



# Performance of commercial Herpes Simplex Virus type-2 (HSV-2) tests on samples from sub-Saharan Africa: A systematic review and meta-analysis



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**Background:** Several commercial type-specific serologic tests are available for Herpes Simplex Virus type 2 (HSV-2). Poor specificity of some tests has been reported on samples from sub-Saharan Africa. To summarise the performance of the tests, we performed a systematic review of publications reporting performance of commercially available HSV-2 tests against a gold standard (Western Blot or monoclonal antibody EIA) on samples from sub-Saharan Africa.

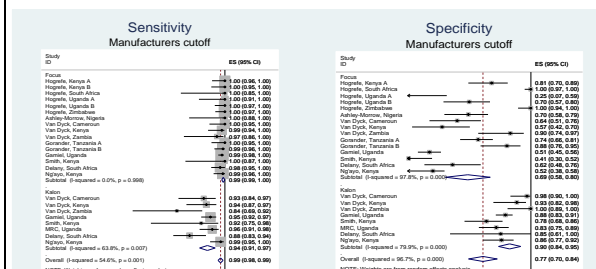
**Methods:** We used random-effects meta-analyses to summarise sensitivity and specificity of the two most commonly evaluated tests: Kalon g2 ELISA and Focus HerpeSelect HSV-2 ELISA. Possible heterogeneity due to HIV infection was explored using meta-regression.

**Results:** We identified **11** eligible papers which included **19** studies of the performance of Focus, **11** of Kalon, **4** of the Monoclonal Antibody EIA (MAb EIA) and **4** of the Biokit test (see **Table 1**).

**Table 1: Performance of HSV-2 serological tests in Africa**

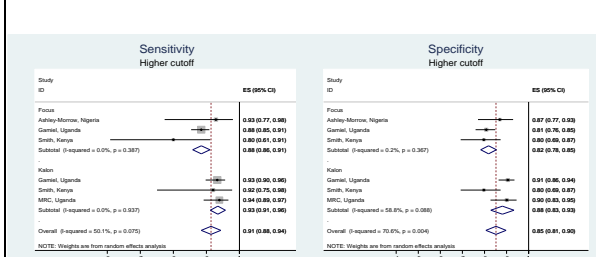
Reference	Year	Population	N	Size	ES	95% CI	Sensitivity	Specificity
<b>Performance of Focus and Kalon HSV-2 tests</b>								
Hughes, Kenya (17)	2000	HIV negative women, age 18 to 45, attending outpatient clinic, Mombasa	100	Focus	1.1	1.09-1.09	100	99.8
Hughes, Kenya (17)	2000	HIV positive women, age 18 to 45, attending outpatient clinic, Mombasa	80	Focus	1.1	1.09-1.09	100	99.9
Hughes, South Africa (17)	2000	Healthy individuals for HIV screening	100	Focus	1.1	1.09-1.09	100	100
Hughes, Uganda (17)	2000	Blood donors, Kampala, 1989	11	Focus	1.1	1.09-1.09	100	100
Hughes, Uganda (17)	2000	HIV negative women aged 15 to 30 in family planning clinic	176	Focus	1.1	1.09-1.09	100	70
Hughes, Zimbabwe (17)	2000	HIV negative women aged 15 to 30 in STD clinic, Harare	124	Focus	1.1	1.09-1.09	100	100
Anthony-Morris, Nigeria (22)	2004	Women aged 15 to 49, Ibadan	97	Focus	1.1	1.09-1.09	100	70
Van Dyck, Cameroon (23)	2004	General adult population, age 15 to 49, Yaoundé, HIV seroprevalence 24%	123	Focus	1.1	1.09-1.09	100	64
Van Dyck, Kenya (23)	2004	General adult population, age 15 to 49, Kisumu, HIV seroprevalence 24%	140	Focus	1.1	1.09-1.09	100	57
Van Dyck, Zambia (23)	2004	General adult population, age 15 to 49, Ndola, HIV seroprevalence 24%	127	Focus	1.1	1.09-1.09	100	62
Gammel, Tanzania (23)	2008	HIV negative blood donors (10 males, 13 females), Dar es Salaam	100	Focus	1.1	1.09-1.09	100	74.3
Gammel, Tanzania (23)	2008	General adult population (10 males, 13 females), Dar es Salaam, HIV seroprevalence 5%	100	Focus	1.1	1.09-1.09	100	88.4
Gammel, Uganda (23)	2008	General population aged 15 to 49 years, Nakuru	800	Focus	1.1	1.09-1.09	100	10.7
Smith, Kenya (23)	2008	HIV negative men 18 to 24 years, Nairobi	100	Focus	1.1	1.09-1.09	100	41
Delany, South Africa (22)	2008	Women attending family planning clinic, Johannesburg, HIV seroprevalence 12%	97	Focus	1.1	1.09-1.09	100	61.9
Ngwen, Kenya (23)	2008	Fishermen aged 18 and above, Kisumu	200	Focus	1.1	1.09-1.09	100	12.3
Van Dyck, Cameroon (23)	2004	General adult population, age 15 to 49, Yaoundé	123	Focus	1.1	1.09-1.09	100	64
Van Dyck, Kenya (23)	2004	General adult population, age 15 to 49, Kisumu	140	Focus	1.1	1.09-1.09	100	57
Van Dyck, Zambia (23)	2004	General adult population, age 15 to 49, Ndola	127	Focus	1.1	1.09-1.09	100	62
Gammel, Uganda (23)	2008	General population, age 15 to 49, Nakuru	100	Focus	1.1	1.09-1.09	100	88.4
Smith, Kenya (23)	2008	HIV negative men, age 18 to 24 years, Nairobi	100	Focus	1.1	1.09-1.09	100	41
Delany, South Africa (22)	2008	Women attending family planning clinic, Johannesburg, HIV seroprevalence 12%	97	Focus	1.1	1.09-1.09	100	61.9
MRC, Uganda (23)	2008	Men and women aged 15 to 49 in general population, Mbarara	260	Focus	1.1	1.09-1.09	100	83.2
Ngwen, Kenya (23)	2008	Fishermen aged 18 and above, Kisumu	200	Focus	1.1	1.09-1.09	100	12.3
<b>Performance of Kalon HSV-2 tests</b>								
Anthony-Morris, Nigeria (22)	2004	Women aged 15 to 49, Ibadan	97	Kalon	2.2	1.09-1.09	93	67
Gammel, Uganda (23)	2008	General population aged 15 to 49 years, Nakuru	800	Kalon	2.2	1.09-1.09	98.4	98.8
Smith, Kenya (23)	2008	HIV negative men 18 to 24 years	100	Kalon	2.2	1.09-1.09	90	80
Gammel, Uganda (23)	2008	General population, age 15 to 49 years, Nakuru	100	Kalon	2.2	1.09-1.09	91.7	92.4
Smith, Kenya (23)	2008	HIV negative men, age 18 to 24 years, Nairobi	100	Kalon	2.2	1.09-1.09	90	80
MRC, Uganda (23)	2008	Men and women aged 15 to 49 in general population, Mbarara	260	Kalon	2.2	1.09-1.09	93.9	93.1
<b>Performance of Biokit HSV-2 tests</b>								
Isipol, Uganda (23)	2000	General adult population, Mbarara	495	Biokit	2.2	1.09-1.09	93	94
Van Dyck, Cameroon (23)	2004	General adult population, age 15 to 49, Yaoundé	123	Biokit	2.2	1.09-1.09	97	94
Van Dyck, Kenya (23)	2004	General adult population, age 15 to 49, Kisumu	140	Biokit	2.2	1.09-1.09	98	96
Van Dyck, Zambia (23)	2004	General adult population, age 15 to 49, Ndola	127	Biokit	2.2	1.09-1.09	100	94
Van Dyck, Cameroon (23)	2004	General adult population, age 15 to 49, Yaoundé	123	Biokit	2.2	1.09-1.09	89	90
Van Dyck, Kenya (23)	2004	General adult population, age 15 to 49, Kisumu	140	Biokit	2.2	1.09-1.09	89	92
Van Dyck, Zambia (23)	2004	General adult population, age 15 to 49, Ndola	127	Biokit	2.2	1.09-1.09	77	87
Gammel, Uganda (23)	2008	General population aged 15 to 49 years, Nakuru	100	Biokit	2.2	1.09-1.09	94	94.1

**Figure 1: Sensitivity and specificity of Focus and Kalon HSV-2 assays in Sub-Saharan Africa**



Focus had high sensitivity (random effects summary estimate **99%**, [95% CI, 99% - 100%]) but lower specificity (**69%**, [58% - 80%]). Kalon had sensitivity of **94%** [91% - 97%] and specificity of **90%** [84% - 95%].

**Figure 2: Sensitivity and Specificity of Focus and Kalon HSV-2 assays at higher cut-off than recommended by manufacturer**

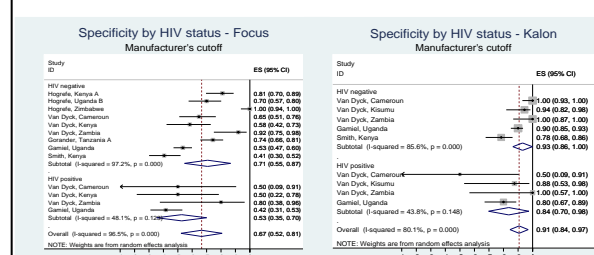


Three studies evaluated a higher cut-off of 3.5 for Focus, which improved specificity to **82%** [78% - 85%].

In collaboration with DFID UK funded SRH & HIV RPC at LSHTM



**Figure 3: Specificity of Focus and Kalon HSV-2 assays by HIV status in Sub-Saharan Africa**



Specificity of Focus was lower among HIV-positive (**53%** [35% - 70%]) vs. HIV-negative individuals (**71%** [55% - 87%]), although this was not statistically significant ( $p=0.2$ ). There was substantial between-study heterogeneity amongst HIV-negatives. There was a similar trend for Kalon, although the difference by HIV status was less marked (specificity in HIV positives **84%** [70% - 98%] vs. **93%** [86% - 100%] in HIV negatives).

**Conclusions:** The **specificity** of commercially available HSV-2 serological tests **using African samples** appears **generally inferior** to that reported from industrialised countries.

There is a **large variation in performance** depending on **geographical location, characteristics of the study populations and HIV serostatus**. Therefore, studies using HSV-2 testing would benefit from an evaluation of test performance in the proposed study population, bearing in mind the aims of the testing e.g. estimation of prevalence, establishing aetiology of genital ulcer, estimating the effect of HSV-2 on risk of HIV acquisition or infectivity. Different assays could be used for different purposes.

**Focus tended to have low specificity** (summary estimate **69%**) compared with the gold standard when using the manufacturer's recommended cut-off (OD=1.1). Kalon tends to perform better when compared with Focus in the same study populations, although performance also varied across studies.

**Improved specificity** was obtained when the **cut-off was increased** above that recommended by the manufacturer (OD>1.5 for Kalon; OD>3.4 for Focus).