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Decreased Inaccuracies in HIV Screening following Strengthening of Quality System: Evidence-based Interventions through the PMTCT Program in Cameroon

Baisse des Erreurs dans les Tests du VIH suite au Renforcement du Système Qualité: Expérience du Programme de PTME au Cameroun

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Mots clés: Test VIH, Assurance Qualité, PTME, Cameroun

ABSTRACT

Objective. To evaluate the evolution in error rates of HIV testing and the quality of HIV testing within the national PMTCT program before and after quality assurance interventions. **Methods.** We conducted a study from 2012 to 2016 among pregnant women in Cameroon. The quality system was evaluated with a checklist. Performance in HIV screening (sensitivity, specificity, positive predictive and negative values) was evaluated using the national reference laboratory as gold standard. Based on quality performance, a package of quality interventions was implemented and evaluated thereafter. **Results.** In 2012 and 2016, 6521 (93.2%) and 6859 (97.99%) eligible pregnant women were enrolled. Following quality interventions between the two surveys, a significant increased performance was reported from 2012 (average score: 56.25%) to 2016 (average score: 79.75%); p=0.0157. Sensitivity in HIV testing increased from 81.2% to 91.4% (p<0.00001); specificity increased from 99.3% to 99.6% (p=0.0058); positive- and negative-predictive values also increased respectively: 90.2% and 98.7% (2012) to 93.5% and 99.5% (2016); p<0.001. **Conclusion.** Evidence-based quality interventions are effective in reducing errors occurred during routine HIV testing. However, increased performance merits further efforts to meet the required standards (97.5% sensitivity and 99.8% specificity). Thus, implementing periodic quality interventions and re-testing of HIV-positive specimens will reduce diagnostic errors.

RÉSUMÉ

Objectif. Evaluer la variation des taux d'erreur dans les tests de VIH et le système qualité dans le programme national de PTME avant et après des interventions programmatiques sur l'assurance qualité. **Méthodes.** Une etude a été menée de 2012 à 2016 chez les femmes enceintes au Cameroun. A l'aide d'un checklist, le système qualité a été évaluaté. La performance diagnostic du VIH (sensitivité, spécificité, valeurs prédictives positive et négative) etait évaluatée les rersultats du laboratoire de référence comme standard. Sur la base de la performance, un paquet d'interventions qualité a été mis en œuvre et son impact évalué entre 2012 et 2016. **Resultats.** En 2012 et 2016, 6521 (93,2%) et 6859 (97,99%) de femmes enceintes eligibles étaient enrolées. Suivant les interventions qualité mises en oeuvre, une amelioration significative de la performance générale a été observée de 2012 (score moyen: 56,25%) à 2016 (score moyen: 79,75%); p=0,0157. La sensibilié du HIV s'est ameliorée significativement de 81,2% à 91,4% (p<0,00001); la spécificité s'est ameliorée significativement de 99,3% à 99,6% (p=0,0058); les valeurs prédictives positive et négative sont passées respectivement de 90,2% et 98,7% (2012) à 93,5% et 99,5% (2016) ; p<0,001. **Conclusion.** Les interventions probantes sur le système qualité se traduisent par baisse significative des erreurs dans le test du VIH en routine. Toutefois, de efforts sont nécessaires pour optimiser les performance vers les seuils standards (sensibilté : 97,5% ; specificité : 99,8%). Instituer une périodicité des interventions qualité et le re-testing des échantillons positifs permettrait de baisser davantage ces erreurs.

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INTRODUCTION

The Cameroonian population was estimated at 22,709,892 by end 2016 [1], in a context of declining HIV epidemics (5.5%-4.3% respectively in 2004-2011) [2,3]. Interestingly, projections indicate continuous decline in the epidemics, from 3.9%, 3.8% to 3.7% respectively in 2015, 2016 and 2017 [4]. In spite of the significant epidemiological decline recorded, HIV remains a generalised epidemic nationwide, with pregnant women serving as the target population for successful interventions toward prevention of mother-to-child transmission of HIV (PMTCT) in Cameroon as part of maternal and child healthcare. Of note, PMTCT program offers a package of activities consisting of antenatal care (ANC), HIV screening among preganant women and their respective partners, linkage of HIV-seropositive women to care for antiretroviral therapy (ART) and management of HIV-vertically exposed infants/children with antirrteorivral prophylaxis and early infant diagnosis of HIV-infection for timely treatment intitiaion [5]. Thus, meeting the expected targets for PMTCT requires regular but accurate HIV screening among pregnant women. Such testing, conducted routinely by health staff whose level of expertise might very considerably, is fundamental for HIV programmatic surveillance [6]. Out of 2,418,139 HIV screening performed in Cameroon among women in 2016, 26% (628,002) were solely within the context of PMTCT [6]. Of note, PMTCT option B+ (i.e. lifelong ART for all pregnant women irrespective of clinical or CD4 staging) was endorsed by Cameroon in 2012 and implemented effectively in 2014 [6-7]. Currently, the national ART programme has adopted the "*Test and Treat*" strategy for all individual tested positive for HIV regardless of CD4-count and clinical conditions [7]. With a wide/rapid scale of ART in this "*Test and Treat*" era, a wrong HIV positivity would directly weaken programme goals due to waste in resources associated with unnecessary ART provision lifelong; furthermore, the psycosocial effects on pateints could be largely detrimental, more prominently in a context of HIV serodiscordant couples. Such psycosocial impariements often lead to conflicting marital/family conditions that result in divorce, suicide, impaired children education, etc. In contrast, false negative results delivered to HIV-infected women has several implications amongwhich: up to 40% risks of MTCT, risks of continuous horizontal HIV transmission unknowingly to sexual partner(s) due to false laboratory report [8-10]. These aformentionned challenges urgently prompt the need of a strengthened quality assurance system for HIV testing for successful HIV prevention and treatment programs.

Our field experience on PMTCT in Cameroon revealed significant disparities in the accurate testing of HIV-infected ANC attendees, with varying performance across geographical settings or overtime (within the same site), most of which are below the WHO benchmark of 97.5% sensitivity and <99.8% specificity [11]. We thus hypothetised that such disparities in routine HIV testing would be as a result of a poor quality management system in place. Hence, identifying the gaps in laboratory quality assurance would serve as a footprint to set-up evidence-based interventions to limit false result delivery to clients. We therefore sought to evaluate the effects of programmatic interventions on quality assurance system and on HIV testing performance of PMTCT-site laboratories nationwide.

MATERIALS AND METHODS

Study design

An interventional and analytical study was conducted as part of the 2012 and 2016 in the 10 regions of Cameroon, targeting for each year a sample of 7000 pregnant women attending their first ANC (ANC-1) in different geographical settings (4000 in urban and 3000 in rural settings).

Brief description of HIV sentinel surveillance survey (SSS)

The HIV SSS is a national representative study implemented in 20 sentinel sites that include 60 SSS routine collection points in health facilities offering routine PMTCT services. In such surveys, PMTCT sites included are chosen based on: (a) geographical locations (urban or rural in each region of the country), (b) performance of ≥60% ANC-1 coverage in the catchment (WHO-recommendation), (c) ability to enroll ≥300-500 pregnant women at ANC1 during the survey period, and (d) presence of ANC and PMTCT services [12]. Per site, preganant women at ANC-1 and aged 15-49 were consecutively enrolled, until the required site sample size is achieved (300 or 500 ANC-1 attendees per site) [12].

Onsite HIV Testing procedure

Plasma samples and sociodemographic data were collected as per the routine clinical practice per site. During the study period, HIV screening was proposed to every ANC-1 attendee according to the serial algorithm recommended by the Ministry of Public Health in Cameroon [13]. After onsite HIV testing, residual plasma were transferred into cryotubes marked with a specific ID code of the participant, and stored at 0°-8°C. Plasma and accompanying sample sheet were then linked by the ID

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code. Labeled samples were then shipped at the National Reference Laboratory (NRL) following universal standards for transport of plasma specimens [14].

A serial algorithm for HIV screening was used in all PMTCT-site laboratories and at the NRL, following the national algorithm for voluntary HIV testing (Figure 1). Briefly, the first test was Determine HIV1/2 (*Abbott, Minato-ku-Tokyo, Japan*); non-reactive samples were repoted as negative while in case of reactivity to test-1, a second test was then used for confirmatory analysis. Onsite, indeterminate HIV results were reported as indeterminate, while specimens with indeterminate/discordant HIV results at the NRL were tested with ELISA, used as tiebreaker. Residual plasma was stored at -70°C at the NRL for quality control or further testing if necessary.
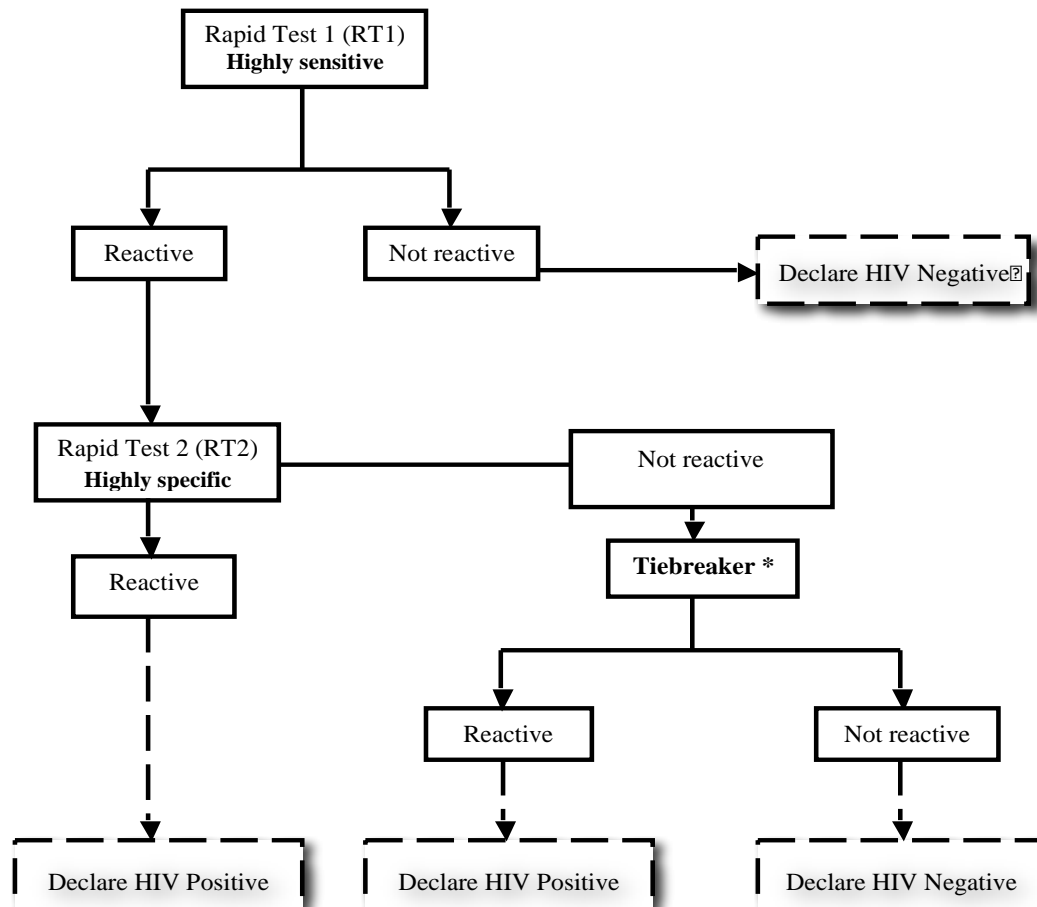

Fig. 1: Algorithm for HIV rapid testing during a voluntary and free counseling

Legend. *: To be checked in a reference laboratory or repeat algorithm with RT1 and RT2 after 3 to 4 weeks interval on a new sample; RT: rapid testing

Assessment of quality indicators

Eight quality indicators were evaluated both in 2012 and 2016 with their resoective threshold for desirable performance: (1) Personnel training and Certification, (2) Physical facility, (3) safety, (4) Pre-testing phase, (5) Testing phase, (6) Post-testing phase, (7) Document and record, (8) External Quality Assessment (EQA).

After the first assessment in 2012, we then implemented interventions on quality assurance in each HIV testing site, which included: (a) staff training on HIV testing algorithm, participation in HIV external quality control (ECQ) or proficiency testing, field supervision of site with persistent suboptimal perofmance.

Assessment of site laboratory performance in HIV testing

Performance of site laboratries in HIV testing was calculated using NRL results as gold standard (Table 1). Based on conclusive negative or positive HIV results obtained testing algortihm by both the site and the NRL, intrinsic performances covering sensitivity and specificity, and extrinsic performances covering positive predictive and negative predictive values, were then calculated, as previously described [15].

$$Reference\ HIV\ Prevalence = 100 \times \frac{a+c}{a+b+c+d} \qquad PMTCT\ HIV\ rate = 100 \times \frac{a+b}{a+b+c+d}$$

$$Sensitivity = 100 \times \frac{a}{a+c} \qquad Specificity = 100 \times \frac{a}{b+d}$$

$$Positive\ Predictive\ Value = 100 \times \frac{a}{a+b} \qquad Negative\ Predictive\ Value = 100 \times \frac{d}{c+d}$$

Legend: PMTCT, prevention of mother-to-child transmission.

Table 1. Calculation of intrinsic and extrinsic performances of HIV testing by PMTCT site laboratories

PMTCT sites results	HIV+	HIV-	Total
	(NRL SSS-HIV test)		
Test +	a	b	a + b
Test -	c	d	c + d
Total	a + c	b + d	a + b + c +d
NRL: National Reference Laboratory			

Ethical statements

Ethical clearance for the surveys was obtained from the Cameroon National Ethics Committee (ref N°2017/03/879/CECNERSH/SP). The privacy of consenting pregnant women and data confidentiality were ensured by the use of ID codes. Data integrity was assured by a double entry and access was restricted for security measures. Onsite HIV test results were offered to pregnant women free of charge, and HIV-positive cases were linked to care for PMTCT services according to national guidelines.

RESULTS

Sociodemographic characteristics of enrolled pregnant women

Out of 7000 pregnant women targeted in the 2012 and 2016 surveys, 6521 (93.2% sampling rate) and 6859 (97.99% sampling rate) eligible ANC-1 attendees were enrolled, respectively. According to age distribution, 49.3% of our participants were aged <25 years in 2012 against 42.9% in 2016. According occupational activities, housewives remained predominant (49.7% in 2012 and 46.47% in 2016), followed by students (14.2% in 2012 and 17.32% in 2016).

Results following interventions on quality assurance

After the 2012 survey, a quality assurance package was implemented in all study sites, regardless their performance (sensitivity, specificity) on HIV testing during the 2012 survey. This quality assurance package yielded the following outcomes of 8 quality indicators, with an overall increased performance between the pre- and post-interventional phases (Figure 2):
- Training on HIV testing of five personnels involved in PMTCT management per site (3 from each urban and 2 from each rural site) using standard operational procedures (SOP) as per the national algorithm, during a 4-day training session: This component helped increased performances at pre-analytical phase (from 60-80%), at analytical phase (55-75%), and at post-analytical phase (80-100%) in these PMTCT-site laboratories;
- EQA was conducted quarterly in all study sites, which entailed HIV re-testing of a panel of samples collected from each site and result comparison to result to the proficiency panel: performance increased from 65% to 95% in these PMTCT-site laboratories;
- Supervision and mentorship programs were conducted quarterly, to ensure monitoring, evaluation and capacity strengthening of each site by laboratory experts. This component helped in increasing performance according to standards of physical facilities (from 80-95%), document recording (40-85%), safety (55-85%);
- Certified/trained staff on HIV testing remained very low (25-30%) even after our interventions.
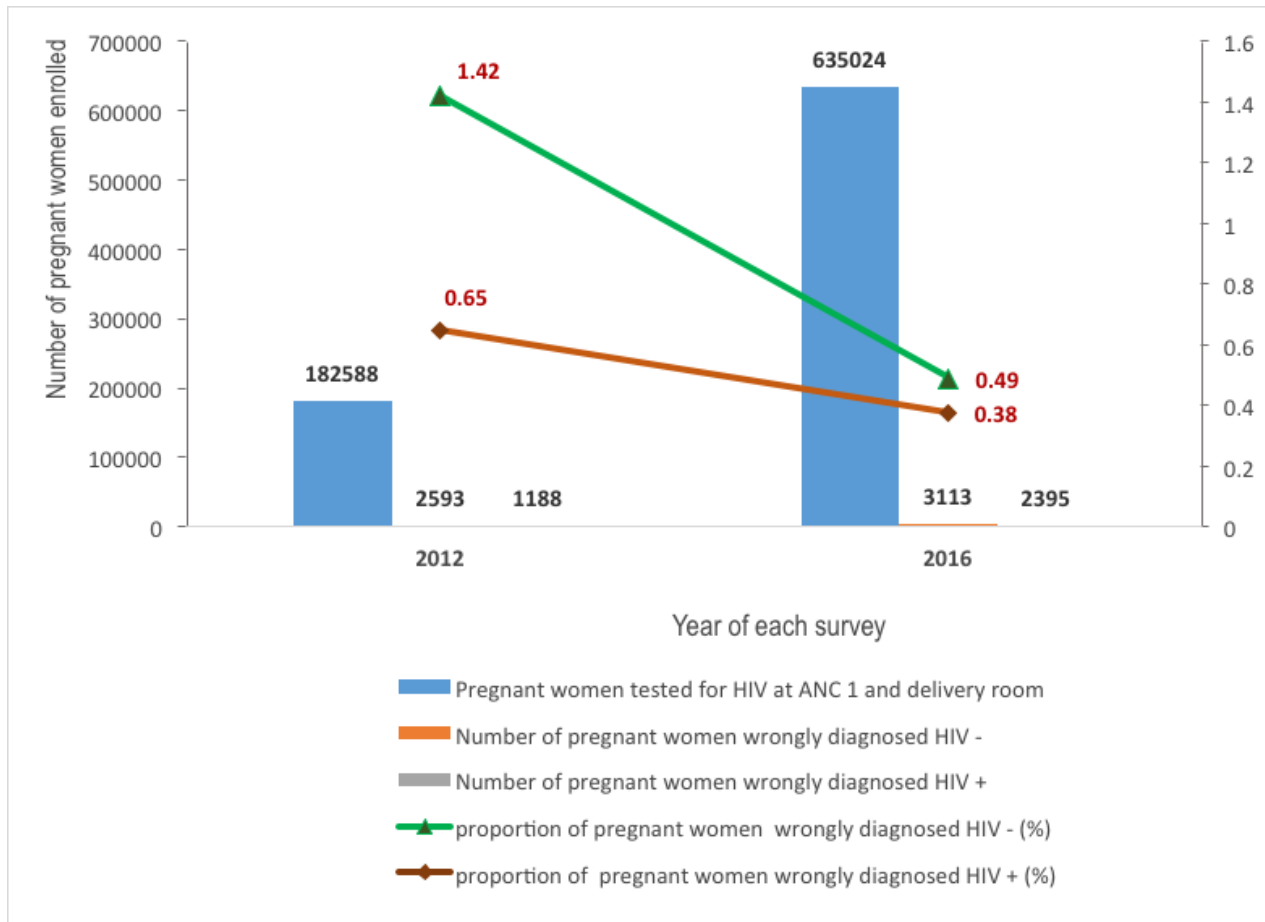
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Fig. 2: Mean performance of PMTCT Sites using the checklist accross 8 quality elements at baseline and last assessment.
Legend: PMTCT, prevention of mother-to-child transmission of HIV

HIV prevalence in 2012 and 2016
Out of 6521 and 6859 ANC-1 attendees enrolled as study participants in 2012 and 2016, the overall prevalence of HIV was 7.8% and 5.7%, respectively, revealing a significant decrease (p<0.0001).

Comparison of Sensitivities and specificities in HIV testing between PMTCT-site laboratories and NRL in 2012 and 2016
Comparing the intrinsic performance in HIV testing between 2012 and 2016, the sensitivity significantly increased with a score of 10.2, from 81.2% in 2012 to 91.4% in 2016 (p<0.00001). Similarly, specificity significantly increased with a score of 0.3, from 99.3% in 2012 to 99.6% in 2016 (p=0.0058). Similar increasing trends were reported in different geographical locations (Urban: from 84.02% to 91.8 %; Rural: from 76.55% to 90.8%). With reference to the WHO benchmarks of 97.5% positive agreement (referred to as sensitivity) and 99.8% negative agreement (referred to as specificity) for countries with HIV prevalence from SSS around 6%, only 2 out of 10 regions (centre and northwest) might be transitioning from HIV-SSS to routine PMTCT data collection for surveillance (Table 2).

At programme-level, inspite of the increased performance in detetcting HIV-infected women (sensitivity: 91.4% in 2016), there was still a gap of 8.6% false HIV-negative results within the frame of PMTCT. At population level, out of 635,024 HIV screening performed in 2016 among ANC-1 attendees (with 5,7% positivity rate and 8.6% false HIV-negative result), 3,113 HIV-infected pregnant women in 2016, representing 0.49% ANC-1 attendees in that same year were wrongly declared HIV-negative and thus not enrolled on ART for PMTCT, due to diagnostic errors. Rates of these diagnostic errors ranged from 1.42% in 2012 down to a significant decrease of 0.49% in 2016 (p< 0.0001).

Programmatically, the national specificity in 2016 (99.6%) revealed that 0.4% ANC-1 attendees wrongly received a positive HIV result, resulting to 0.38% false HIV-negative results (i.e. 2395 pregnant women receiving a false HIV-negative result

nationwide: 635024 (ANC1) x [1 – 0.057] (i.e. 1 – positivity rate) x 0.4% (false positive) = 2395. Thus, in the current era of PMTCT option B+, these pregnant women were wrongly enrolled on lifelong ART due to diagnostic errors. Rates of these diagnostic errors ranged from 0.65% in 2012 down to a significant decrease of 0.38% in 2016 (p< 0.0001).

At regional-level, there was an overall decreasing rate of diagnostic errors, indicated by significant increasing performance of sensitivity (Centre, Northwest, South and Southwest). Of note, only two regions revealed a decreasing sensitivity (Far North and West regions). In terms of specificity, mainly 3 regions had a significant increasing performance (Littoral, Far North and Southwest regions).

Comparison of positive and negative predictive values in HIV testing between PMTCT-site laboratories and NRL in 2012 and 2016

Overall, from 2012 (pre-interventions) to 2016 (post-interventions), performance of both the positive predictive (PPV) and the negative predictive values (NPV) increased considerably (Table 3).

Table 3: Comparison of extrinsic performances by geographical locations in 2012 vs. 2016.			
Region	**Extrinsic performance**	**2012 assessment**	**2016 assessment**
Adamaowa	Positive predictive value	87.1%	91.3%
	Negative predictive value	99.1%	99.8%
Centre	Positive predictive value	100%	96.3%
	Negative predictive value	97.1%	99.8%
East	Positive predictive value	96.9%	96.5%
	Negative predictive value	98.6%	98.7%
North	Positive predictive value	88%	89.5%
	Negative predictive value	98.7%	99.7%
Littoral	Positive predictive value	87.7%	87.5
	Negative predictive value	97.7%	99.6%
South	Positive predictive value	80%	80%
	Negative predictive value	95.8%	99.5%
West	Positive predictive value	92.9%	93.8%
	Negative predictive value	100%	99.1%
Northwest	Positive predictive value	92.0%	95.5%
	Negative predictive value	99.2%	100%
Southwest	Positive predictive value	88.5%	96.6%
	Negative predictive value	98.1%	99.7%
Far-North	Positive predictive value	84.4%	100%
	Negative predictive value	99.7%	99.2%
National performance	Positive predictive value	90.2%	93.5%
	Negative predictive value	98.7%	99.5%

Regarding PPV, the overall performance increased nationwide from 90.2% in 2012 to 93.5% in 2016, p<0.001. Interestingly, only 40% (4/10) of regions met the target of 90% desirable performance for PPV in 2012, against 70% (7/10) of regions in 2016, with a statistically significantly difference pre- and post-interventions (p<0.001).

Regarding NPV, the overall performance increased nationwide from 98.7% in 2012 to 99.5% in 2016, p<0.001. Interestingly, only 40% (4/10) of regions met the target of 99% desirable performance for NPV in 2012, against 90% (9/10) of regions in 2016, with a statistically significantly difference pre- and post-interventions (p<0.001).

The decrease in diagnostic errors between 2012 and 2016, expressed by a reduction in HIV false positive results (-0.93) and in HIV false negative results (-0.27), also underscores the impact of our intervention on quality assurance system in place (Figure 3).
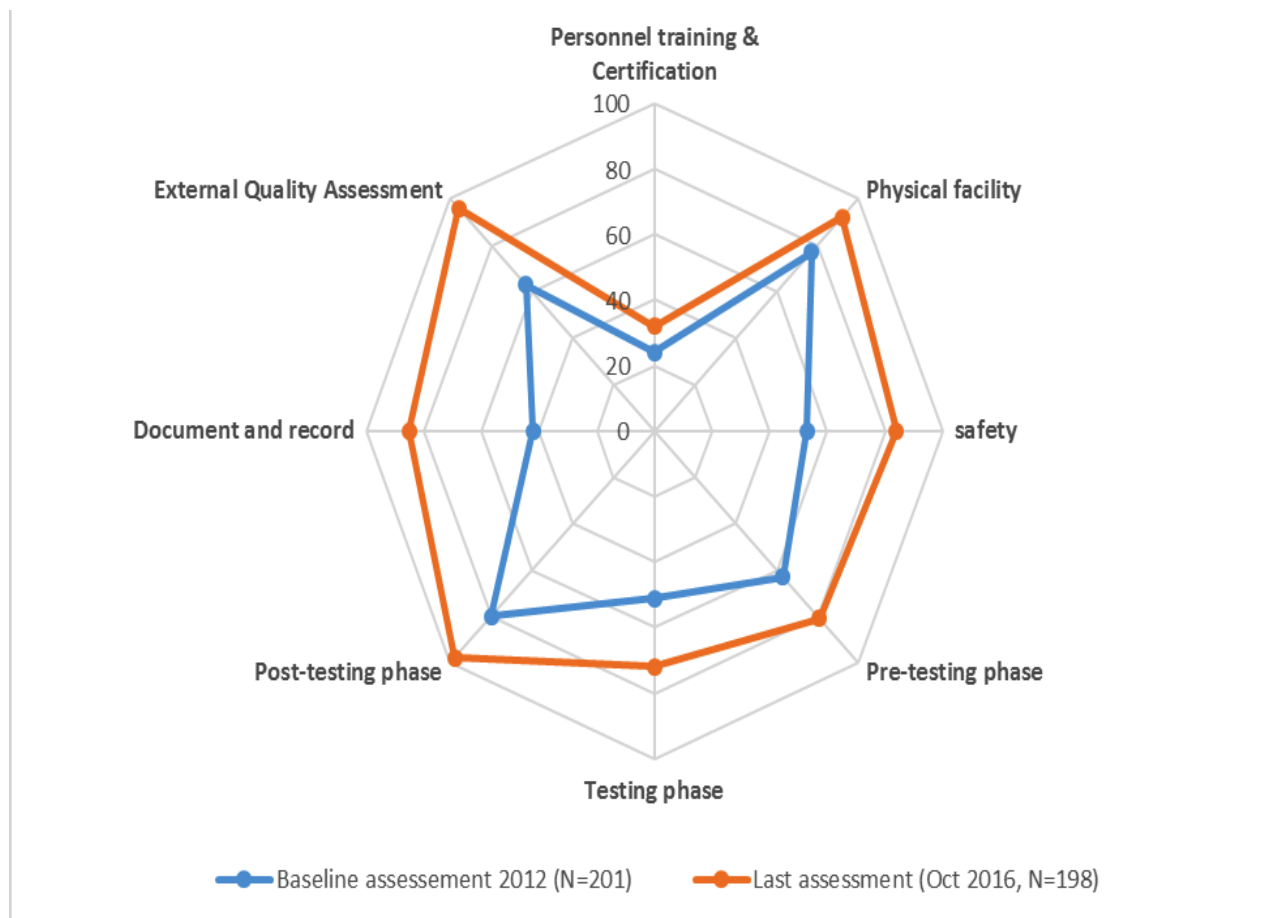
Fig. 3: Comparison of false positivity and false negativity in 2012 and in 2016.

DISCUSSION

In order to strengthen the quality of HIV screening in RLS like Cameroon, we sought to evaluate the effect of quality interventions on the performance of PMTCT laboratories. Briefly, laboratories dedicated to PMTCT services represent a suitable platform for a proof-of-concept in strengthening the quality assurance, based on the large and consistent number of samples routinely process for HIV testing. Thus, evidence generated within the PMTCT program could be translated for implementation in the "test-and-treat" era like Cameroon [7]. Throughout the two HIV diagnostic accuracy surveys, the use of the same testing algorithm also ensures comparatibility of the generated data [13,14]. It therefore becomes evident to ascertain the potential impact of our international package on HIV quality assurance system. This interventional package entails essentially staff training on HIV testing, participation in EQA, documentation and recording, safety and quality of physical facility in each PMTCT site [11]. The high acceptability of HIV testing throughout the two surveys among these pregnant women in Cameroon underlines the effectiveness of current PMTCT strategies, due to continuous counselling by trained staff within the health system [16,17]. Of note, several reports also highlited the efficiency of counseling in ensuring maternal adherence to PMTCT. Of note, the "Opt-Out" approach used within the frame of PMTCT for HIV counselling and screening, as well as screening free of any charges in Cameroon, might be the driven factors of this excellent performance in HIV acceptability by pregnant and brestfeeding women [18]. This is in contrast with a previous study attributing this excellent performance compulsory HIV testing in health facilities [19].

Despite the significant decline in the national prevalence of HIV among Cameroonian pregnant women in 2012 (7.8%) and 2016 (5.7%), the reported rates of infection confirm the public health concern of HIV-infection during pregnancy and the consideration of Cameroon as part of the global PMTCT high priority countries [17]. Thus, accurate diagnosis of HIV-infection during preganancy would largely contribute in closing the gaps among the

undiagnosed people living with HIV, hence contributing toward universal diagnosis within the communities [17,18].

When comparing the intrinsic performance in HIV testing prior (2012) and post-interventions (2016), there was a susbstantial increase in the sensitivity (from 81.2% to 91.4%), indicating an improved capacity of the site laboratories in providing reliable positive results [11,12]. This implying that our interventions had an upgrading effect on the previous performance of PMTCT-site laboratories. Similarly, the capacity of these laboratories in providing reliable HIV negative results (specificity) was also improved significantly from 99.3% to 99.6%. Regarding geographical locations, performance increased similarly both within rural (from 84.02% to 91.8 %) and urban (from 76.55% to 90.8%).

Altogether, these findings support the significance of programmatic interventions on the performance of HIV testing within the health system laboratories [7,13,16,17]. However, despite these encouraging outcomes, the overall performance remains below the World Health Organisation (WHO) benchmarks of 97.5% positive agreement (referred to as sensitivity) and 99.8% negative agreement (referred to as specificity) for countries with HIV prevalence from SSS around 6% [20]. Similar to records found in countries like Zimbabwe, there is need to further strengthen quality assurance of rapid HIV testing and data collection practices, while using regions with good performance (only 20 out of 10 regions: centre and northwest) to prioritise transitioning from SSS to PMTCT-routine HIV surveillance system [21].

Beside improvements in sensitivity and specificity of HIV testing, the extrinsic performances also revealed that the probability of a pregnant woman receiving a positive HIV result when she is really infected (PPV) also increased nationwide (from 90.2% to 93.5%) after our interventions, with a remarkable increment of regions scoring an excellent performance following our interventions (desirable performance found in 40% of regions in 2012 and 70% regions in 2016). Likewise, the probability of a pregnant woman receiving a negative HIV result when she is really uninfected (NPV) also increased nationwide (from 98.7% to 99.5%) after our interventions, with a remarkable increment of regions scoring an excellent performance following our interventions (desirable performance moving found 40% regions in 2012 to 90% regions in 2016) [20].

With current HIV testing performance at programme level, about 2,395 ANC-1 attendees would be wrongly receiving a positive HIV result, indicating uneccessary enrolment on lifelong ART due to diagnostic errors, while 3,113 HIV-infected pregnant women would be wrongly declared HIV-negative and thus not enrolled on ART for PMTCT, due to diagnostic errors, which in turn suggest ongoing risks of HIV vertical transmission [11,20,21].

At regional-level, there was an overall decreasing rate of diagnostic errors, indicated by significant increasing sensitivity performance in 4 regions (Centre, Northwest, South and Southwest); while only two regions experienced a decreasing sensitivity (Far North and West regions).

A major strength of our study is the use of same sentinel sites during the two surveys [11,20] and the use of HIV rapid tests that were selected based on their excellent diagnostic performance recently obtained on diverse HIV strains in the same country, which include HIV types 1 and 2, as well as groups M, N and O of VIH-1 [22]. A limitation to our study was the inability to delineate, within the interventional package, the key components that were largely associated with the increased performance. However, we assume the driven factors would be training in HIV testing (pre, per, and post-analysis), participation in EQA and monitoring-evaluation. Further studies would therefore consider these aspects in order to capitalise on meeting the required WHO-target performance [20].

CONCLUSION

Interventions on the QA system in PMTCT-laboratories are very relevant in reducing errors occurred during routine HIV testing. Despite the significant decline in testing errors, further quality improvements are required to meet the desired performace of 97.5% sensitivity and 99.8% specificity with the 5.7% HIV prevalence in SSS. Thus, transitioning to routine PMTCT-data for surveillance is not yet encouraged. Nonetheless, sites with desirable performance should share their experience on specific quality indicators associated with accuracy in HIV rapid testing, prior to transitioning confidently to surveillance using routine PMTCT data in Cameroon.

CONFLICT OF INTEREST:

There is no conflict of interest to declare.

FUNDING:

ETHICAL APPROVAL:

Ethical clearance for the surveys was obtained from the Cameroon National Ethics Committee (ref N°2017/03/879/CECNERSH/SP).

AUTHORS' CONTRIBUTIONS

Designed the study: SCB, JF, CKN, AM, JDA, MNN, AN, ACZKB, JBEN
Collected the data: CKN, JDA, AM, SCB, JF, YM
Analyzed or interpreted the data: SCB, JF, CKN, AM, MNN, AN, ACZKB, JBEN, IP, YM, VC, LB, PTB
Revised the paper: SCB, JF, CKN, AM, JDA, MNN, AN, ACZKB, JBEN, IP, PTB, YM, VC, LB
Approved the final version submitted: All the authors.

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Table 2: Comparison of intrinsic performances (Sensitivity, specificity) by geographical locations in 2012 and in 2016.

Region	Year	Urban			Rural			National				
		Number of pregnant women enrolled	Se	Sp	Number of pregnant women enrolled	Se	Sp	Number of pregnant women enrolled	Se	Comparison Site vs NRL (P-Value)	Sp	Comparison Site vs NRL (P-Value)
Adamawa	2012	412	87.5	99.8	301	76.48	98.9	713	81.8	0.069	99.4	0.227
	2016	475	93.3	99.5	202	100	100	677	95.5		99.7	
Centre	2012	317	88.6	100	244	50	100	561	78.3	**0.001**	100	0.113
	2016	541	97.7	99.6	137	100	100	678	98.1		99.7	
East	2012	303	93.8	100	327	69.6	99.6	630	79.5	0.146	99.8	0.315
	2016	317	93.1	99.6	380	82.4	99.7	697	87.3		99.7	
Far North	2012	382	92.6	99.1	296	100	99.2	678	93.1	0.052	99.2	**0.001**
	2016	327	73.3	100	355	85.7	100	682	77.3		100	
Littoral	2012	402	77.5	99.1	272	82.6	98.3	674	79.4	0.229	98.8	0.051
	2016	448	100	99.8	169	66.7	99.4	617	87.5		99.6	
North	2012	427	65.2	99.2	300	87.5	100	727	71	0.063	99.6	0.318
	2016	406	93.8	99.5	312	66.7	100	718	89.5		99.7	
Nothwest	2012	392	90.63	99.7	302	89.5	98.9	694	90.2	**0.019**	99.3	0.201
	2016	353	100	99.7	323	100	99.7	676	100		99.7	
West	2012	398	100	99.7	294	100	99.55	692	100	**0.002**	99.7	0.246
	2016	402	57.1	99.7	271	98.6	100	673	71.4		100	
South	2012	321	56.25	99.5	152	61.1	96.9	473	58.8	**0.002**	98.5	0.298
	2016	246	83.3	98.8	472	100	98.8	718	90.3		98.9	
Southwest	2012	380	85.72	98.5	299	78.3	99.2	679	83.1	**0.007**	98.8	**0.034**
	2016	411	95.5	99.1	300	97.3	100	711	96.6		99.7	
National performance	2012	3734	84.02	99.5	2787	76.6	99.2	6521	81.2	**<0.001**	99.3	**0.006**
	2016	3926	91.8	99.6	2921	90.8	99.8	6847	91.4		99.6	
	Se: sensitivity.	Sp: specificity:.		NRL: National Reference Laboratory.								