PREVALENCE OF HIGH-RISK HPV INFECTION AND E6/E7 ONCOPROTEINS AMONG RWANDAN HIV-INFECTED WOMEN SCREENED FOR CERVICAL CANCER

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Background

- Invasive Cervical Cancer (ICC) is the 4th most frequently diagnosed and 4th leading cause of cancer death in women worldwide
- 570000 new cases and 311000 deaths in 2018
- In most lower HDI countries, it ranks 2nd after breast cancer
- Most commonly diagnosed in 28 countries
- Leading cause of cancer death in 42 countries, most of them in SSA

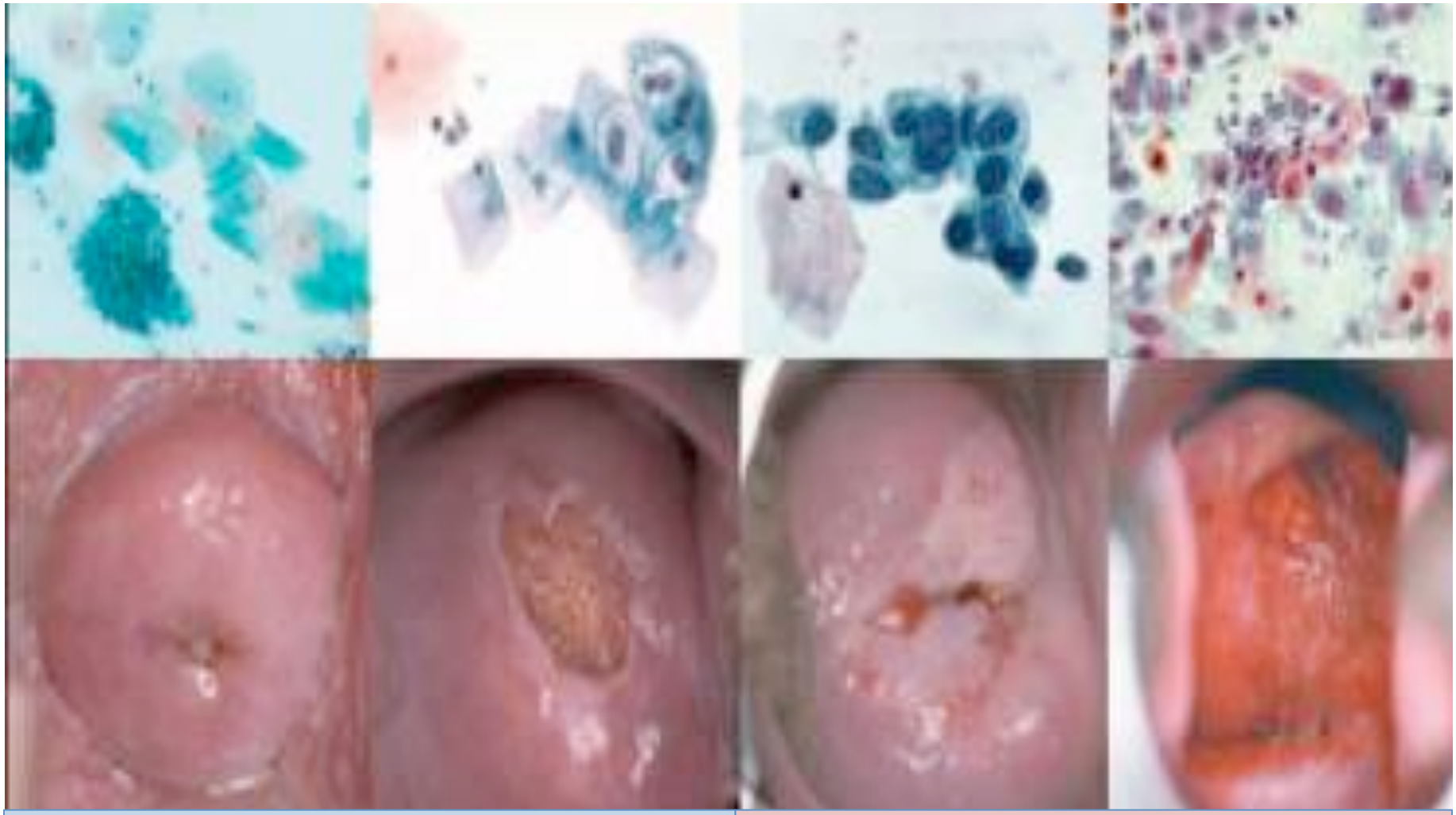
Background (Cont'd)

- The introduction of effective Pap-based screening in some, mostly high-income, countries in the mid- to late-20th century has led to steady decreases in ICC incidence and mortality in those countries
- More than 80% of all ICC occurs in LMICs where high-coverage, Pap-based screening has never been successfully implemented
- Need for prevention modalities in LMICs
- WLWH are at higher risk for ICC than the general population
- ICC classified as an AIDS defining illness (CDC 1993)
- HPV is virtually the necessary, but not sufficient, cause of ICC
- 12 oncogenic types classified as group 1 carcinogens by IARC

Natural history of HPV

- The natural history of HPV and cervical carcinogenesis can be represented by a simple, causal schema of four, reliably-measured stages
- 1) HPV acquisition
- 2) HPV persistence
- 3) progression to precancer (CIN3/AIS), and
- 4) ICC
- The key step in cervical carcinogenesis is overt, measurable HPV persistence, which even after a year or two strongly predicts the development of cervical precancer and cancer (CIN3+)

Cervical Carcinogenesis



Transient infection | Persistent HPV

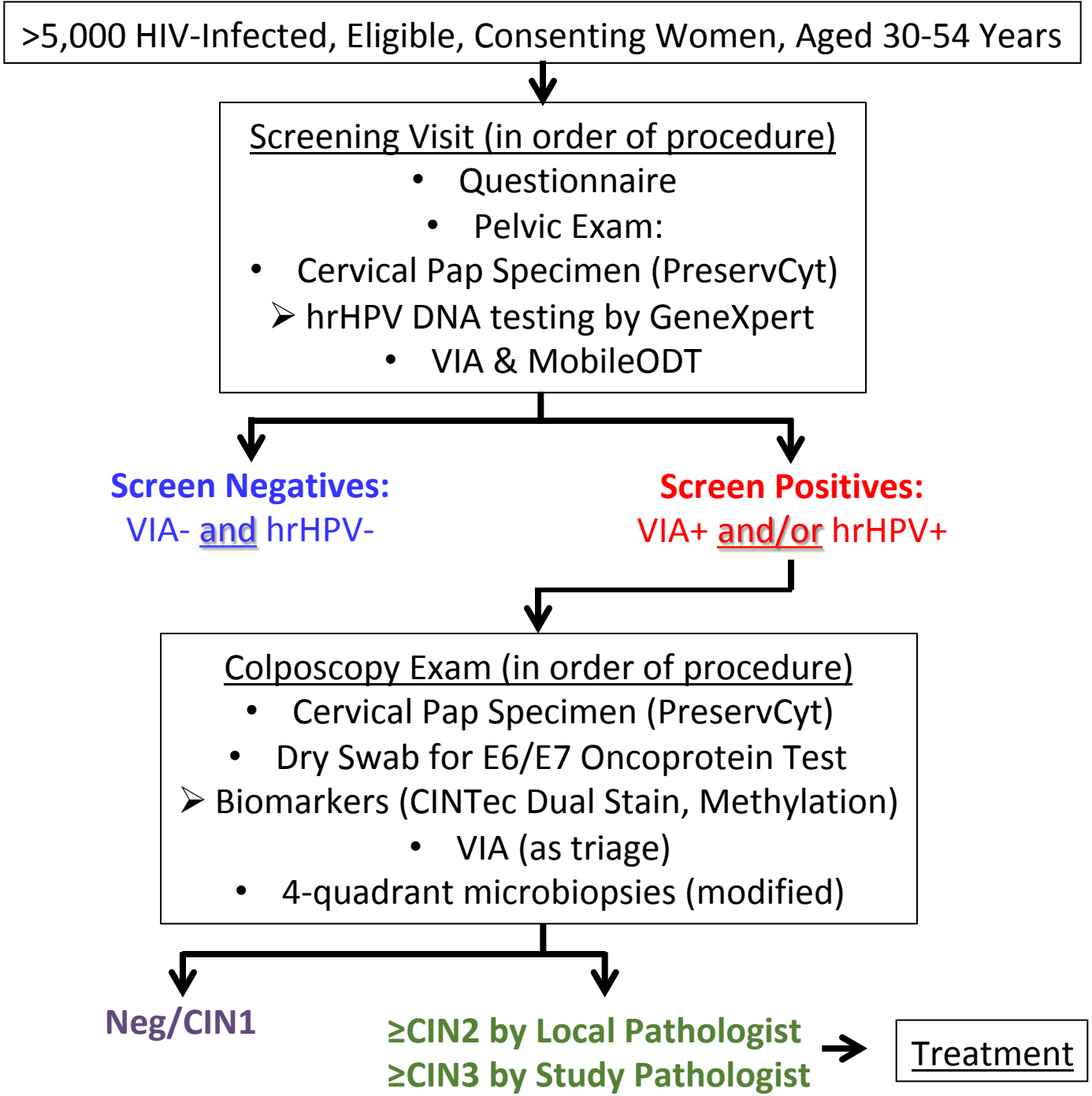
Normal cervix —INFECTION→ HPV-infected cervix —PROGRESSION→ Precancer —INVASION→ Cancer

HPV-infected cervix —CLEARANCE→ Normal cervix

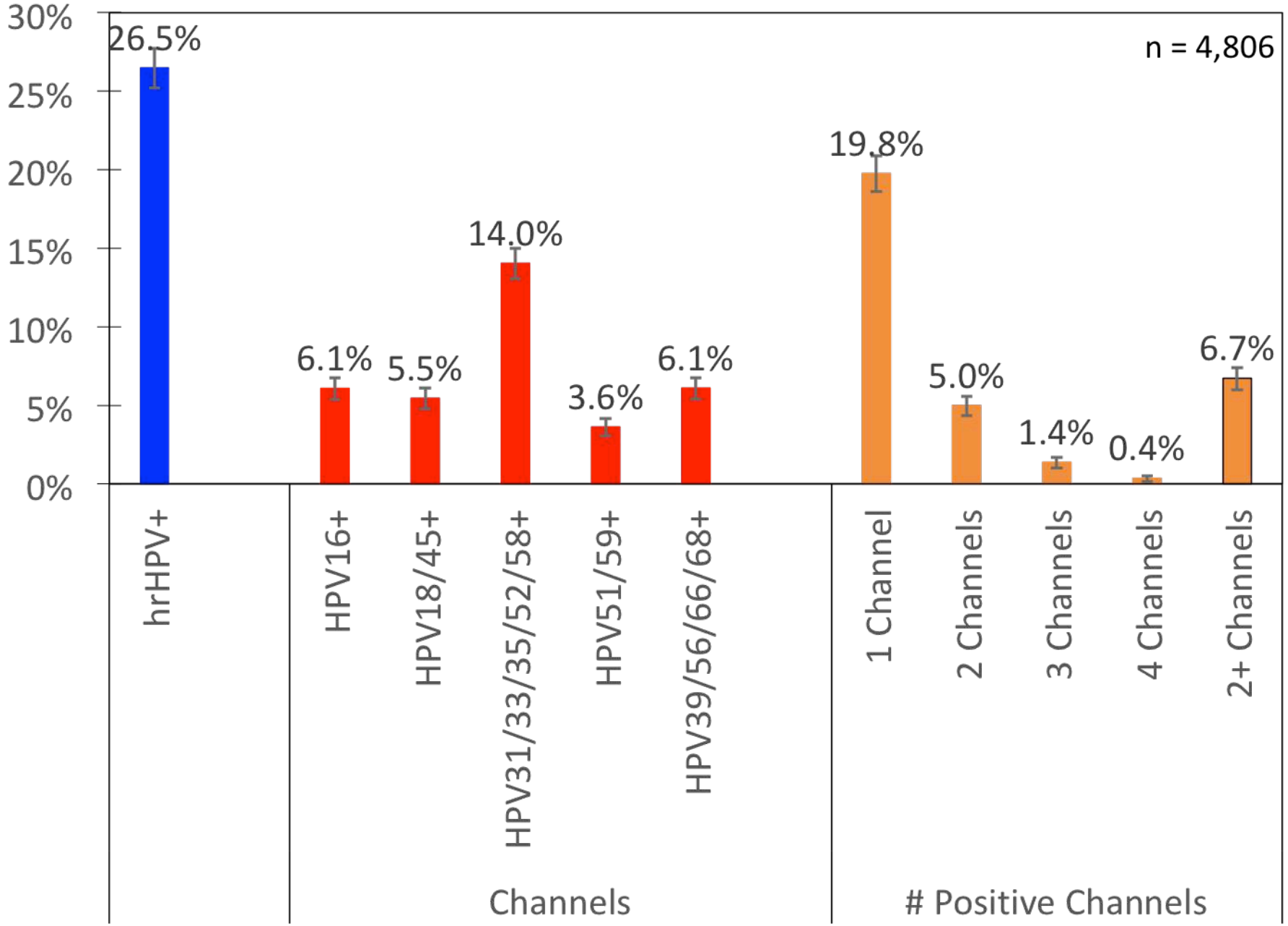
Precancer —REGRESSION?→ HPV-infected cervix

Objective

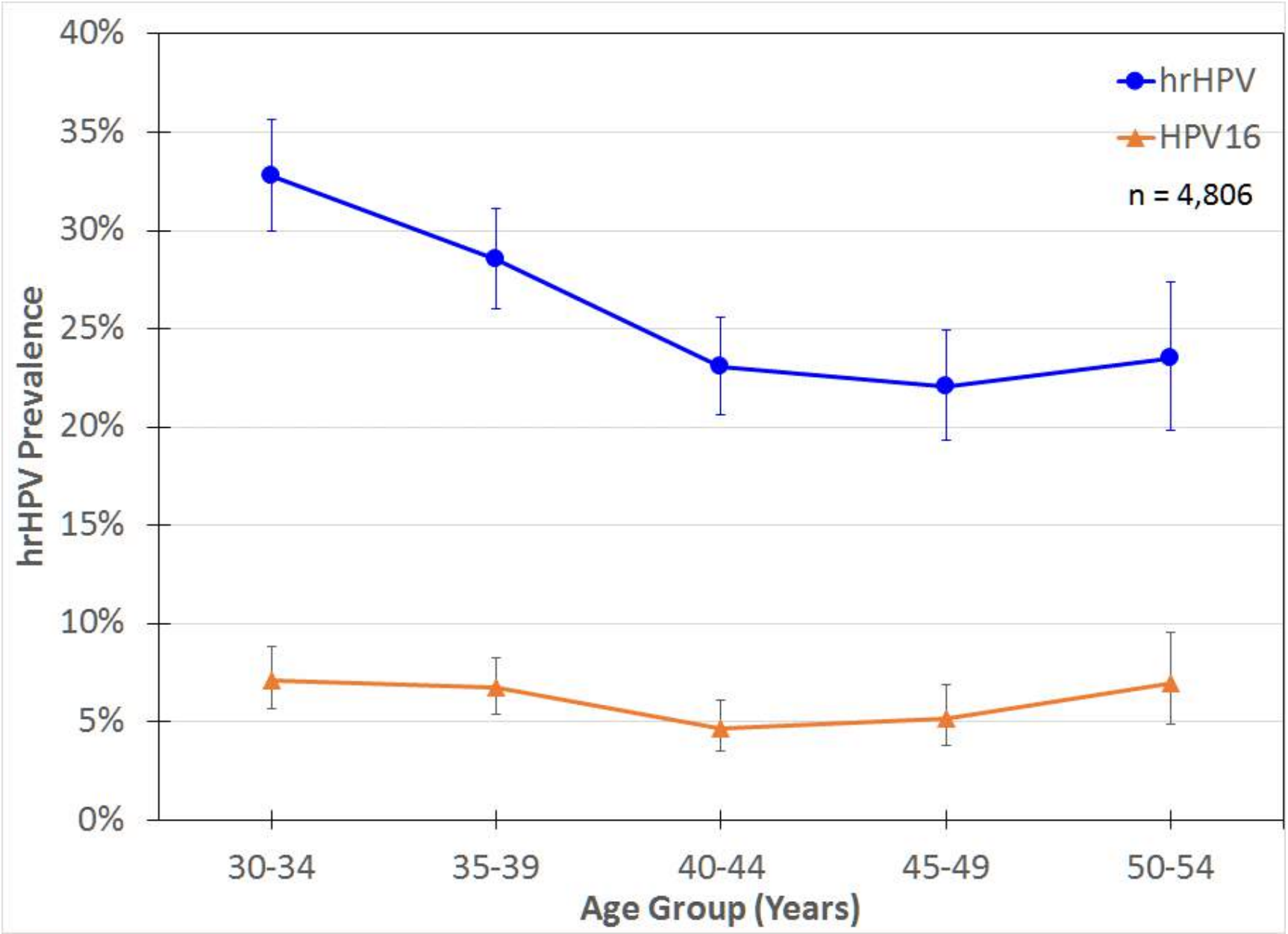
To compare the clinical performance of different screening methods (i.e., HPV DNA and VIA) and biomarkers for triage (e.g. E6/E7 Oncoprotein, Dual Stain, and Host and Viral Genomic Methylation) of screen-positive, HIV+ women living in Rwanda.


>5,000 HIV-Infected, Eligible, Consenting Women, Aged 30-54 Years
Screening Visit (in order of procedure)
• Questionnaire
• Pelvic Exam:
• Cervical Pap Specimen (PreservCyt)
➢ hrHPV DNA testing by GeneXpert
• VIA & MobileODT
Screen Negatives:
VIA- and hrHPV-
Screen Positives:
VIA+ and/or hrHPV+
Colposcopy Exam (in order of procedure)
• Cervical Pap Specimen (PreservCyt)
• Dry Swab for E6/E7 Oncoprotein Test
➢ Biomarkers (CINTec Dual Stain, Methylation)
• VIA (as triage)
• 4-quadrant microbiopsies (modified)
Neg/CIN1
≥CIN2 by Local Pathologist
≥CIN3 by Study Pathologist
Treatment

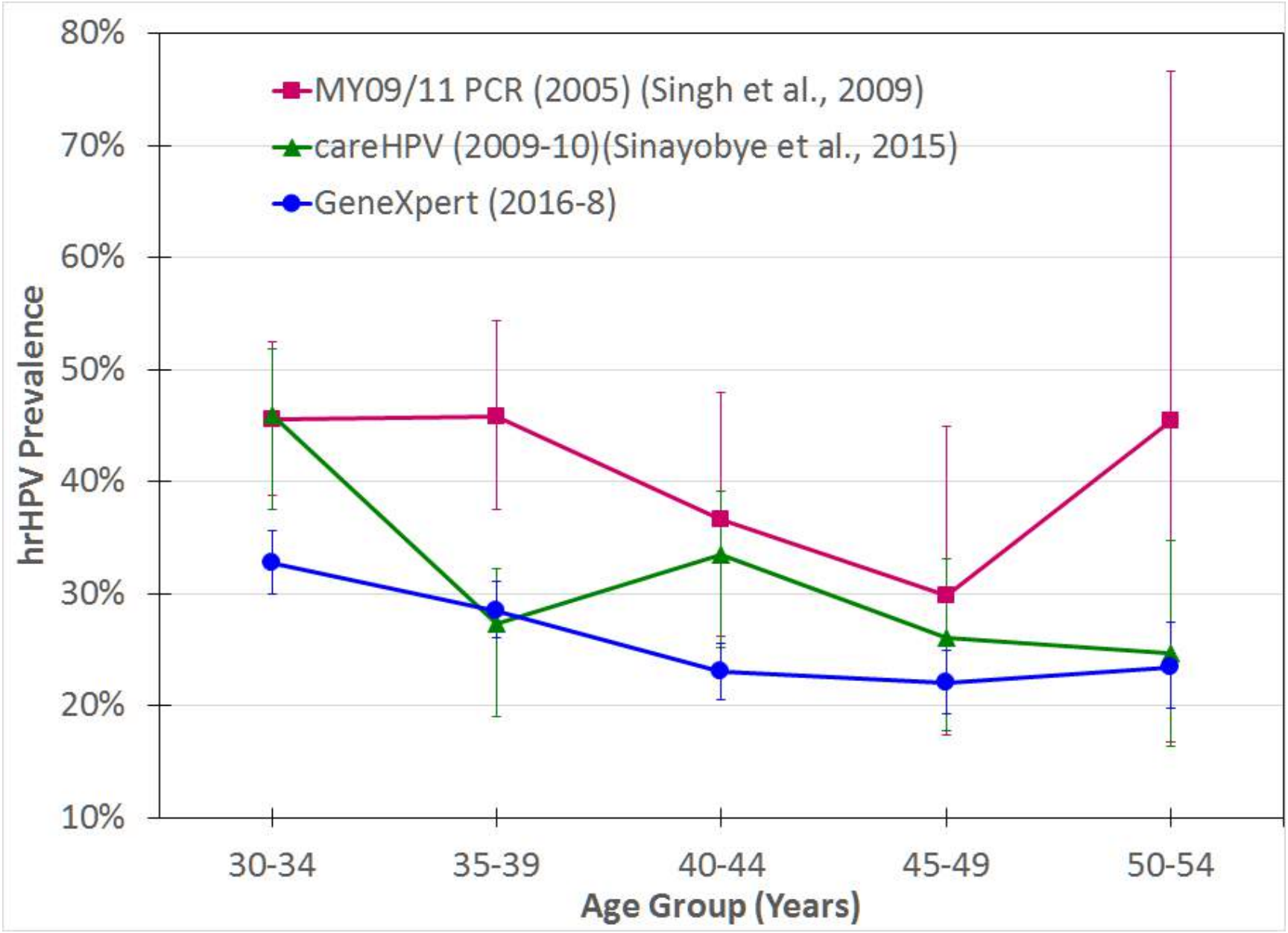
HPV Prevalence



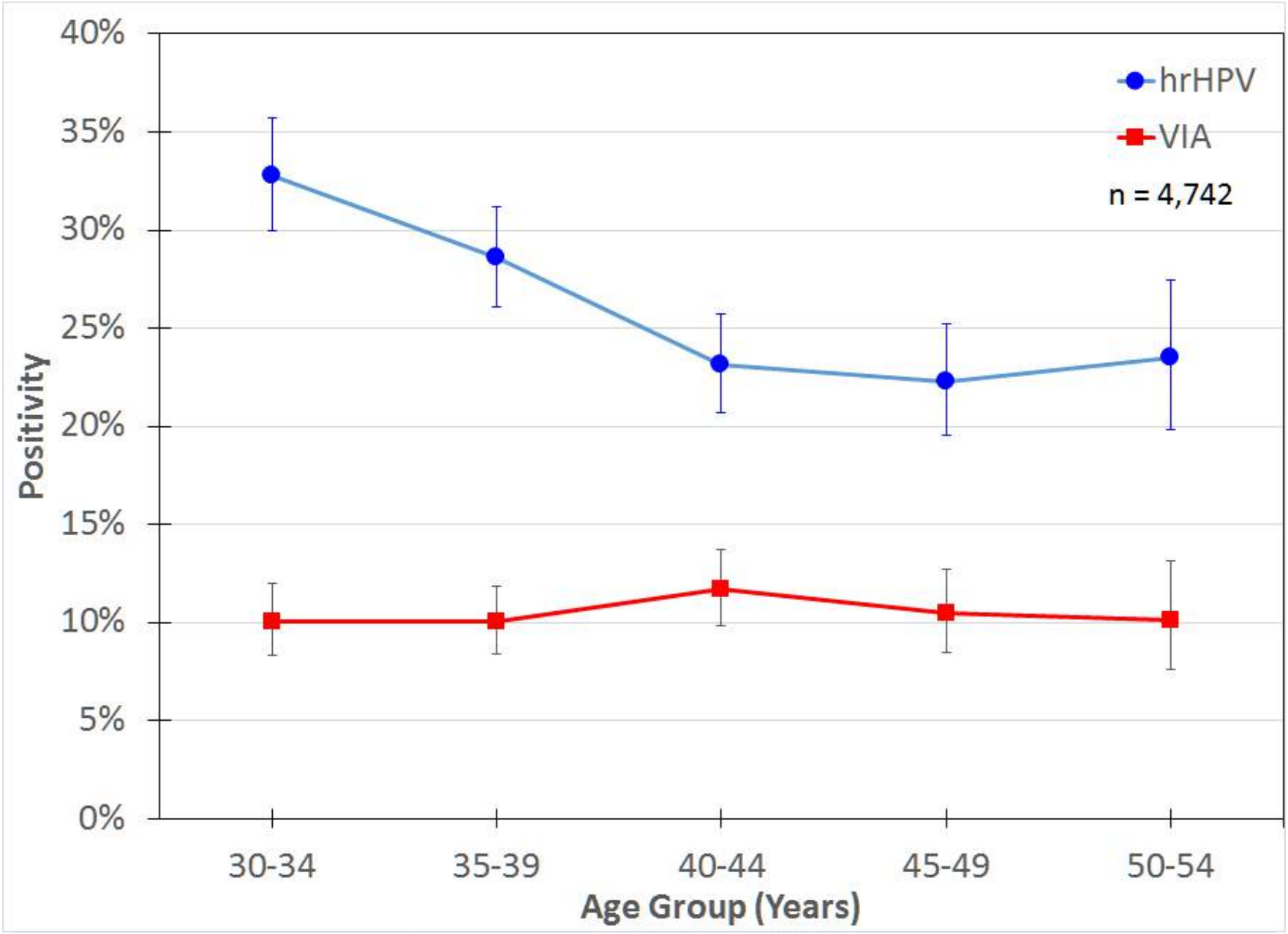
Age Group-Specific hrHPV and HPV16 Prevalence



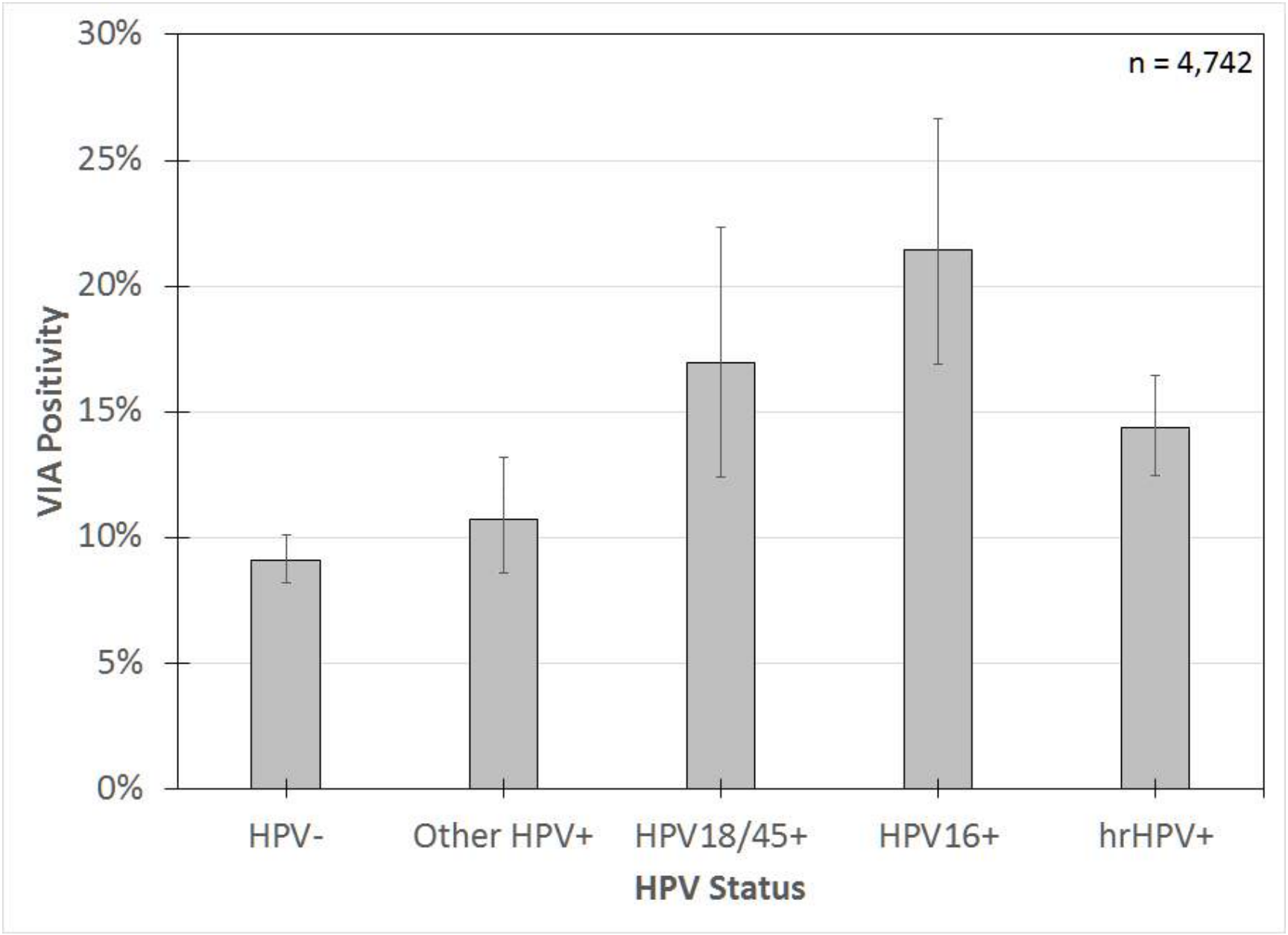
Age Group-Specific hrHPV Prevalence By Study



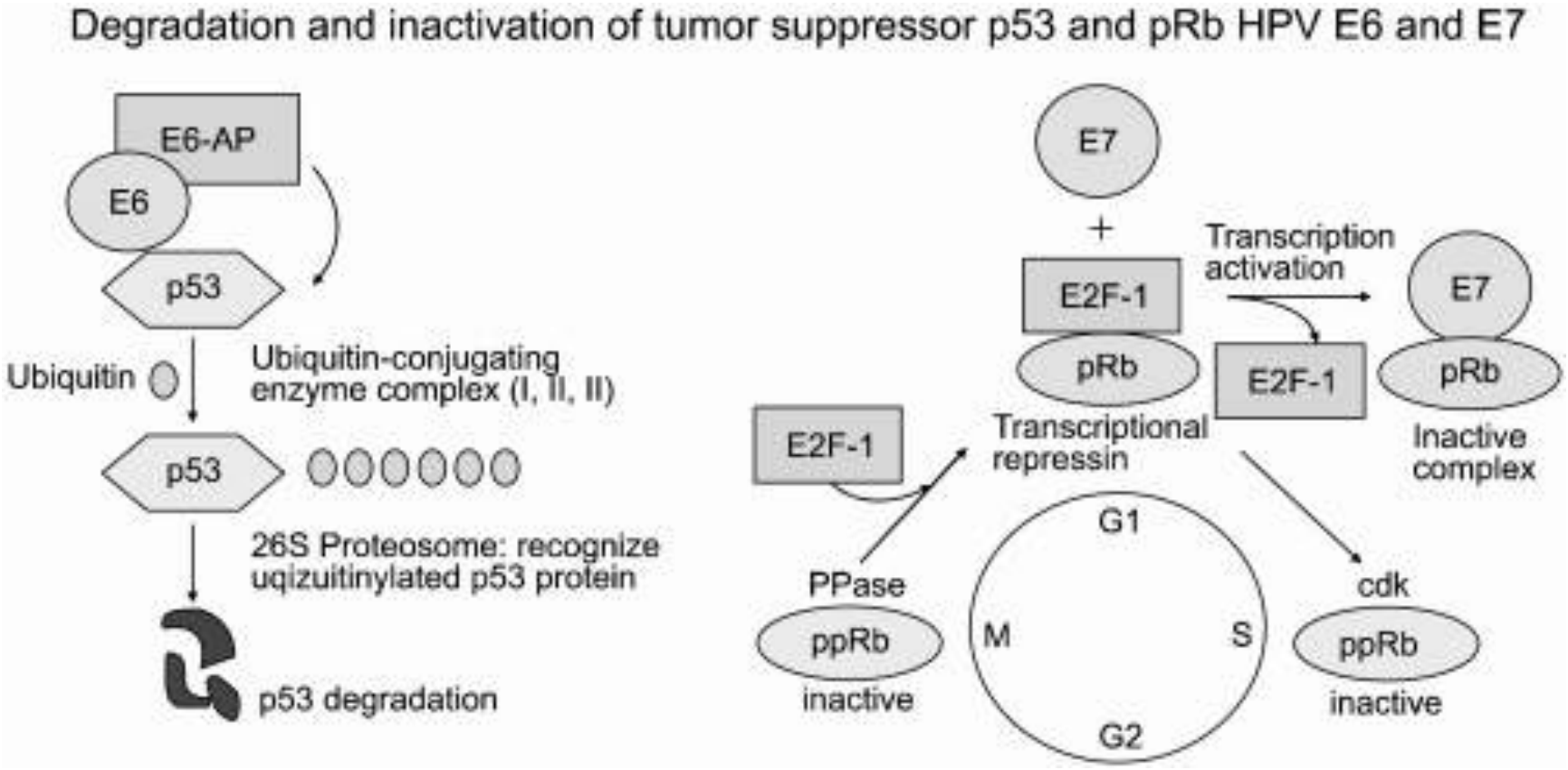
hrHPV and VIA Positivity by Age Group



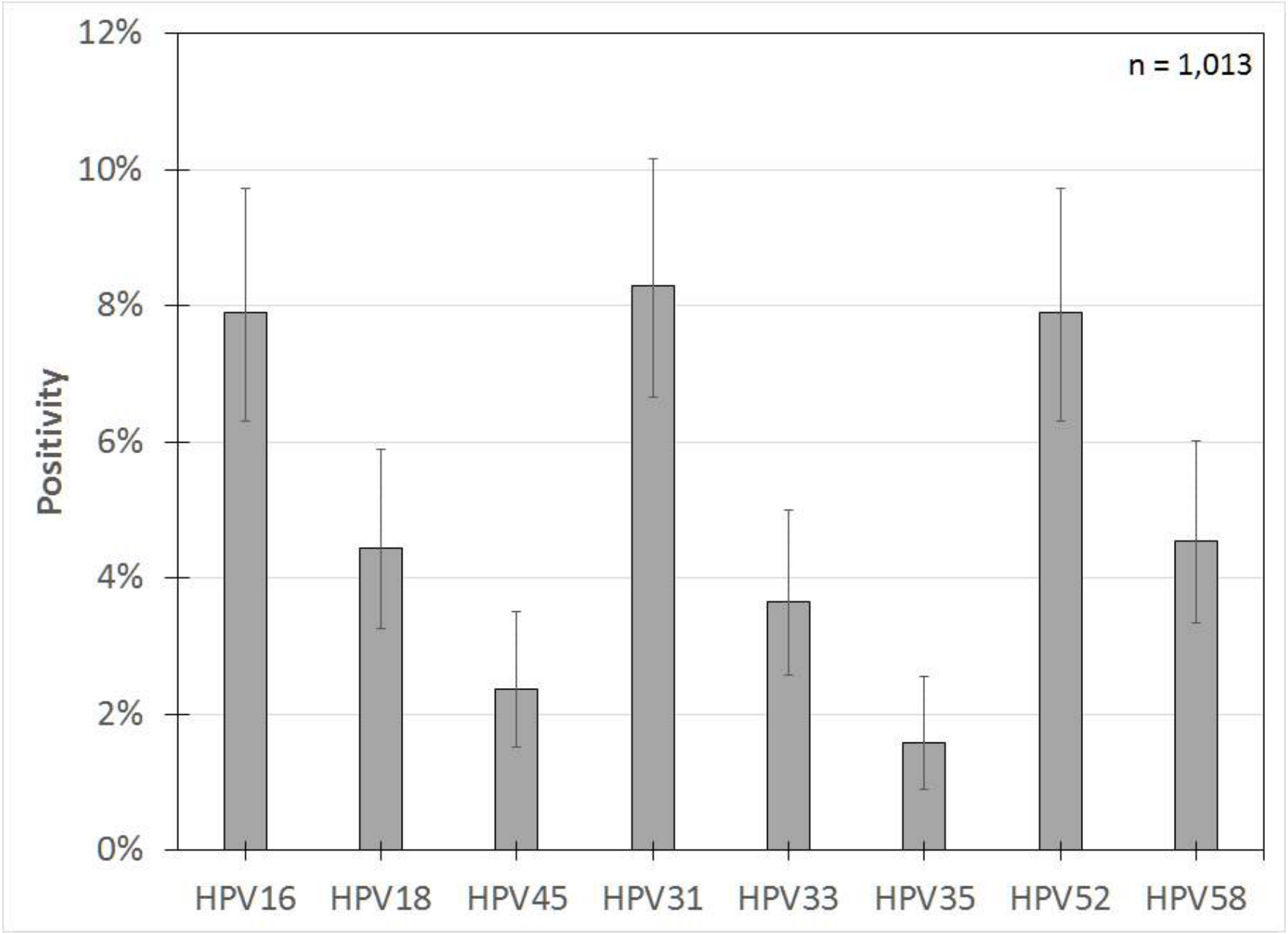
VIA Positivity by HPV Status



E6/E7 oncoproteins expression



Type-Specific E6/E7 Positivity



HPV E6/E7 vs. DNA Among Colposcopy Patients* (p_{trend} <0.001 for all)

		Total Positivity		Paired Results			
DNA Status:		Pos	----	Pos	Pos	Neg	Neg
E6/E7 Status:		----	Pos	Pos	Neg	Pos	Neg
HPV16	n	169	80	73	96	7	837
	%	16.7%	7.9%	7.2%	9.5%	0.7%	82.6%
HPV18 & 45	n	157	66	53	104	13	842
	%	15.6%	6.5%	5.2%	10.4%	1.3%	83.1%
HPV31, 33, 35, 52, & 58	n	422	234	186	236	48	543
	%	41.7%	23.1%	18.4%	23.3%	4.7%	53.6%

*HPV DNA and/or VIA positive

N=1,013

HPV E6/E7 vs. DNA by Group

		HPV E6/E7 Positivity (Hierarchical)		
		HPV31, 33, 35, 52, & 58+	HPV18 & 45+	HPV16+
hrHPV DNA Positivity (Hierarchical)	Other hrHPV+	119	4	2
	HPV31, 33, 35, 52, & 58+	**38**	3	3
	HPV18 & 45+	13	**49**	0
	HPV16+	19	4	**73**
	Total	189	60	78

Type Fidelity:	38/189	49/60	73/78
	20%	82%	91%

Conclusions

1. The prevalence of hrHPV is 26.5% among our study population.
2. hrHPV prevalence decreases with age ($p_{trend}<0.0001$) but HPV 16 prevalence does not.
3. hrHPV prevalence appears to be decreasing over the last decade, perhaps due to better HIV management and care.
4. As expected, E6/E7 positivity is lower than HPV DNA but very specific for the positive types by each test.
5. The study is ongoing but enrollment target of 5,000 achieved.
6. Pathology results to compare with clinical outcome will soon be available.

Acknowledgements

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Protocol published

Murenzi G, Dusingize J-C, Rurangwa T, Sinayobye J d'Amour, Munyaneza A, Murangwa A, et al. Protocol for the study of cervical cancer screening technologies in HIV-infected women living in Rwanda. BMJ Open [Internet]. 2018;8(8):e020432. Available from: http://bmjopen.bmj.com/lookup/doi/10.1136/bmjopen-2017-020432

https://www.ncbi.nlm.nih.gov/pubmed/30082342

MANY THANKS FOR
YOUR KIND ATTENTION