

An Age-Stratified Risk Score to Predict HIV Acquisition in Young South African Women

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INTRODUCTION

In sub-Saharan Africa (SSA) young women aged 15-24 years are disproportionally affected by HIV, contributing nearly 25% of all new infections in the region (1). Prioritizing highest risk women in HIV hyperepidemic settings, remains important for optimized introduction and scale of new prevention methods like oral PrEP. We assessed the performance of a risk score derived from the VOICE cohort (2) using the CAPRISA 004 dataset, and modified the score for age-specific prediction.

METHODS

We validated a risk score that was initially developed in the VOICE study and modified the score with other predictors of risk in the CAPRISA 004 dataset. The CAPRISA 004 1% tenofovir gel trial followed 889 sexually active HIV negative women, 18-40 years-old at 2 sites in KwaZulu-Natal. Given the trial’s efficacy of 39%, only participants in the CAPRISA 004 placebo arm (n=444) were used in this analysis.

Initial Risk Score (IRS) Validation

- Participant’s total IRS scores were calculated by summing the individual score for each of the 7 analogous VOICE items measured at baseline in the CAPRISA 004 cohort (Table 1; VOICE Model) for a maximum score of 11.

RESULTS

There were 60 HIV infections among the 444 women with 660.7 PYs of follow-up (incidence= 9.08/100 PY, 95% CI 7.05, 11.70). Women <25-years-old (N=302, 68%) accounted for 47 infections (incidence= 10.57/100 PY, 95%CI 7.94, 14.06). The remaining women ≥25 years (N=142) accounted for 13 infections (incidence= 6.02/100 PY, 95%CI 3.50, 10.37).

IRS Performance

- Majority of participants (N=431, 97%) had complete data for the 7 items in the IRS.
- The discriminative power of the IRS was good overall (AUC: 0.66, 95% CI 0.54, 0.74) and for women <25 years (AUC 0.69, 95% CI 0.60, 0.78). The IRS could not predict HIV acquisition in women ≥25 years (AUC: 0.49, 95% CI 0.30, 0.63)

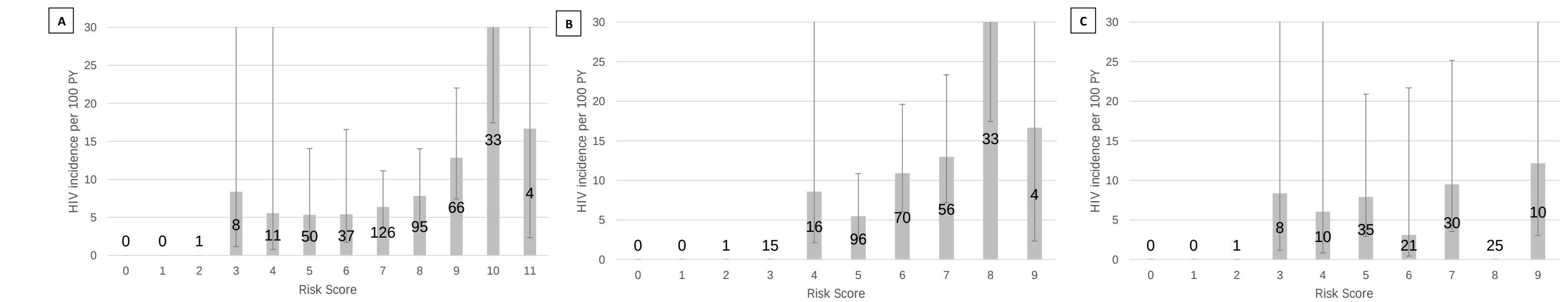


Figure 1. The number of women in each risk score category and HIV incidence by IRS value using the risk score in the entire sample (N=431) (A), and among women <25 years-old (B) (N=291), and women ≥25 years (N=140) (C)

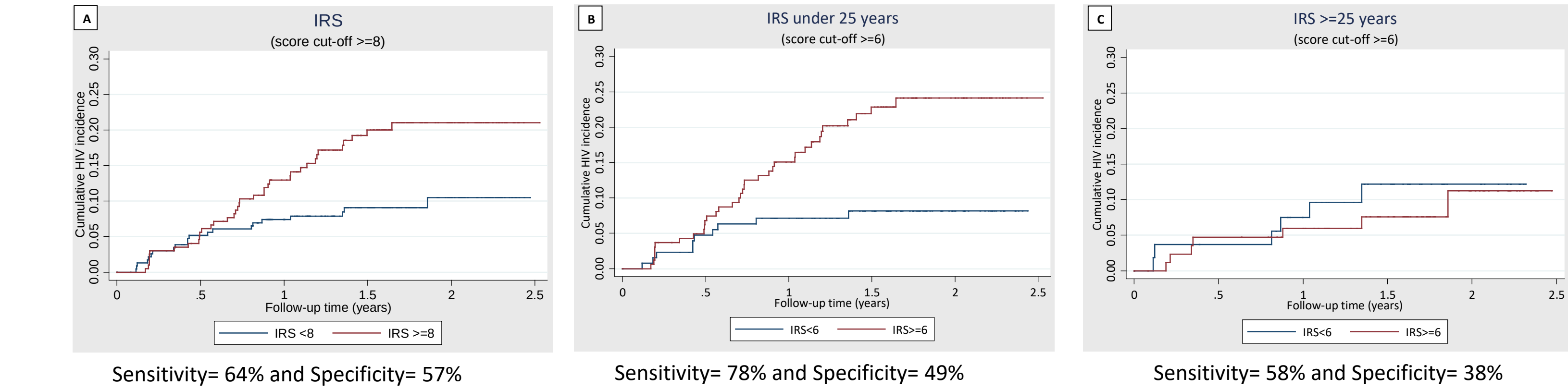


Figure 2. Cumulative HIV incidence over study time at risk score cut offs of ≥8 for IRS (A), ≥6 for IRS under 25 years old (B) and ≥6 for IRS ≥25 years old (C)



Figure 3. The number of women in each risk score category and HIV incidence among women <25 years-old by MRS value (A), and by PHRS score value (B) (N=291)

Risk Factor Analysis

- In univariate analysis for all women, out of the 7 IRS factors, only “partner exclusivity” was independently significantly associated with HIV infection (Table 1). In younger women, responding “yes” that your partner has other partners (HR=9.92, CI 1.31, 75.1), casual partnerships (HR=2.39, 95%CI 1.22, 4.70) and HSV-2 seropositivity (HR=2.50, 95%CI 1.40, 4.48) were significantly associated. None of the 7 IRS factors independently predicted HIV infection in women ≥25 years.
- The age-stratified MRS showed the most predictive score for women <25 years included HSV-2, casual partnerships, and partner exclusivity (AUC: 0.70, 95%CI: 0.60, 0.79) (Figure 3 A). The PHRS had an AUC of 0.62 (95%CI 0.56, 0.68) (Figure 3 B).

LIMITATIONS

- Curable STIs at baseline were not diagnosed with laboratory assays. Self-report of STIs and syndromic management were used as proxies.
- The small sample size limits the power of the exploratory analysis to make inference, particularly with the age-stratified analyses. For our exploratory scores we did not pursue internal validation due to the small sample size and therefore susceptible to statistical biases
- To include as many failures as possible in our analysis, we assessed the score’s predictability over the entire study follow-up, as opposed to one year as proposed by *Balkus et al.* However, when we limited to one year, the estimates were similar, but confidence bounds expanded indicating reduced precision.

Statistical Analysis

- IRS and age-stratified score performances (max score = 9 within age strata, <25 years versus ≥25 years) were assessed by generating the HIV incidence per 100 person-years (PYs) in each risk score category; calculating time-dependant area under the receiver operating curve (AUC); and sensitivity (Sen) and specificity (Spec) at different score cut-offs.
- The un/adjusted effects of the 7 risk score items included in the score, as well as others of interest, were evaluated using Cox Proportional hazards for their association with HIV acquisition. Common methods for developing clinical prediction rules were used to create a modified risk score [(MRS) includes: partner exclusivity, casual partnerships, and HSV status; max score=5] and a public health use risk score [(PHRS) excludes non-routine HSV serotesting] among women <25 years, and evaluated using the same methods as described for external validation of the IRS.
- Complete set analysis using Pearson’s chi-squared tests to compare differences of key demographics was performed.
- Time-dependant ROC curves were calculated using R v.3.4.0, all other statistical analyses were performed using Stata v.13.

Table 1. Univariate Analysis in all women (N=431) and multivariate analyses of factors associated with HIV acquisition in the IRS (N=431), those <25 years (MRS), and those <25 years of age removing clinical factors (PHRS) (N=291)

Factors	Univariate Analysis		Multivariate Analysis			
	Placebo Arm	VOICE model (IRS)	<25 model (MRS)		<25 model (PHRS)	
	HR (95% CI)	aHR (95% CI)	score value	aHR (95% CI)	score value	aHR (95% CI)
Age						
<25	1.74 (0.94, 3.22)**	0.41 (0.20, 0.80)*	2			
≥25 (Ref)	1.00	1.00	0	-	-	-
Income source						
Partner (Ref)	1.00	1.00	0			
Other	0.50 (0.18, 1.38)	0.44 (0.16, 1.24)	1	-	-	-
Married or living with						
Partner (Ref)	1.00	1.00	0			
Parents or other	0.94 (0.43, 2.07)	1.49 (0.63, 3.55)	2	-	-	-
Partner(s) has other partners*						
No (Ref)	1.00	1.00	0	1.00	0	1.00
Don't know	3.43 (1.06, 11.1)*	4.02 (1.22, 13.3)*	2	7.56 (1.03, 55.7)*	3	6.45 (0.88, 47.32)**
Yes	3.85 (1.12, 13.2)*	3.77 (1.07, 13.3)*	2	7.86 (1.02, 60.3)*	3	8.84 (1.16, 67.25)*
Abnormal discharge in last 30 days						
No (Ref)	1.00	1.00	0			
Yes	0.97 (0.56, 1.69)	1.09 (0.62, 1.91)	1	-	-	-
HSV-2 positive						
No (Ref)	1.00	1.00	0	1.00	0	
Yes	1.54 (0.92, 2.60)**	2.10 (1.19, 3.68)*	2	2.54 (1.39, 4.63)*	1	-
Alcohol use before sex last 30 days						
No (Ref)	1.00	1.00	0			
Yes	1.26 (0.75, 2.11)	1.31 (0.77, 2.23)	1	-	-	-
Casual partners in last year						
None	1.00			0.02	0	1.00
≥1	1.91 (1.02, 3.60)*	-	-	2.19 (1.09, 4.39)*	1	2.10 (1.06, 4.16)*
Total			11		5	
AIC		678.76		480.92		499.20

*Indicates a p-value <0.05, **p-value <0.1

CONCLUSIONS

In this high incidence population, the ability of the IRS to predict incident HIV infections was comparable to previous findings (AUC=0.66 vs. 0.58-0.71) (2). However, a cut-off where women were at a substantially low risk of HIV infection could not be determined (e.g., incidence <3%) (3). Age-stratified analysis showed that associations with HIV were in younger women (18-24 years of age), suggesting that there could be more value to characterizing age-specific risk, especially since age is not a modifiable risk factor. Importantly, HSV-2 had a strong relationship with HIV in this study, which is consistent with a large body of evidence. HSV-2 testing should be done whenever possible in young women; however, most clinical settings do not currently offer and likely will not offer HSV-2 testing as part of their routine health services. Although based on exploratory analyses that require external validation before implementation, the MRS and PHRS could offer simpler risk tools that use behavioural and partner characteristics. These tools can be used for PrEP counselling, to increase risk perception and to focus interventions on modifiable risk factors; yet, relatively lower risk women still had high HIV incidence suggesting a need for further modification to these tools or to offer PrEP to anyone at risk in hyperepidemic settings.

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DISCLAIMER: The content in this abstract are those of the authors and do not necessarily reflect the views of the United States Agency for International Development or the United States Government.

REFERENCES

- UNAIDS. Global AIDS UPDATE. Unaid [Internet]. 2016;17 Suppl 4:S3-11. Available from: <http://pesquisa.bvsaalud.org/portal/resource/pt/mdl-15080170>
- Balkus J, Brown E, Palanee T, Nair G, Gafoor Z, Zhang J et al. An Empiric HIV Risk Scoring Tool to Predict HIV-1 Acquisition in African Women. JAIDS Journal of Acquired Immune Deficiency Syndromes. 2016;72(3):333-343.
- Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIVinfection: recommendations for a public health approach [Internet]. 2nd ed. Geneva: World Health Organization; 2016. Available from: <http://www.who.int/hiv/pub/prep/policy-brief-prep-2015/en>