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Comparative performance of Cobas 4800 and 5800 assays with Cobas 6800 assay for detecting/genotyping high-risk HPV in cervical samples: An interlaboratory evaluation in Maputo, Mozambique

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Abstract:

Background: High-risk (hr) human papillomaviruses (HPV) testing is immensely important in elucidating molecular epidemiology of HPV infections and has become an essential part of current clinical practice in the management of the precancerous lesions and cervical cancer risks. Evaluation of HPV testing systems suitable for large-scale organized cervical screening programs is required. Very little is known about the diagnostic performance of the Cobas assays in resource-limited settings, particularly in Mozambique. We evaluated the concordance of the Cobas 4800 and Cobas 5800 assays with the Cobas 6800 assay for detecting high-risk HPV genotypes in clinician-collected cervical samples.
Methodology: In Mozambique, HPV-based cervical cancer screening is being regionally implemented and is currently well established in Maputo using the Cobas 4800, Cobas 5800 and Cobas 6800 assays. A random subset of 124 samples from women older than 18 years attending organized cervical cancer screening and previously tested for hrHPV-DNA using Cobas 4800 and Cobas 5800, were used for a subsequent analysis on Cobas 6800.
Results: Our results showed a good-to-high overall concordance of the Cobas 4800 and Cobas 5800 tests with Cobas 6800 test, showing strong Cohen's kappa values (95%, κ=0.89, 95% CI: 0.80–0.98, for Cobas 4800 versus Cobas 6800; and 100%, κ=1.00, 95% CI: 1.00–1.00 for Cobas 5800 versus Cobas 6800). Similar performance to detect HPV-16, HPV-18, and the 12 other hrHPV genotypes was observed.
Conclusion: The global performance to detect the 14 hrHPV genotypes was not significantly different between the three Cobas assays, which supports their suitability for use in large centralized laboratories included within population-based cervical cancer screening programs in resource-limited settings.

Keywords. Cervical cancer screening, HPV testing; Cobas assays; Performance; Interlaboratory comparison

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Performances comparatives des tests Cobas 4800 et 5800 avec le test Cobas 6800 pour la détection/génotypage des HPV à haut risque dans des échantillons cervicaux: Une évaluation interlaboratoires à Maputo, Mozambique

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Résumé:

Contexte: Le test des papillomavirus humains à haut risque (hrHPV) est d'une importance majeure pour élucider l'épidémiologie moléculaire des infections à HPV. Il est devenu un élément essentiel de la pratique clinique actuelle pour la prise en charge des lésions précancéreuses et des risques de cancer du col de l'utérus. L'évaluation des systèmes de dépistage du HPV adaptés aux programmes de dépistage cervical organisé à grande échelle est nécessaire. Très peu de données existent concernant la performance diagnostique des tests Cobas dans les contextes à ressources limitées, en particulier au Mozambique. Nous avons évalué la concordance des tests Cobas 4800 et Cobas 5800 avec le test Cobas 6800 pour la détection des génotypes hrHPV dans des échantillons cervicaux prélevés par des cliniciens.
Méthodologie: Au Mozambique, le dépistage du cancer du col de l'utérus basé sur le HPV est mis en œuvre à l'échelle régionale et est actuellement bien établi à Maputo grâce aux tests Cobas 4800, Cobas 5800 et Cobas 6800. Un sous-ensemble aléatoire de 124 échantillons de femmes âgées de plus de 18 ans, participant à un programme organisé de dépistage du cancer du col de l'utérus et préalablement testées pour l'ADN hrHPV avec les tests Cobas 4800 et Cobas 5800, a été réanalysé avec le test Cobas 6800.
Résultats: Nos résultats ont montré une concordance globale bonne à élevée des tests Cobas 4800 et Cobas 5800 avec le test Cobas 6800, avec des valeurs de kappa de Cohen élevées (95%, κ= 0,89, IC 95%: 0,80–0,98, pour Cobas 4800 versus Cobas 6800; et 100%, κ=1,00, IC 95%: 1,00–1,00 pour Cobas 5800 versus Cobas 6800). Des performances similaires ont été observées pour la détection du HPV-16, du HPV-18 et des 12 autres génotypes hrHPV.
Conclusion: Les performances globales pour la détection des 14 génotypes hrHPV n'ont pas montré de différences significatives entre les trois tests Cobas, ce qui confirme leur pertinence pour une utilisation dans les laboratoires centralisés de grande envergure intégrés aux programmes de dépistage du cancer du col de l'utérus dans les contextes à ressources limitées.

Mots-clés: Lésions cervicales; Dépistage HPV; Tests Cobas; Performance; Comparaison interlaboratoires

Introduction:

Human papillomavirus (HPV) is one of the most common sexually transmitted viruses worldwide and accounts for approximately 7.7% of all cancers in developing countries, predominantly cervical cancer, resulting in over 75,000 new cases and 50,000 deaths annually in sub-Saharan Africa (1,2). Infection with oncogenic types of HPV is the causative factor of nearly all (>99%) cases of cervical cancer (1,3). Fifteen genotypes (including HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82) are classified as oncogenic types of HPV, well known as high-risk HPV (hrHPV), and three genotypes (HPV 26, 53 and 66) are considered probably carcinogenic (4, 5).

Mozambique is among the countries with the highest burden of HPV infection, HIV and cervical cancer. Each year, over 5,300 new cases of cervical cancer and more than 3,800 deaths are registered (6), disproportionally affecting women living with HIV/AIDS (7,8). HPV infection is common among Mozambican women, with data indicating considerable prevalence rates of hrHPV (HPV 16, 18, 31, 33, 35, 45, 51, 52, and 58), varying from 26.3% to 75.9%, according to studies (9–13).

After the WHO Global strategy for the elimination of cervical cancer was launched (14), hrHPV-based tests have been increasingly adopted, as primary or co-test for cervical cancer screening, and for monitoring of the effectiveness of HPV vaccination (15,16). The key feature of hrHPV-based tests for cervical cancer screening is their high sensitivity and accuracy for screening women at risk for cervical lesions, as well as for detecting high-grade cervical intraepithelial neoplasia (CIN2+) and cervical cancer (CC), particularly in women above 30 years of age (16–18).

In Mozambique, the National Cancer Control Program, Ministry of Health has recently introduced (in Maputo) the pilot implementation of hrHPV testing in primary cervical screening to comply with the WHO guidelines. Although there have been many pilot projects and studies using several HPV tests (12,13, 19), the assay actually in use within the government healthcare system is the recently developed Cobas 5800/6800/8800 HPV DNA for use on the Cobas 5800/6800/8800 systems (20). The Cobas 4800 HPV DNA test which has been successfully deployed for primary HPV-based screening (21,22), was introduced for hrHPV screening in a cervical screening service at the DREAM program, Sant'Egídio (12). This test is for use on the Cobas 4800 system; an automated system that has been a reference standard for HPV screening programs due to its high sensitivity, reliability and ability to predict CIN2+ or worse (23–25).

Current guidelines recommend that, in order to enable testing in large centralized laboratories and ensure diagnostic accuracy, clinically validated HPV assays should be used (14,17). The aim of this study was to evaluate

the performance concordance of Cobas 4800 and Cobas 5800 tests with Cobas 6800 test for the detection and genotyping of hrHPV, using an interlaboratory comparative approach. Yet, there is no information on the performance concordance of these tests, nor on their clinical validation in the Mozambican context.

Materials and method:

Study design, population and ethical considerations:

This is a cross-sectional retrospective study, under the scope of activities of laboratory quality management in 2023 and 2024, of two molecular laboratories (DREAM Sant' Egidio laboratory and laboratory of Mavalane General Hospital), in Maputo, Mozambique. The DREAM Laboratory is accredited by the Portuguese Institute for Accreditation (IPAC) in accordance with ISO 15189 standards.

This study used samples from volunteer women aged >18 years, recruited at the DREAM Health Center in Zimpeto between July 2021 and May 2023 as part of a larger hrHPV screening study (HPV-ISI). The parent study evaluated the feasibility of hrHPV testing as a primary screening method, compared with the visual inspection with acetic acid (VIA) approach (12), and was conducted within the context of a routine cervical cancer screening program.

The HPV-ISI study was approved by the Mozambican national ethical committee (ref. 688/CNBS/20; amendment nº176/CNBS/22). Furthermore, due to the need to use the collected data for academic purposes, additional approval was obtained from the Institutional Review Board of the Eduardo Mondlane University–Faculty of Medicine and Maputo Central Hospital, Mozambique (ref. CIBSFM & HCM/01/2024). Informed written consents were obtained from all the participants, and all the samples and data were anonymized.

Samples and HPV testing:

A random subset of 124 samples was selected from a larger cohort of 1,323 previously tested for hrHPV-DNA at the DREAM Sant'Egidio laboratory using the Cobas 4800 system (Roche Diagnostics), from 2021-2023 (12) and Cobas 5800 in 2023. Only samples with valid hrHPV-DNA test results on both Cobas 4800 and Cobas 5800 were selected and included in the subset for the interlaboratory evaluation by subsequent analysis on Cobas 6800. Limited laboratory test resources were the primary reason for the choice of the sample size. Samples without age data and those from participants aged under 18 years were excluded.

The samples were collected by a trained health professional using cervical brush into a 20 mL liquid-based cytology media (Roche Cell Collection Medium), then followed by hrHPV DNA test using Cobas 4800/5800 assays. After testing, samples were stored at –20°C, until sent to the laboratory of Mavalane General Hospital, for a second/interlaboratory testing, using the Cobas 6800 HPV assay (Roche Diagnostics/Molecular Systems).

The Cobas 4800/5800/6800 tests are a real-time PCR based assays targeting hrHPV L1 gene and human β-globin gene as an internal control. All three tests allow the detection of 14 hrHPV types, genotyping HPV16 and HPV18 and reporting other 12 hrHPVs (including HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) as a "pooled" result in the same channel. The testing was carried out according to the manufacturer's instructions (20,26). If internal control was not amplified, samples were referred as invalid.

Statistical analysis:

Statistical analysis was performed using SPSS 30 software (IBM Corp., Armonk, New York, USA) and GraphPad QuickCalcs (https://www.graphpad.com/quickcalcs/). Quantitative variables were presented as median with interquartile range (IQR), and categorical variables were summarized with the number and percentage of participants in each category. A 2-tailed *p* value of <0.05 was considered significant.

McNemar's test and Cohen's kappa (κ) statistics were calculated to, respectively, assess differences in the proportion of positive samples and the level of agreement between the Cobas tests for detecting the 14 hrHPV types. The strength of agreement was classified according to the criteria described by Landis & Koch (27). Simple agreement was calculated by adding the agreement of the positive and negative results for both techniques; complete and partial discordant results were evaluated.

Results:

Of the 124 samples selected and included in the subset for the interlaboratory evaluation using Cobas 6800 system at the laboratory of Mavalane General Hospital, 94 samples (47 hrHPV-positive and 47 hrHPV-negative) had been previously tested with the Cobas 4800, while 30 samples (15 hrHPV-positive and 15 hrHPV-negative) had been tested with the Cobas 5800.

The median (IQR) age of the sampled participants was 42 (35–48) years, of whom the majority (61.3%) belonged to women aged 30-45 years, followed by 31.5% for >45 years, and 4.8% for 18-30 years. Information on age were missing for 3 (2.4%) participants. The median interval between sample collection

and testing was 5 days (IQR: 2–6 days) for Cobas 4800 and 10 days (IQR: 8–12 days) for Cobas 5800 at the DREAM Sant'Egidio laboratory, whereas for the testing with Cobas 6800 at the Mavalane General Hospital laboratory, it took 76 days (IQR: 59–202 days) for samples tested with Cobas 4800, and 17.5 days (IQR: 16–19 days) for those tested with Cobas 5800.

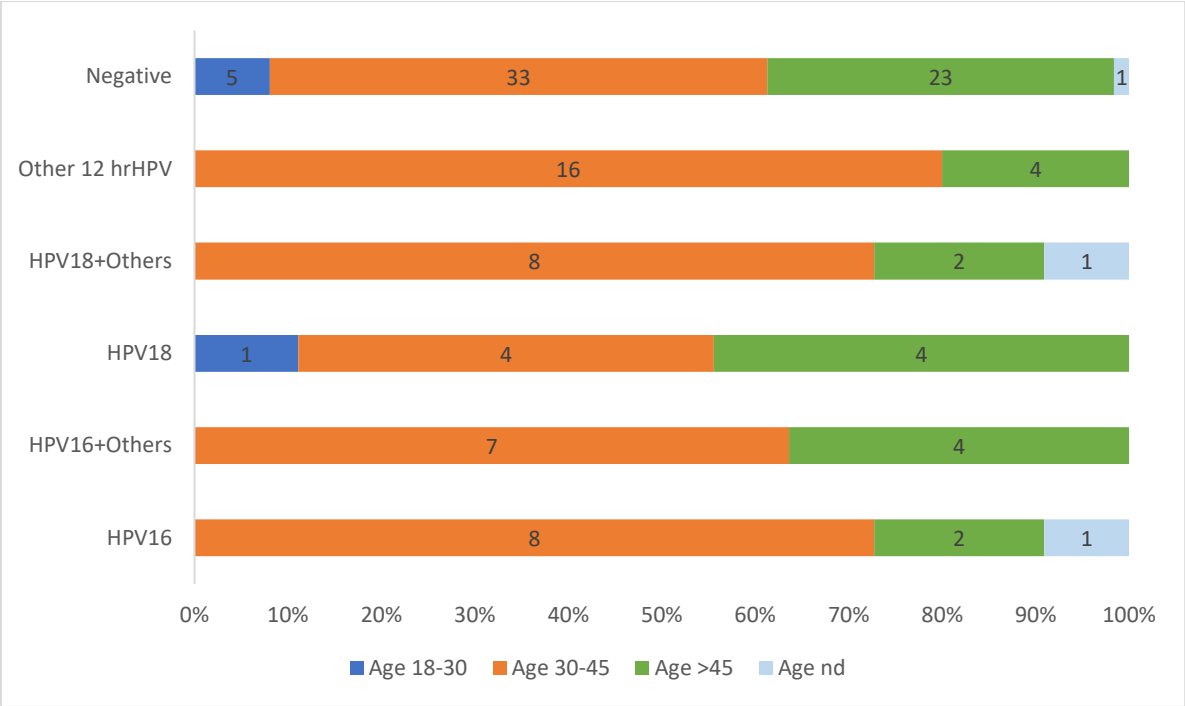
All 124 samples were tested with the three Cobas HPV DNA tests (4800, 5800 and 6800), and none of the samples failed for hr-HPV testing. Among the 94 samples tested with Cobas 4800 versus Cobas 6800, the prevalence of HPV16 alone, HPV18 alone, HPV16 with 'Other hrHPV', HPV18 with 'Other hrHPV', and 'Other hrHPV' types was not significantly different between the 2 tests: 11% versus 12% (p=0.82), 9.6% versus 8.5% (p=0.80), 8.5% versus 8.5% (p=1.00), 9.6% versus 10.6% (p=0.81), and 10.6% versus 10.6% (p=1.00), respectively.

A similar observation was found for the 30 samples tested with Cobas 5800 versus Cobas 6800, with prevalence of HPV16 with 'Other hrHPV', HPV18 with 'Other hrHPV', and 'Other hrHPV', accounting for 10%, 6.7%, and 50.0%, respectively, in both tests. HPV16 alone and HPV18 alone were not detected (Table 1). Fig 1 presents the overall distribution of hrHPV by age group, showing a considerable positivity rate among women aged 30-45 years.

Table 1: Prevalence of human papillomavirus (HPV) types 16 and 18 and other 12 high-risk HPV types found between Cobas 4800 and Cobas 6800 tests, and between Cobas 5800 and Cobas 6800 tests

hrHPV Type		**Cobas 4800 vs Cobas 6800 (n=94)**			**Cobas 5800 vs Cobas 6800 (n=30)**		
		c4800 n (%)	**c6800 n (%)**	***p* value[a]**	**c5800 n (%)**	**c6800 n (%)**	***p* value[b]**
All hrHPV							
	Negative	47 (50.0)	46 (48.9)	0.88	15 (50.0)	15 (50.0)	1.00
	Positive	47 (50.0)	48 (51.1)		15 (50.0)	15 (50.0)	
HPV16 alone							
	Negative	83 (88.3)	82 (87.2)	0.82	30 (100)	30 (100)	-
	Positive	11 (11.7)	12 (12.8)		0 (0)	0 (0)	
HPV18 alone							
	Negative	85 (90.4)	86 (91.5)	0.80	30 (100)	30 (100)	-
	Positive	9 (9.6)	8 (8.5)		0 (0)	0 (0)	
HPV16 + other hrHPV[c]							
	Negative	86 (91.5)	86 (91.5)	1.00	27 (90.0)	27 (90.0)	1.00
	Positive	8 (8.5)	8 (8.5)		3 (10.0)	3 (10.0)	
HPV18 + other hrHPV[c]							
	Negative	85 (90.4)	84 (89.4)	0.81	28 (93.3)	28 (93.3)	1.00
	Positive	9 (9.6)	10 (10.6)		2 (6.7)	2 (6.7)	
Other hrHPV types[c]							
	Negative	84 (89.4)	84 (89.4)	1.00	15 (50.0)	15 (50.0)	1.00
	Positive	10 (10.6)	10 (10.6)		15 (50.0)	15 (50.0)	

HPV: human papillomavirus; hrHPV: high-risk human papillomavirus; (-): not Applicable
[a]Calculated by Chi-square test but using Fisher exact test (given the relatively small total sample size: n=94 per group) a p value of 1.00 was observed for all comparisons
[b]Calculated by Fisher exact test (given the relatively small total sample size: n=30 per group)
[c]12 HPV types: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, "pooled" in the same channel



Other (s) 12 HPV types include 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, "pooled" in the same channel; HPV= human papillomavirus; hrHPV = high-risk human papillomavirus; nd = not determined/available

Fig 1: Overall distribution of hrHPV positivity by age interval

Further statistical analyses for method comparison were also performed on all samples; separately for Cobas 4800 versus Cobas 6800, and Cobas 5800 versus Cobas 6800, with an overall concordance of detecting any hrHPV of 94.68% (agreement on 89/94 samples, Kappa=0.89; 95% confidence interval: 0.80–0.98), and 100.0% (agreement on all 30 samples, Kappa=1.00), respectively. The concordance of the results between Cobas 4800 versus Cobas 6800 for detection of HPV16 alone, HPV18 alone, HPV16 with 'Other hrHPV', HPV18 with 'Other hrHPV', and 'Other hrHPV' types was 98.9%, 98.9%, 100%, 98.9%, and 95.7%, respectively (Table 2).

Five samples were discordant; (i) 1 for HPV16 positivity and 2 for 'Other hrHPV' positivity were missed by Cobas 4800 and detected by Cobas 6800; and (ii) 2 for 'Other hrHPV' positivity, detected by Cobas 4800, were missed by Cobas 6800. Additionally, one sample was partially discordant; Cobas 4800 detected only HPV18 while Cobas 6800 detected HPV18 with 'Other hrHPV' (Table 3). The 'Other hrHPV' was the most common type missed by the 2 methods (5/6 cases). In contrast, for Cobas 5800 versus Cobas 6800, all results were 100.0% concordant (absence of discordance); same agreement index were observed for genotyping HPV16+ 'Other hrHPV' and HPV 18+ 'Other hrHPV' (Table 2).

The agreement (Cohen kappa) between Cobas 4800 versus Cobas 6800 for detection of HPV16 alone, HPV18 alone, HPV16 with 'Other hrHPV', HPV18 with 'Other hrHPV', and 'Other hrHPV' types was 0.95 (CI: 0.85–1.00), 0.94 (CI: 0.81–1.00), 1.00 (CI: 1.00–1.00), 0.94 (CI: 0.83–1.00) and 0.78 (CI: 0.57–0.99), respectively. The performance to positively detect HPV-16 (alone/with 'Other hrHPV'), HPV-18 (alone/with 'Other hrHPV'), and 'Other hrHPV' were not significantly different between the 2 tests (McNemar test, $p>0.05$) (Table 2). In total, the global performance to detect any of the 14 hrHPV types was not significantly different (McNemar test, $p=1.00$).

Discussion:

This study aimed to evaluate, within an interlaboratory quality assessment process, the concordance of Cobas 4800 and Cobas 5800 tests with Cobas 6800 test in detecting and genotyping high-risk human papillomavirus (hrHPV) in 124 cervical samples (94 for Cobas 4800 *versus* Cobas 6800; and 30 for Cobas 5800 *versus* Cobas 6800), from women aged 18 years or older, screened for hrHPV in a cervical cancer screening service. To the best of our knowledge, this is the first study evaluating the diagnostic performance of the Cobas tests within the recently introduced pilot implementation of hrHPV testing in primary cervical screening in Maputo, Mozambique.

The results demonstrate a high level of agreement between Cobas 4800 and Cobas

Table 2: Agreement and performance between Cobas 4800 and Cobas 6800 tests, and between Cobas 5800 and Cobas 6800 tests in detecting Human Papillomavirus (HPV) types 16 and 18 and other 12 high-risk types

hrHPV Type		Number (%)	Cohen Kappa Test (95% CI)	McNemar Test
Cobas 4800 vs Cobas 6800 (n=94)				
All hrHPV				
	Concordant	89 (94.7)	0.89 (0.80–0.984)	1.00
	Discordant	5 (5.3)		
HPV16 alone, n (%)				
	Concordant	93 (98.9)	0.95 (0.85–1.00)	1.00
	Discordant	1 (1.1)		
HPV18 alone, n (%)				
	Concordant	93 (98.9)	0.94 (0.81–1.00)	1.00
	Discordant	1 (1.1)		
HPV16 + other hrHPV[a], n (%)				
	Concordant	94 (100)	1.00 (1.00–1.00)	-
	Discordant	0 (0)		
HPV18 + other hrHPV[a], n (%)				
	Concordant	93 (98.9)	0.94 (0.83–1.00)	1.00
	Discordant	1 (1.1)		
Other hrHPV types[a], n (%)				
	Concordant	90 (95.7)	0.78 (0.57–0.99)	1.00
	Discordant	4 (4.3)		
Cobas 5800 vs Cobas 6800 (n=30)				
All hrHPV[b]				
	Concordant	30 (100)	1.00 (1.00–1.00)	-
	Discordant	0 (0)		

Cohen Kappa test and McNemar test were performed to compare the agreement and the performance of the 2 methods to detect HPV-16, HPV-18, the other hrHPV types, and the 12 hrHPV types "pooled" in the same channel.
HPV: human papillomavirus; hrHPV: high-risk human papillomavirus; CI: Confidence interval; (-): not Applicable
[a]12 HPV types: 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, "pooled" in the same channel.
[b]Including for genotypes detection; All results between Cobas 5800 and Cobas 6800 tests were 100% concordant (absence of discordance)
–: same values of Cohen Kappa index and McNemar test were observed for hrHPV genotyping (HPV16 + other hrHPV and HPV18 + other hrHPV)

Table 3: Discordant and partial discordant results in the comparison of results between Cobas 4800 and Cobas 6800 tests*

Sample ID	Any hrHPV		hrHPV types		Result classification
	Cobas 4800	Cobas 6800	Cobas 4800	Cobas 6800	
11012	Negative	Positive	-	HPV16	Discordant
10891	Negative	Positive	-	Other hrHPV[a]	Discordant
1883	Negative	Positive	-	Other hrHPV[a]	Discordant
9839	Positive	Negative	Other hrHPV[a]	-	Discordant
9911	Positive	Negative	Other hrHPV[a]	-	Discordant
3193	Positive	Positive	HPV18	HPV18+Others[a]	partial discordant

HPV: human papillomavirus; hrHPV: high-risk human papillomavirus.
[a]12 HPV types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68, "pooled" in the same channel.
(*): All results between Cobas 5800 and Cobas 6800 tests were 100% concordant (absence of discordance)

5800 tests with the Cobas 6800 test across both laboratories, showing an overall concordance (95%, for Cobas 4800 *versus* Cobas 6800; and 100%, for Cobas 5800 *versus* Cobas 6800), which indicates an almost perfect agreement (27,28). These findings support the interchangeability of the three platforms in clinical and epidemiological hrHPV screening and surveillance programs. It is widely accepted that, to ensure a robust and highly reliable

test performance in clinical settings, the candidate assay must demonstrate inter-laboratory agreement with a lower confidence limit of no less than 87% (17).

The distribution of hrHPV types, including HPV 16, HPV 18, and Other hrHPV types, was largely comparable between both methods, with no statistically significant differences observed in their detection frequencies. Notably, the detection concordance for HPV16 and HPV-18, the two most oncogenic HPV genotypes, reached 98.9%, underscoring both platforms reliability in identifying these high-risk types. The complete agreement observed in cases with co-infection of HPV16 and Other hrHPV further reinforces the robustness of both assays in multi-type detection scenarios.

The discrepancies between the assays were minimal. Only five samples showed discordant results, with the Cobas 6800 slightly outperforming the Cobas 4800 by detecting three additional positive cases (one HPV16 and two Other hrHPV). Two samples were detected exclusively by the Cobas 4800, and one sample was partially discordant with differing co-infection profiles. The marginally higher detection of Other hrHPV by the Cobas 6800 could be attributed to its technological enhancements over the 4800 system, including analytical sensitivity and automation design, which allows for improved nucleic acid extraction and amplification (17,20,29). However, the difference was not statistically significant, and the kappa agreement for Other hrHPV was slightly lower compared to other genotype categories, suggesting a modest variation in detecting non-HPV16/18 genotypes, which are often present at lower viral loads (30). Similar discrepancies were also reported in other studies (23,24).

The age distribution of hrHPV positivity aligns with epidemiological patterns, where the highest burden of hrHPV was observed among women aged 30–45 years. This reinforces the importance of targeting this age group for primary HPV screening, especially in low- and middle-income settings where cervical cancer remains a leading cause of mortality among women (31,32).

One important procedural difference between the two laboratories involved in this study was the storage time between sample collection and testing. Samples processed at the Mavalane General Hospital laboratory had a significantly longer storage interval (median of 76 days for samples previously tested with Cobas 4800, and 17.5 days for those tested with Cobas 5800) compared to those at the DREAM Sant'Egidio (median of 5 days for Cobas 4800 and 10 days for Cobas 5800). Despite this, there was no impact on assay performance, underscoring the stability of cervical specimens in liquid-based cytology collection media under appropriate storage conditions, as previously reported (33–35).

Our findings support previous studies that have shown strong agreement between Cobas platforms (20,23,24,36), emphasizing their validity in clinical practice. Importantly, while the Cobas 4800 system is a medium throughput (384 samples/day), the Cobas 5800 and Cobas 6800 offers improved workflow efficiency, higher throughput (528 and >1500 samples/day, respectively), and reduced hands-on time, making it particularly suitable for large-scale screening programs and molecular testing for other viruses (20,26). Similar conclusions were also reached by studies that clinically evaluated the performance according to the Meijer criteria, and observed high agreement (>98%) for the two assays, and that clinical sensitivity and specificity met the non-inferiority criteria defined to consider an HPV assay as suitable for large-scale laboratory use (23,24,36).

This study has some limitations. The relatively small sample size, due to limited laboratory test resources, archival sample-based testing and the single-country setting may limit generalizability. Additionally, sequencing confirmation of discordant samples was not performed, which could have helped clarify the true-positive status. Nonetheless, the high concordance metrics and low number of discrepancies suggest these limitations did not significantly impact the conclusions.

Conclusion:

Based on the results of this study, all three Cobas platforms – 4800, 5800, and 6800 – demonstrated high concordance in detecting and genotyping high-risk HPV in cervical samples. These findings support the suitability of each platform for use in routine hrHPV screening programs and underscore the Cobas 6800 as a reliable, high-throughput option particularly well-suited for scaling up cervical cancer prevention efforts.

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Contribution of authors:

AS, TC and JS conceptualized and designed the study, acquired, analyzed and interpreted the data. All the authors drafted, revised, read, provided critical feedback and approved the manuscript.

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Data availability:

The data that support the findings made in this study can be made available from the corresponding author on request.

Disclaimer:

The views expressed in this study are those of the authors and are not an official position of the laboratories administrative; DREAM Program, Community of Sant'Egidio and Mavalane General Hospital.

References:

1. de Martel, C., Plummer, M., Vignat, J., and Franceschi, S. Worldwide burden of cancer attributable to HPV by site, country and HPV type. Int J Cancer. 2017; 141 (4): 664–670. doi/10.1002/ijc.30716.
2. Mboumba Bouassa, R. S., Prazuck, T., Lethu, T., et al. Cervical cancer in sub-Saharan Africa: a preventable noncommunicable disease. Expert Rev Anti Infect Ther. 2017; 15 (6): 613–627. doi: 10.1080/14787210.2017.1322902.
3. Walboomers, J. M. M., Jacobs, M. V., Manos, M. M., et al. Human papillomavirus is a necessary cause of invasive cervical cancer worldwide. J Pathol. 1999; 189 (1): 12–19. doi:10.1002/(SICI)1096-9896(199909)189:1<12::AID-PATH431>3.0.CO;2-F.
4. Muñoz-Bello, J. O., Carrillo-García, A., and Lizano, M. Epidemiology and Molecular Biology of HPV Variants in Cervical Cancer: The State of the Art in Mexico. Int J Mol Sci. MDPI; 2022; 23. doi: 10.3390/ijms23158566.
5. Arbyn, M., Tommasino, M., Depuydt, C., and Dillner, J. Are 20 human papillomavirus types causing cervical cancer? J Pathol. 2014; 234 (4): 431–435. doi: 10.1002/path.4424.
6. Bruni, L., Albero, G., Serrano, B., et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in Mozambique. Summary Report. 2023. www.hpvcentre.net.
7. Carrilho, C., Fontes, F., Tulsidás, S., et al. Cancer incidence in Mozambique in 2015–2016: data from the Maputo Central Hospital Cancer Registry. Euro J Cancer Prev. 2019; 28 (4): 373–376. doi: 10.1097/CEJ.0000000000000457.
8. Batman, S., Rangeiro, R., Monteiro, E., et al. Expanding Cervical Cancer Screening in Mozambique: Challenges Associated with Diagnosing and Treating Cervical Cancer. JCO Glob Oncol. 2023; (9). https://ascopubs.org/doi/10.1200/GO.23.00139
9. Edna Omar, V., Orvalho, A., Nália, I., et al. Human papillomavirus prevalence and genotype distribution among young women and men in Maputo city, Mozambique. BMJ Open. 2017; 7 (7): e015653. doi: 10.1136/bmjopen-2016-015653.
10. Bule, Y. P., Silva, J., Carrilho, C., et al. Human papillomavirus prevalence and distribution in self-collected samples from female university students in Maputo. Int J Gynecol Obstetr. 2020; 149 (2): 237–246. doi: 10.1002/ijgo.13126.
11. Maueia, C., Murahwa, A., Manjate, A., et al. Identification of the human papillomavirus genotypes, according to the human immunodeficiency virus status in a cohort of women from Maputo, Mozambique. Viruses. 2021; 14 (1): 24. doi: 10.3390/v14010024.
12. Sineque, A., Catalao, C., Ceffa, S., et al. Screening approaches for cervical cancer in Mozambique in HIV positive and negative women. Euro J Cancer Prev. 2023; 32 (5): 431- 437. doi: 10.1097/CEJ.0000000000000802.
13. Salcedo, M. P., Lathrop, E., Osman, N., et al. The Mulher Study: cervical cancer screening with primary HPV testing in Mozambique. Int J Gynecol Cancer. 2023; 33 (12): 1869.
14. World Health Organization. Introducing and scaling up testing for human papillomavirus as part of a comprehensive programme for prevention and control of cervical cancer: A step-by-step-guide. World Health Organization; 2020. https://iris.who.int/bitstream/handle/10665/336668/9789240015166-eng.pdf. (Accessed May 8, 2025).
15. Arbyn, M., Snijders, P. J. F., Meijer, C. J. L. M., et al. Which high-risk HPV assays fulfil criteria for use in primary cervical cancer screening? Clin Microbiol Infect. 2015; 21 (9): 817–826. doi: 10.1016/j.cmi.2015.04.015.
16. Ronco, G., Dillner, J., Elfström, K. M., et al. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. Lancet. 2014; 383 (9916): 524–532. doi: 10.1016/S0140-6736(13)62218-7.
17. Meijer, C. J. L. M., Berkhof, J., Castle, P. E., et al. Guidelines for human papillomavirus DNA test requirements for primary cervical cancer screening in women 30 years and older. Int J Cancer. 2009; 124 (3): 516–520. doi: 10.1002/ijc.24010.
18. Stanczuk, G., Baxter, G., Currie, H., et al. Clinical validation of hrHPV testing on vaginal and urine self-samples in primary cervical screening (cross-sectional results from the Papillomavirus Dumfries and Galloway-PaVDaG study). BMJ Open. 2016; 6 (4): e010660. doi: 10.1136/bmjopen-2015-010660.
19. de Oliveira, C. M., Salcedo, M. M. P., Mariano, A., et al. HPV testing for cervical cancer screening in Mozambique: Challenges and recommendations. J Glob Health Rep. 2022; 6: e2022007. doi:10.29392/001c.32432.
20. Roche Molecular Systems Inc. Cobas ® HPV Qualitative nucleic acid test for use on the Cobas ® 5800/6800/8800 Systems. Doc Rev. 09652736001-01. 2023. https://elabdoc-prod.roche.com/eLD/api/downloads/f5944ece-fcae-ee11-2191-005056a772fd?countryIsoCode=XG. (Accessed May 8, 2025).
21. Heideman, D. A. M., Hesselink, A. T., Berkhof, J., et al. Clinical Validation of the Cobas 4800 HPV Test for Cervical Screening Purposes. J Clin Microbiol. 2011; 49 (11): 3983–3985. doi: 10.1128/JCM.05552-11.
22. Lamin, H., Eklund, C., Elfström, K. M., et al. Randomised healthcare policy evaluation of organised primary human papillomavirus screening of women aged 56–60. BMJ Open. 2017; 7 (5): e014788. doi: 10.1136/bmjopen-2016-014788.
23. Frayle, H., Gori, S., Rizzi, M., et al. HPV testing for cervical cancer screening: Technical improve

ment of laboratory logistics and good clinical performance of the Cobas 6800 in comparison to the 4800 system. BMC Womens Health. 2019; 19 (1): 47. doi: 10.1186/s12905-019-0743-0.

24. Sundström, K., Lamin, H., and Dillner, J. Validation of the Cobas 6800 human papillomavirus test in primary cervical screening. PLoS One. 2021; 16 (2): e0247291. doi: 10.1371/journal.pone.0247291.
25. Liu, S. S., Chan, K. K. L., Wei, T. N., et al. Clinical performance of the Roche Cobas 4800 HPV test for primary cervical cancer screening in a Chinese population. PLoS One. 2022; 17 (8): e0272721. doi: 10.1371/journal.pone.0272721.
26. Roche Molecular Systems Inc. Cobas ® HPV Test for use on the Cobas ® 4800 System. Doc Rev. 05641268001-12 2016 https://www.accessdata.fda.gov/cdrh_docs/pdf10/p100020s017c.pdf. (Accessed May 8, 2025).
27. Landis, J. R., and Koch, G. G. The measurement of observer agreement for categorical data. Biometrics. 1977; 33 (1): 159.
28. Miot, H. A. Análise de concordância em estudos clínicos e experimentais. J Vasc Bras Soc Bras Ang e Cir Vasc. 2016: 15: 89–92. doi: 10.1590/1677-5449.004216.
29. Ogilvie, G. S., Krajden, M., van Niekerk, D. J., et al. Primary cervical cancer screening with HPV testing compared with liquid-based cytology: results of round 1 of a randomised cont rolled trial – the HPV FOCAL Study. Br J Cancer. 2012; 107 (12): 1917–1924. doi: 10.1038/bjc.2012.489.
30. Castle, P. E., Solomon, D., Wheeler, C. M., et al. Human Papillomavirus Genotype Specificity of Hybrid Capture 2. J Clin Microbiol. 2008; 46 (8): 2595–2604. doi:10.1128/JCM.00824-08.
31. Arbyn, M., Weiderpass, E., Bruni, L., et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health. 2020; 8 (2): e191–e203. doi: 10.1016/S2214-109X(19)30482-6. Erratum in Lancet Glob Health. 2022; 10 (1): e41. doi: 10.1016/S2214-109X(21)00554-4.
32. Bruni, L., Albero, G., Serrano, B., et al. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Human Papillomavirus and Related Diseases in the World. Summary Report. 2023. www.hpvcentre.net.
33. Castle, P. E., Solomon, D., Hildesheim, A., et al. Stability of archived liquid-based cervical cytologic specimens. *Cancer*. 2003; 99 (2): 89–96. doi: 10.1002/cncr.11058.
34. Agreda, P. M., Beitman, G. H., Gutierrez, E. C., et al. Long-Term Stability of Human Genomic and Human Papillomavirus DNA Stored in BD SurePath and Hologic PreservCyt Liquid-Based Cytology Media. J Clin Microbiol. 2013; 51 (8): 2702–2706. doi: 10.1128/JCM.00759-13.
35. Gilbert, L., Oates, E., and Ratnam, S. Stability of Cervical Specimens in SurePath Medium for Human Papillomavirus Testing with the Roche Cobas 4800 Assay. J Clin Microbiol. 2013; 51 (10): 3412–3414. doi: 10.1128/JCM.01391-13.
36. Saville, M., Sultana, F., Malloy, M. J., et al. Clinical Validation of the Cobas HPV Test on the Cobas 6800 System for the Purpose of Cervical Screening. J Clin Microbiol. 2019; 57 (2): e01239-18. doi: 10.1128/JCM.01239-18