10 μl of DNA was amplified with the biotin-labeled GP5+/6+ primer set. The GP5+/6+ amplimers were subsequently genotyped by the *digene* HPV Genotyping LQ test using xMAP technology for high-throughput screening (Qiagen, Hilden, Germany) according to the manufacturer's instructions (18).

For the comparison of the two collection systems, only the 14 hrHPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68 were evaluated. Comparing the presence of hrHPV between the samples, results were classified as identical, concordant, or discordant. If all genotypes were the same in both samples, the results were called identical. If analyses showed at least one identical genotype in both samples, the results were called

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TABLE 1 Agreement in hrHPV positivity (14 hrHPV genotypes) in self-sampled dry Evalyn Brush samples compared to physician-obtained samples with SPF_{10}-DEIA-$LiPA_{25}$ in relation to the diagnoses

Diagnosis	*n*	hrHPV positivity[a] detected by SPF_{10} in:				κ (95% CI)	*P* value
		Dry Brush and physician-obtained samples	Physician-obtained samples only	Dry Brush samples only	Neither of the two systems		
Negative[b]	70	21	7	3	39	0.695 (0.522–0.868)	0.344
BMD[c]	28	15	0	5	8	0.632 (0.360–0.904)	0.063
CIN 1	9	4	1	1	3	0.550 (0.001–1.000)	1.500
CIN 2	13	11	0	0	2	1.000 (1.000–1.000)	2.000
CIN 3	14	11	2	0	1	0.440 (0–1.000)	0.500
Total	134	62	10	9	53	0.715 (0.597–0.834)	1.000

[a] Values indicate the number of samples.
[b] Two of these results were not obtained at the same time as the sample for HPV analysis was obtained.
[c] Three of these results were not obtained at the same time as the sample for HPV analysis was obtained; one of these samples was a vagina top smear. BMD, borderline or mild dyskaryosis.

concordant. Genotype results were called discordant when the genotypes were different.

Statistical analysis. The level of agreement was determined using Cohen's kappa statistics. The two-tailed McNemar's test was used for mutual comparison of positivity rates. The level of statistical significance was set at 0.05. All analyses were performed using SPSS version 17.0 for Windows (Chicago, IL). Cytology and histology data were used to investigate clinically relevant differences in hrHPV detection.

This study was approved by the local medical ethical committees of both hospitals.

RESULTS

A self-collected sample and a subsequent conventional physician-taken cervical smear were obtained from 134 women (mean age, 40 years [standard deviation {SD}, 9.5 years]; range, 21 to 66 years). For 44 of the 134 women, histology results were available. Of the 44 biopsy specimens, 8 contained normal tissue, 9 had a CIN1 lesion, 13 a CIN2 lesion, and 14 a CIN3 lesion. Cytology results were available for all women. If a histology diagnosis was available, this was used in the analyses of hrHPV detection in relation to cytohistological diagnosis. Five of the cytology results were not obtained during the same visit as that in which the sample for HPV analysis was obtained. Of these five women, three had an earlier smear with borderline dyskaryosis and two had an earlier negative result. These earlier results were used as the diagnoses in the analyses of hrHPV detection for women without concurrent cytohistological diagnoses.

SPF_{10} PCR-DEIA-$LiPA_{25}$ system. Table 1 shows the SPF_{10} PCR-DEIA-$LiPA_{25}$ results in relation to the cytohistological diagnoses. The hrHPV positivity rate in physician-taken samples was 72/134 (54%) using the SPF_{10}-DEIA-$LiPA_{25}$ system. By comparison, 71 (53%) of the self-samples were hrHPV positive with SPF_{10}-PCR. Ten women were SPF_{10} positive in the physician-taken samples but negative in self-samples, and 9 women tested positive in self-samples only but negative on the physician-taken sample. Fifty-three women were hrHPV negative in both samples. These differences in hrHPV results were observed in all diagnostic categories. There was no difference in the percentage of HPV positivity and the number of discordant cases between the specimens that were tested after 2 weeks to 1 month and the specimens that were tested after 2 to 6 months (data not shown). There was good agreement for hrHPV detection using SPF_{10}-DEIA-$LiPA_{25}$ between the self-sample and the physician-taken sample (kappa value [κ] = 0.715; 95% confidence interval [CI], 0.597 to 0.843; $P = 1.000$) with 85.8% concordance. Of the 62 samples that were SPF_{10} positive in the physician-taken sample and the self-sample, 41 (66%) showed identical hrHPV genotypes, 18 (29%) showed concordant hrHPV genotypes, and 3 (5%) showed discordant genotypes. In the concordant cases, in 7/18 (39%) cases the self-sample detected an additional hrHPV genotype and in 5/18 (28%) cases an additional hrHPV type was detected in the physician-taken sample. In the 6 other cases, one or two genotypes were replaced by one or two other genotypes in the other sample. In 3 discordant cases, the physician-taken samples showed HPV types 52, 56, 31, and 39/68/73 ($LiPA_{25}$ cannot distinguish between these types), whereas the self-samples showed HPV types 16, 31, and 16, respectively.

The 72 physician-taken samples and 71 self-samples that were SPF_{10}-DEIA positive were genotyped by $LiPA_{25}$. Only the 14 hrHPV types were considered. Table 2 shows that the overall agreement for hrHPV genotyping between physician-taken samples and self-samples was good (κ = 0.691; 95% CI, 0.617 to 0.766; $P = 1.000$). No statistically significant differences were found. From the 72 hrHPV-positive physician-taken samples, 25 (35%) contained a multiple infection with two or more hrHPV types, compared to 20/71 (28%) in the self-samples.

GP5+/6+-LQ. Table 3 shows the GP5+/6+-LQ test results in relation to the cytohistological diagnoses. With GP5+/6+-PCR, hrHPV was detected in 58 (43%) of 134 physician-taken samples. A similar number of self-samples tested hrHPV positive (56/134 [42%]; $P = 0.815$). Ten samples were found GP5+/6+ positive in physician-taken samples but negative in self-samples. Only two of these physician-taken samples were also SPF_{10} positive. Both were negative by SPF_{10} in self-samples. With GP5+/6+-PCR, hrHPV was detected in eight self-samples that were negative in the physician-taken sample. For 68 women both samples were hrHPV negative, and for 48 women both samples were hrHPV positive. None of the diagnostic categories showed a significant difference in hrHPV detection. The concordance for hrHPV detection using GP5+/6+-LQ between self-samples and physician-taken samples was 86.6%, with good agreement (κ = 0.725; 95% CI, 0.607 to 0.843; $P = 0.815$).

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TABLE 2 Comparison of hrHPV genotyping by SPF_{10}-DEIA-$LiPA_{25}$ in physician-obtained and dry Evalyn Brush samples

Genotype	hrHPV positivity[a] detected by SPF_{10}-$LiPA_{25}$ in:				κ value (95% CI)	*P* value
	Dry Brush and physician-obtained samples	Physician-obtained samples only	Dry Brush samples only	Neither of the two systems		
HPV16	13	1	3	117	0.850 (0.706–0.994)	0.625
HPV18	8	2	0	124	0.881 (0.719–1.000)	0.500
HPV31	8	3	6	117	0.604 (0.369–0.839)	0.508
HPV33	5	1	0	128	0.905 (0.721–1.000)	1.000
HPV35	2	1	0	131	0.796 (0.407–1.000)	1.000
HPV39	2	4	2	126	0.378 (0–0.770)	0.687
HPV45	2	0	0	132	1.000 (1.000–1.000)	2.000
HPV51	7	0	4	123	0.763 (0.540–0.985)	0.125
HPV52	5	5	5	119	0.460 (0.177–0.743)	1.000
HPV56	4	3	3	124	0.548 (0.226–0.870)	1.000
HPV58	1	1	0	132	0.663 (0.044–1.000)	1.000
HPV59	4	4	0	126	0.653 (0.339–0.967)	0.125
HPV66	9	1	4	120	0.763 (0.563–0.962)	0.375
HPV68/73	1	2	2	129	0.318 (0–0.812)	1.000
HPV39/68/73	0	2	0	132	NC[b]	0.500
Any type	71	30	29	1,880	0.691 (0.617–0.766)	1.000

[a] Values indicate the number of samples.
[b] NC, this quantity cannot be calculated.

All GP5+/6+-positive samples were genotyped by LQ. Only the 14 hrHPV types were considered. The results are shown in Table 4. The 48 samples that were GP5+/6+-LQ positive in both the physician-taken sample and the self-sample did not show discordant genotypes, 37/48 samples (77%) had identical hrHPV genotypes, and 11/48 (23%) had concordant hrHPV genotypes. We found good agreement for hrHPV genotyping between physician-taken samples and self-samples (κ = 0.768; 95% CI, 0.691 to 0.846; $P = 0.110$). A multiple infection with two or more genotypes was found in 24% (14/58) of the physician-taken samples and 25% (14/56) of the self-samples.

Detection rate of CIN2+. CIN2+ was present in 27 women (20.1%). The sensitivities for the detection of CIN2+ in physician-obtained samples with the SPF_{10} and the GP5+/6+-PCR were 88.9% and 81.5%, respectively, and in the self-samples 81.5% and 74.1%, respectively (Table 5). The specificities for the detection of CIN2+ samples in physician-taken samples with the SPF_{10} and the GP5+/6+-PCR were 55.1% and 66.4%, respectively, and in the self-samples 54.2% and 66.4%, respectively.

No significant difference in the sensitivity for the detection of CIN2+ could be found between the physician-taken samples and the self-samples with both detection methods (for SPF_{10}, $P = 0.500$; and for GP5+/6+, $P = 0.625$).

Questionnaires. Of the 134 questionnaires, 127 (95%) were returned for analysis. The results from the questionnaires are shown in Table 6. From this group, 124 (98%) women rated their experience with the brush as good to excellent. The instructions for using the Evalyn Brush were considered good to excellent by 124 (98%) of the 127 women, and 125 (98%) women rated the convenience of using this self-sampling device as good to excellent. Most women ($n = 120$ [95%]) preferred self-sampling to physician sampling because it was simple, easy, and less painful than a physician-collected smear. Also women that never used tampons judged their experience with the brush as very good.

TABLE 3 Agreement in hrHPV positivity (14 hrHPV genotypes) in self-sampled dry Evalyn Brush samples compared to physician-obtained samples with GP5+/6+-LQ in relation to the diagnoses

Diagnosis	*n*	hrHPV positivity[a] detected by GP5+/6+ in:				κ value (95% CI)	*P* value
		Dry Brush and physician-obtained samples	Physician-obtained samples only	Dry Brush samples only	Neither of the two systems		
Negative[b]	70	13	4	4	49	0.689 (0.490–0.889)	1.273
BMD[c]	28	12	1	3	12	0.716 (0.460–0.971)	0.625
CIN 1	9	4	2	0	3	0.571 (0.098–1.000)	0.500
CIN 2	13	9	1	1	2	0.567 (0.032–1.000)	1.500
CIN 3	14	10	2	0	2	0.588 (0.107–1.000)	0.500
Total	134	48	10	8	68	0.725 (0.607–0.843)	0.815

[a] Values indicate the number of samples.
[b] Two of these results were not obtained at the same time as the sample for HPV analysis was obtained.
[c] Three of these results were not obtained at the same moment as the sample for HPV analysis was obtained; one of these samples was a vagina top smear. BMD, borderline or mild dyskaryosis.

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TABLE 4 Comparison of hrHPV genotyping by GP5+/6+-LQ in physician-obtained and dry Evalyn Brush samples

Genotype	hrHPV positivity[a] detected by GP5+/6+-LQ in:				κ value (95% CI)	*P* value
	Dry Brush and physician-obtained samples	Physician-obtained samples only	Dry Brush samples only	Neither of the two systems		
HPV16	11	4	3	116	0.729 (0.539–0.920)	1.000
HPV18	7	1	1	125	0.867 (0.686–1.000)	1.000
HPV31	6	3	2	123	0.686 (0.427–0.945)	1.000
HPV33	5	1	0	128	0.905 (0.721–1.000)	1.000
HPV35	2	0	0	132	1.000 (1.000–1.000)	2.000
HPV39	2	0	1	131	0.796 (0.407–1.000)	1.000
HPV45	2	0	0	132	1.000 (1.000–1.000)	1.000
HPV51	4	3	1	126	0.651 (0.334–0.969)	0.625
HPV52	1	1	1	131	0.492 (0–1.000)	1.000
HPV56	4	4	0	126	0.653 (0.339–0.967)	0.125
HPV58	2	1	0	131	0.796 (0.407–1.000)	1.000
HPV59	3	0	1	130	0.853 (0.570–1.000)	1.000
HPV66	8	2	1	123	0.830 (0.642–1.000)	1.000
HPV68	0	1	0	133	NC[b]	1.000
Any type	56	21	11	1,658	0.768 (0.691–0.846)	0.110

[a] Values indicate the number of samples.
[b] NC, this quantity cannot be calculated.

Women also liked the option of self-sampling because it was time saving, as no visit to the clinician was needed. The most frequent reason (6/7 [86%]) for preferring the physician-taken smear was that the women considered it more reliable. Among the women who preferred self-sampling to physician sampling, 2/120 (2%) nevertheless considered the physician-taken sample more reliable and 3/120 (3%) questioned whether they had performed the test correctly. Women commented on the appearance of the Evalyn Brush and said that they liked the color.

DISCUSSION

The dry self-samples showed good agreement with the physician-taken samples in hrHPV detection with both the analytically sensitive SPF_{10}-PCR and the clinically validated GP5+/6+-PCR. Our results indicate that self-sampling using the dry Evalyn Brush system is as good as a physician-taken smear for hrHPV detection. Our results are in line with previous studies showing repeatedly that self-collected cervicovaginal samples are as reliable as clinician-collected specimens for hrHPV detection (9, 12, 19, 26, 28, 37–39, 44).

Previous HPV self-sampling studies have used a variety of collection devices and HPV DNA tests. The concordance between the dry brush system and physician sampling in this study was 85.8% with SPF_{10} and 86.6% with GP5+/6+. This is comparable with the mean concordance calculated in the meta-analysis of Petignat et al. (87%) (39) and with the more recent review of Schmeink et al. (85.2%) (44). The kappa statistic showed good agreement between self-sampling and physician sampling for hrHPV in this study (κ = 0.715 and κ = 0.725). This agreement was higher than the mean κ obtained by Schmeink et al. (κ = 0.60) (44) and by Petignat et al. (κ = 0.66) (39). In our study, the sensitivities for CIN2+ did not differ significantly between the self-samples and the physician-taken samples. Some previous publications reported that self-sampling has a lower sensitivity than clinician sampling for HPV detection (2, 8, 17, 33, 37, 45, 51, 52), but these results have not been consistently found (9, 22, 26). The difference in sensitivity between studies might be due to differences in collection devices (brush, swab, tampon, or lavage), populations (screening population or women with an abnormal Pap smear), and the HPV DNA tests used. Schmeink et al. concluded that PCR-based HPV testing shows better results than studies performed with HC2. From our results, it appears that the use of an analytically sensitive test, like the SPF_{10}, results in a lower specificity than that obtained with the less sensitive GP5+/6+. Further studies are needed to determine the most suitable test in different populations.

The Evalyn Brush is a well-accepted self-sampling method for HPV detection according to 98% of women who used this device because it is easy to use, time saving, and more comfortable than collection by a physician. This self-sampling device was specifically designed to improve women's confidence in, and the convenience of, self-sampling. Indeed, 95% of women preferred self-sampling to physician sampling. The few women in our study who

TABLE 5 Sensitivity and specificity for the two collection devices with the SPF_{10} and the GP5+/6+-system for the detection of CIN2+

Characteristic	Physician-obtained samples[a]		Dry Brush samples[a]	
	SPF_{10}	GP5+/6+	SPF_{10}	GP5+/6+
Sensitivity	88.9% (24/27)	81.5% (22/27)	81.5% (22/27)	74.1% (20/27)
Specificity	55.1% (59/107)	66.4% (71/107)	54.2% (58/107)	66.4% (71/107)

[a] Values in parentheses are number of samples in which CIN2+ was detected/total number.

TABLE 6 Questionnaire results

Question topic	Excellent		Very good		Good		Moderate		Poor	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Experience	43	34	39	31	42	33	3	2	0	0
Instructions	46	36	35	28	43	34	3	2	0	0
Convenience	45	35	45	35	35	28	1	1	1	1
Convenience compared to physician-taken smear	56	44	30	24	34	27	5	4	2	1

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preferred clinician sampling specified their main reason as fear of inadequate self-sampling. This is in line with findings of previous studies (14, 23, 28, 40, 49). Acceptability of the self-sampling device may be important for women who ignore the invitation to attend the national cervical cancer screening program or in settings without organized cervical screening programs (27). Use of the Evalyn Brush may help increase the participation rate for cervical screening programs.

A limitation of this study is that it was performed in a hospital setting. Self-sampling is shown to be accepted well by women with a history of an abnormal Pap smear, but this study population is not representative of the broader population of women not participating in screening. Therefore, this study cannot be generalized to such a population. Another theoretical limitation is that the self-sample was always obtained before the physician-taken smear. This was done to avoid interference with HPV detection by the lubricating gel used on the speculum. The order of sampling could influence the amount of HPV DNA sampled, but Harper et al. (21) showed in a randomized controlled trial that the order of sampling did not influence the result. Third, the number of patients included in this study is small. The response rate and performance of the Evalyn Brush are currently being investigated in nonresponders to the Netherlands national screening program.

In conclusion, although the number of women included in this study was limited, the dry-stored Evalyn Brush showed good agreement for hrHPV detection with the physician-taken smears and is a well-accepted self-sampling device. Clinical validation and evaluation of the acceptability of this self-sampling device in screening populations should be the next step.

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