

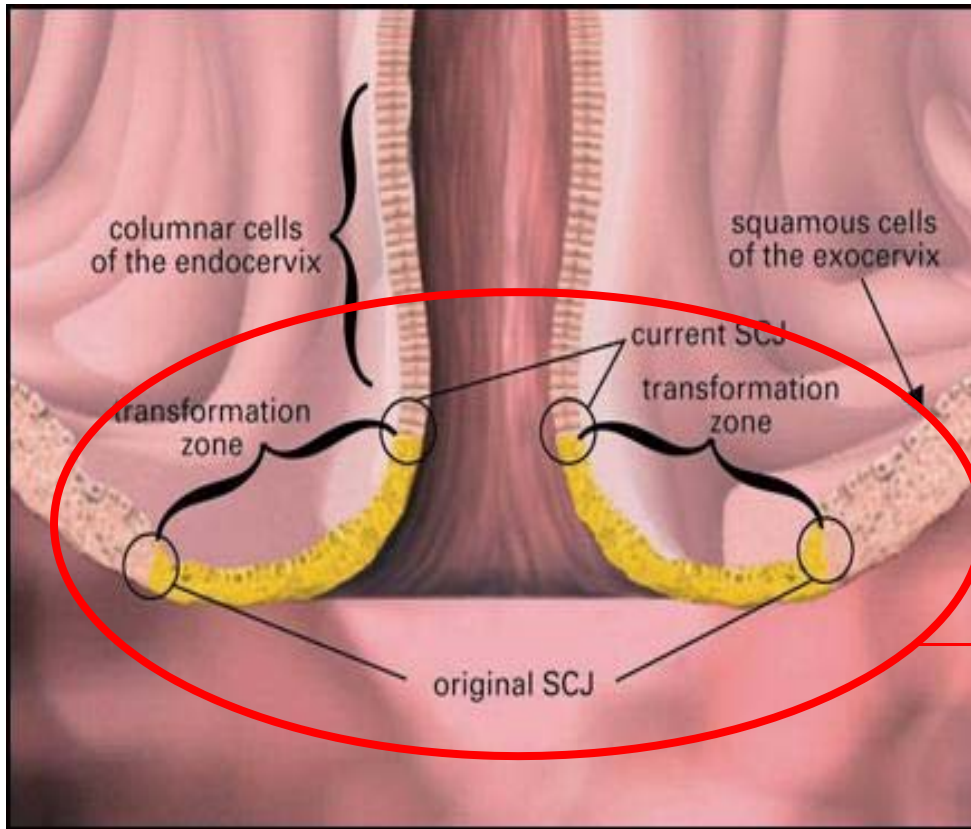
High Prevalence Of Cervical Squamous Intraepithelial Lesions In Women On Antiretroviral Therapy In Cameroon:

Is Targeted Screening Feasible?

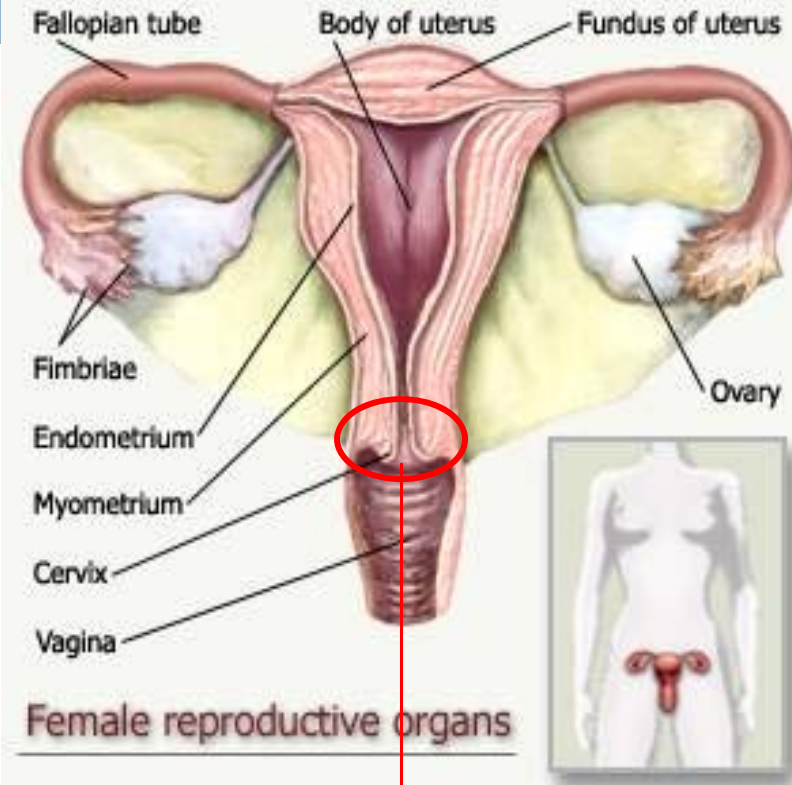
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Cervical cancer - Pathogenesis

Transformation Zone



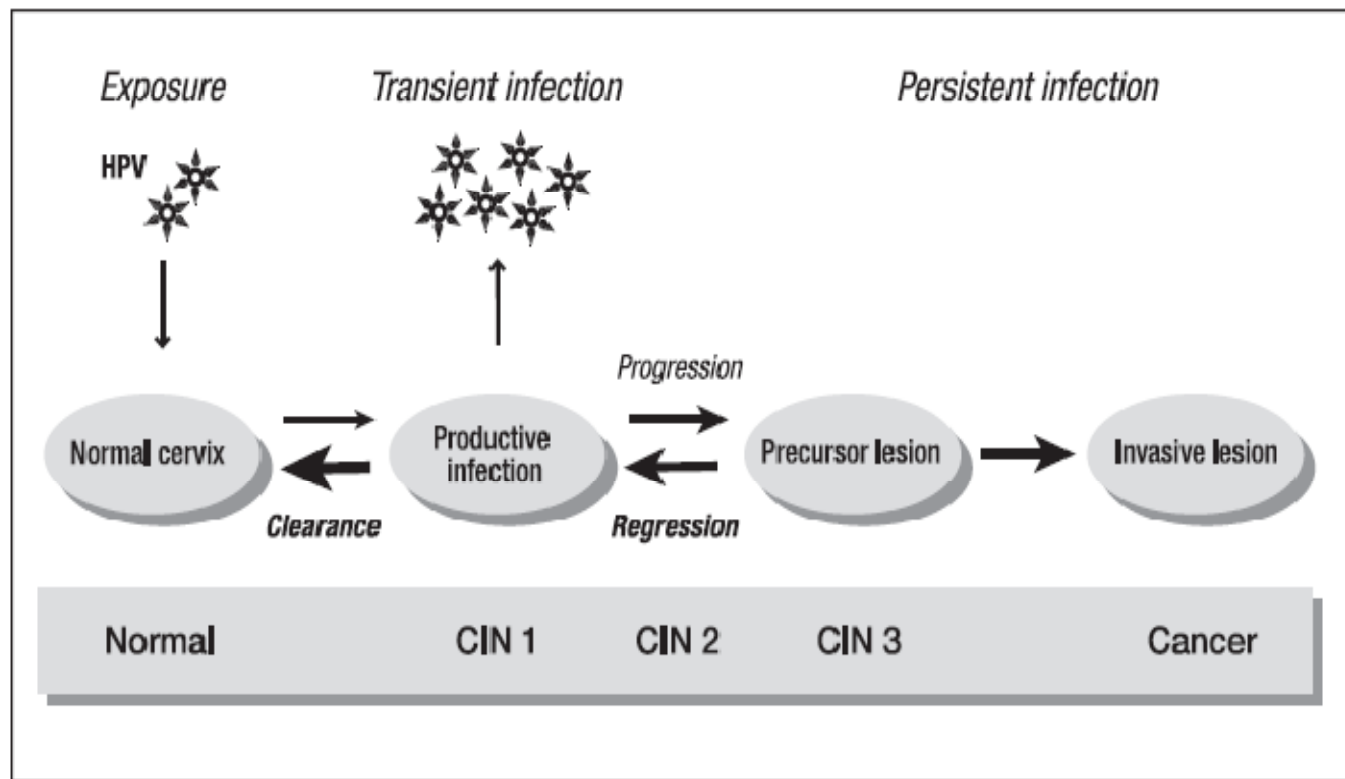
Credit: Merck & Co., Inc.



Credit: Choice to Live With, Inc.

Cervical cancer - pathogenesis

- Natural history from HPV infection to invasive cancer



CIN: cervical intraepithelial lesion

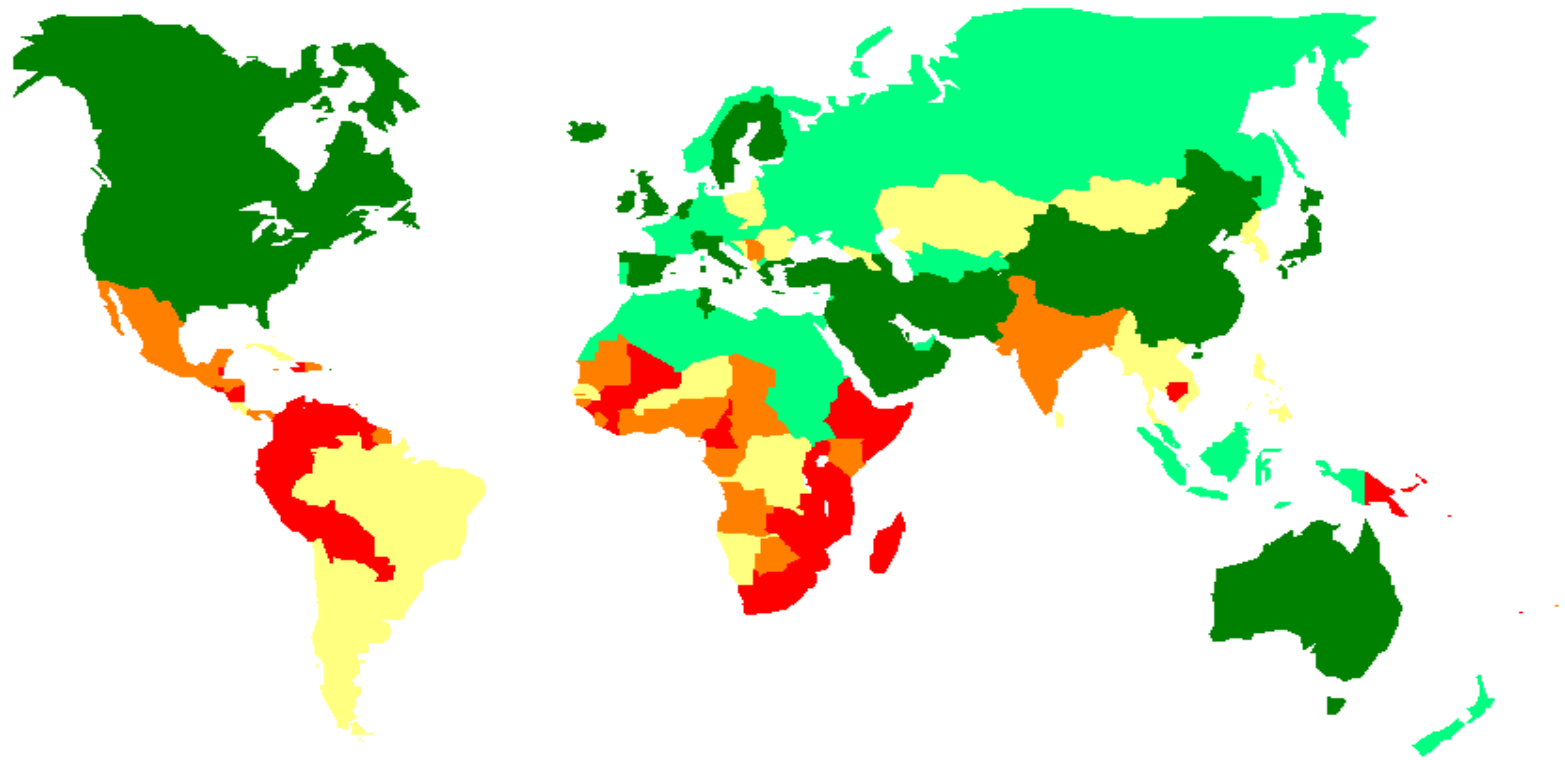
Classification of cervical precancerous lesions/cancer

Cytological classification (used for screening)		Histological classification (used for diagnosis)	
Pap	Bethesda system	CIN	WHO descriptive classifications
Class I	Normal	Normal	Normal
Class II	ASC-US ASC-H	Atypia	Atypia
Class III	LSIL	CIN 1 including flat condyloma	Koilocytosis
Class III	HSIL	CIN 2	Moderate dysplasia
Class III	HSIL	CIN 3	Severe dysplasia
Class IV	HSIL	CIN 3	Carcinoma in situ
Class V	Invasive carcinoma	Invasive carcinoma	Invasive carcinoma

CIN: cervical intraepithelial neoplasia; LSIL: low-grade squamous intraepithelial lesion; HSIL: high-grade squamous intraepithelial lesion; ASC-US: atypical squamous cells of undetermined significance; ASC-H: atypical squamous cells: cannot exclude a high-grade squamous epithelial lesion.

Cervical cancer epidemiology – incidence

Incidence of Cervix uteri cancer: ASR (World) (All ages)

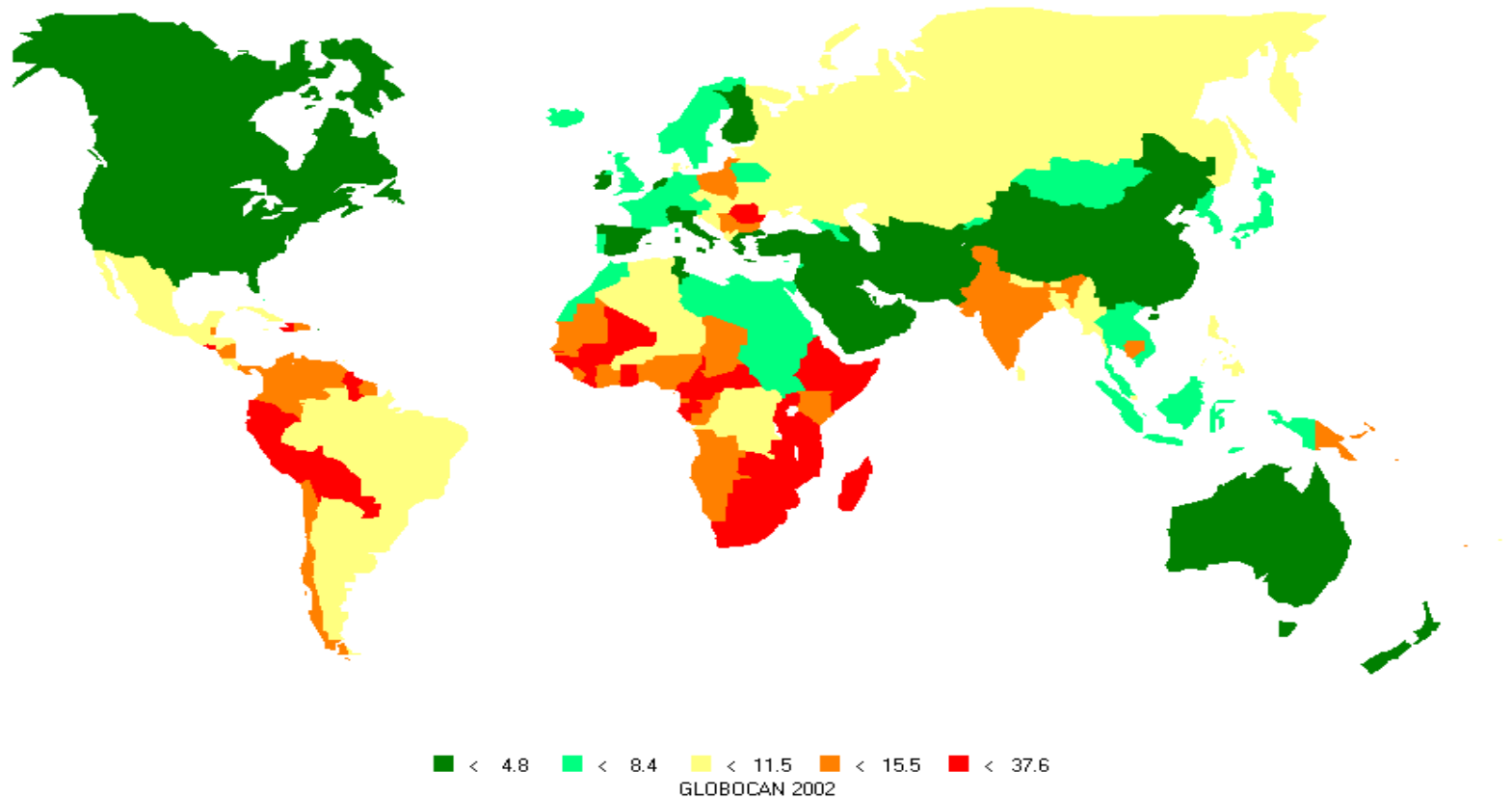


■ < 9.3 ■ < 16.2 ■ < 26.2 ■ < 32.6 ■ < 87.3
GLOBOCAN 2002

□ Worldwide: 500,000 cases annually

Cervical cancer epidemiology-mortality

Mortality from Cervix uteri cancer: Crude rate (All ages)

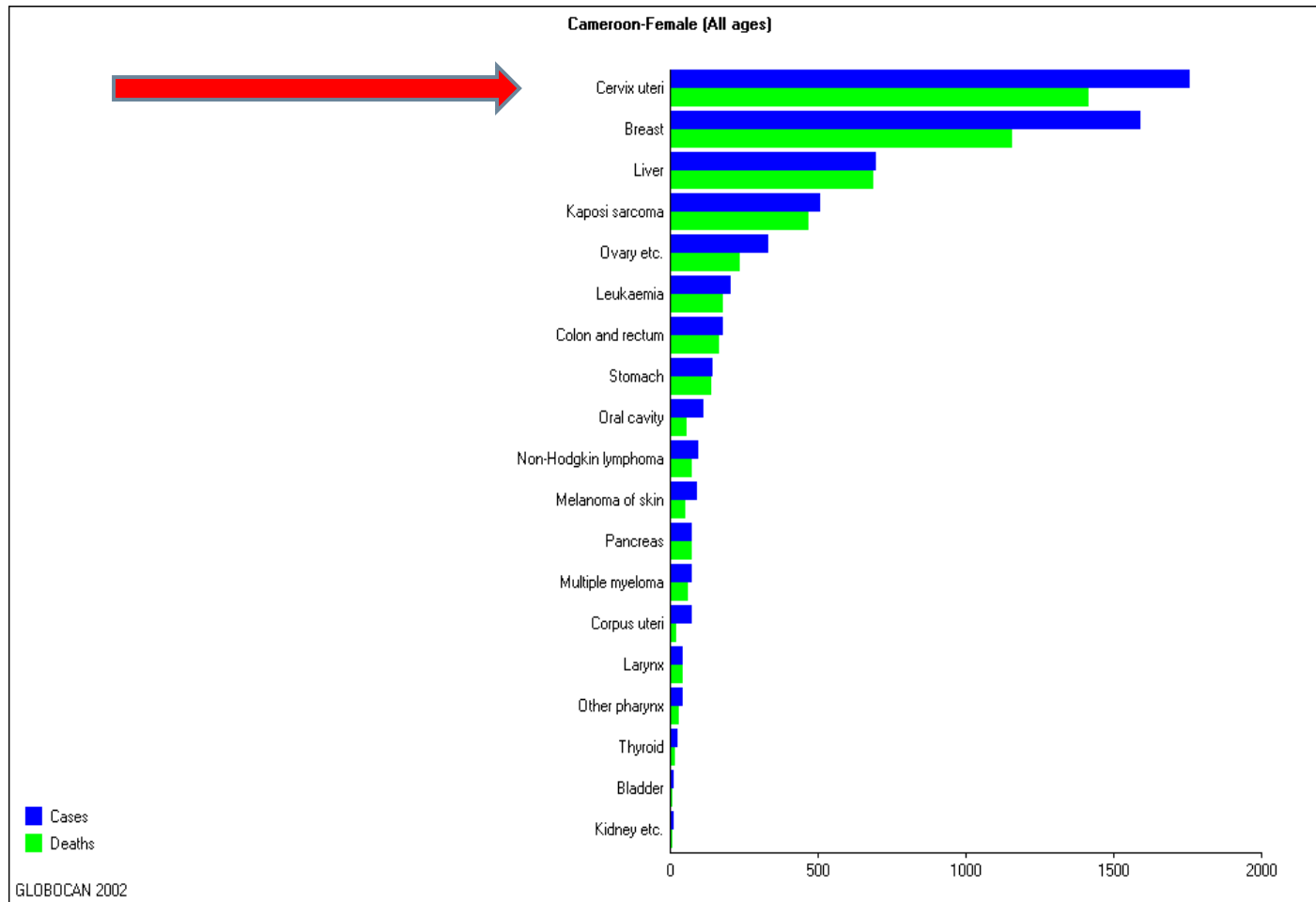


□ Worldwide 300,000 deaths annually

Cervical cancer - epidemiology

- Second cause of cancer in women
- Second cause of cancer deaths in women
- Annually:
 - 630 million HPV infections
 - 30 million low-grade lesions
 - 10 million of high-grade lesions
 - 500,000 cervical cancer cases
 - 300,000 deaths

Cancer epidemiology: Cameroon



Incidence and mortality of cancers in females in Cameroon

HIV and Cervical cancer

- **Invasive cervical cancer is AIDS-defining**
- **Pathogenesis of ICC in HIV-infected**
 - **HPV**
 - **Higher HPV incidence (both STDs)**
 - **Higher HPV Persistence**
 - **Precancerous lesions**
 - **Higher prevalence**
 - **Higher incidence**
 - **Faster progression LSIL to HSIL**

HIV in women in Cameroon

- 6% prevalence
- Access to HAART increasing
- No systematic screen for cervical cancer
- Potential for increased cervical cancer mortality
with increased survival

Why screen in HIV positive women

- ARV treatment: expected longer survival
- Unlike some other cancers (ex. KS), immune restoration with HAART does not substantially halt the progression of lesions to cancer
- Screening effective in detecting precancerous lesions and reducing cancer incidence
- Precancerous lesions can be treated with relatively cheaper techniques requiring modest training and infrastructure

Overall goal

- To evaluate the need for cervical cancer screening in HIV-positive women in Cameroon and assess the potential for targeted screening

Specific aims

- **To determine the prevalence, severity and predictors of SIL in HIV-positive women on antiretroviral therapy in Cameroon**
- **Develop and assess risk scores for clinical use**

Why targeted screening



- ▣ **Potentially cost and time effective**
- ▣ **Reduce false positives and false negatives**

Methods

- Cross-sectional design
- Setting: three HIV-care clinics in Cameroon
- Eligibility criteria
 - ▣ Aged 18 years +
 - ▣ Within a year of initiating HAART
 - ▣ Non-pregnant and not bleeding
- 282 women recruited
 - ▣ Estimate margin of error of $<1.5\%$ at any prevalence

Data collection

- Patient assessment
 - ▣ Demographic and clinical characteristics

- Laboratory assessment
 - ▣ Cervical cytology and Pap smear
 - Conventional method

 - ▣ Quality control/validation

Variables

□ Outcomes

- Prevalent SIL
- Prevalent ASC-H/HSIL

□ Predictors

- Marital status
- Rural/Urban residence
- Parity
- Age
- Hormonal contraception
- Exposure to tobacco smoke
- CD4 count
- AIDS clinical stage

Statistical analysis

- Univariate analysis
 - ▣ Description of outcomes, potential predictors and other patient characteristics

- Bivariate analysis
 - ▣ Unadjusted POR and 95% CI for each predictor
 - ▣ Linearity of the log-odds for continuous variables
 - Graphical methods (Lowess)
 - LR test of fitness of quadratic term in model

Statistical analysis

- Multivariate analysis
 - All models unconditional logistic models
 - Predictive models
 - Full model
 - Reduced model based on backward elimination
 - Stop based on $p\text{-value} < 0.05$ or $> 10\%$ change in c-statistic
 - Risk score development
 - Based on integers proportional to model slope coefficients
 - Assessment of risk scores
 - Estimation of errors associated with each cut-off



Results



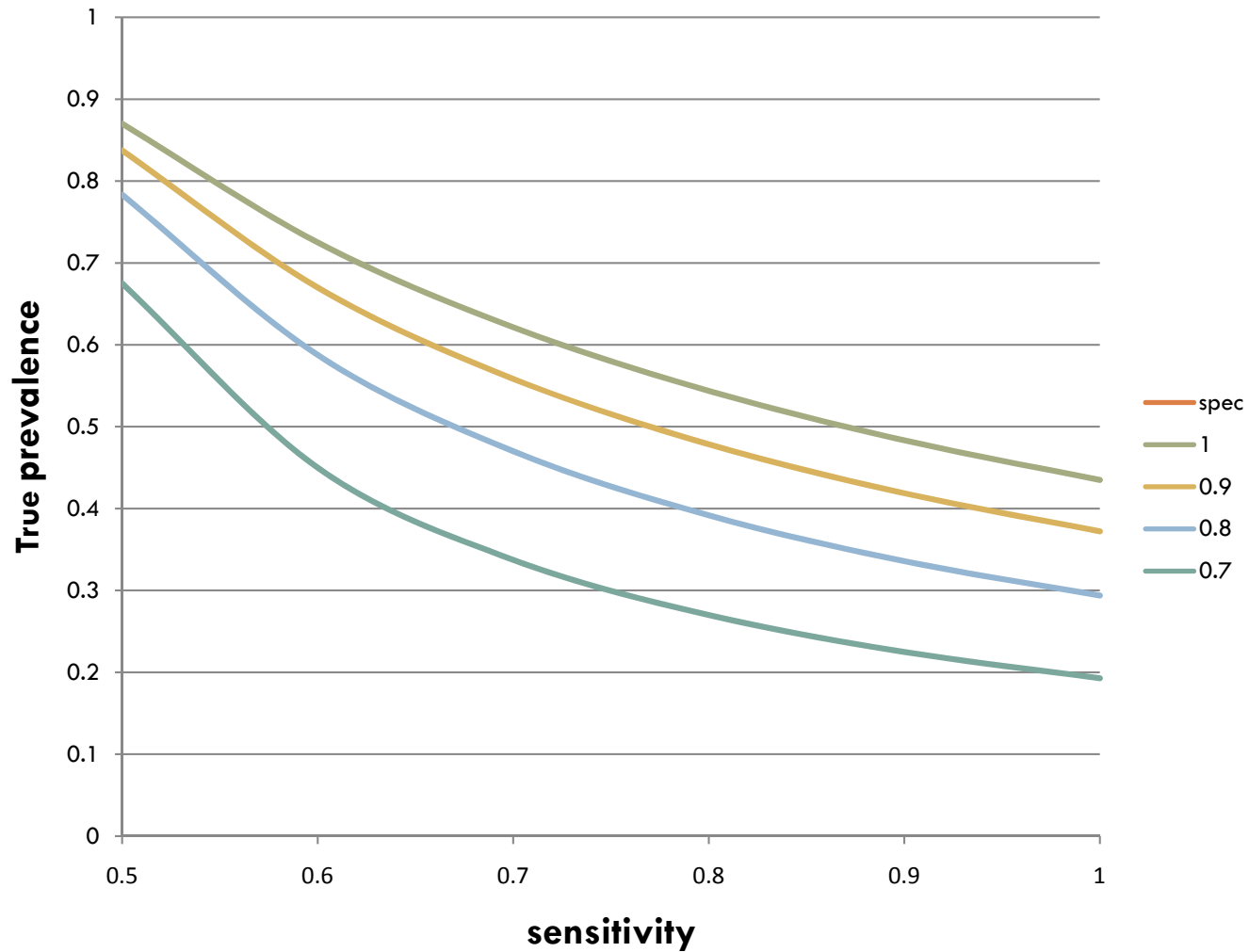
Characteristics of 282 participants

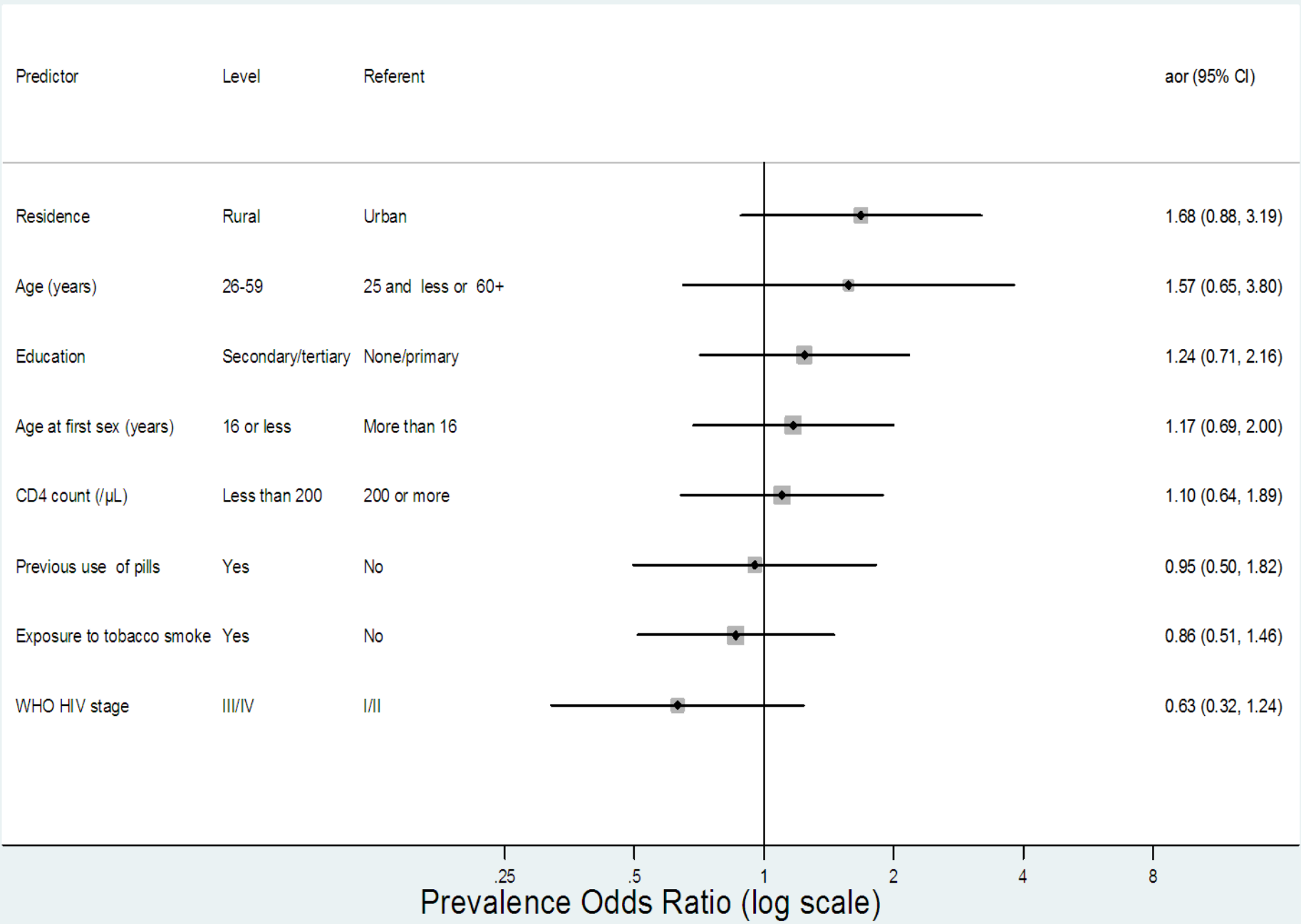
- Age mean of 36 years range 19 - 68
- HIV diagnosis for 18 months range 0 -136
- CD4 count median 176 IQR 100 – 271
- WHO HIV stage III/IV in 80.9%
- Previous Pap smear in only 2.1%

Prevalence and severity

- SIL in 43.5% (95%CI: 37.5, 49.6%)
 - ▣ ASCUS 0.7% (95%CI: 0.09, 2.3%)
 - ▣ LSIL 25.0% (95%CI: 20.0, 30.5%)
 - ▣ ASC-H 14.5% (95%CI: 10.6, 19.2%)
 - ▣ HSIL 3.3% (95%CI: 1.5, 6.1%)

Sensitivity analysis of prevalence





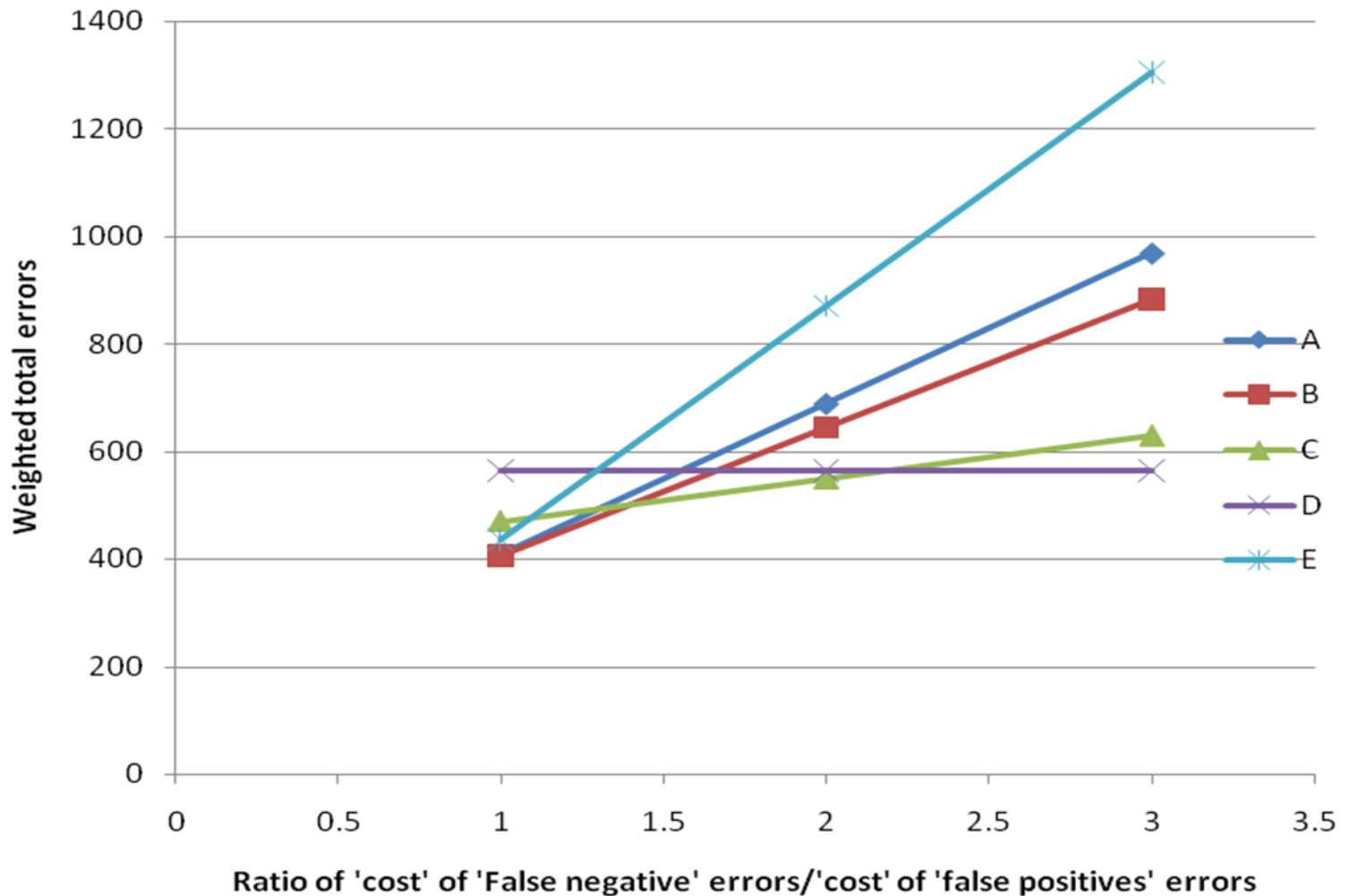
Risk score for predicting presence of lesions

Characteristic	Score
Full model for predicting prevalent SIL	
HIV diagnosed within 1 year	2
Age at first sex less than or equal 16 years	2
Not exposed to tobacco	2
Secondary/tertiary education	2
Rural residence	5
WHO HIV Stage I/II	5
Age 26-59 years	5
TOTAL	23

Performance of Risk score

Targeted proportion to screen	Cut-off score	SENS (%)	SPEC (%)	PPV (%)	NPV (%)	Total unweighted** errors (per 1000 women)
Risk score for any SIL						
Screen 25%	> 14	35.7	77.0	54.0	61.3	410
Screen 50%	> 11	45.2	70.4	53.6	62.9	406
Screen 75%	> 8	81.7	30.9	47.2	69.1	470
Universal screening (100%)*	None	100.0	0.0	43.5	NA	565
No screening (0%)*	None	0.0	100.0	NA	56.5	435

Errors associated with screening strategies



Limitations and strengths

Limitations

- **Not representative of whole country**
- **Measurement error associated with limitations of a Pap smear**
- **Limited number of covariates**
- **No data on HPV and Histology**

Strengths

- **Primary data collection**
- **Trained interviewers and cytologist**
- **Clinically relevant predictors**

Conclusion

- High prevalence of SIL in women initiating antiretroviral therapy in Cameroon.
 - ▣ need for screening in this population.

- No accurate demographic or clinical predictor of SIL
 - ▣ alternative affordable screening options need to be explored.

- A prospective study of the long-term evolution of these lesions and their determinants is needed

Acknowledgements



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- **Others**

Thank You!

