

Pregnancy and HIV Risk

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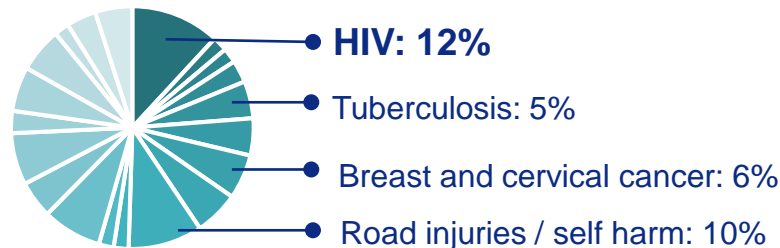
Take home points

- Pregnancy is a time of heightened HIV risk
 - HIV risk during pregnancy is likely 2-3 times greater than non pregnant times
- Postpartum may also be a time of heightened risk
 - HIV risk during postpartum may be as high as 4 times greater than non pregnant times
- Increases in risk are likely due to behavioral and biological factors

HIV and women

- Disproportionate HIV risk

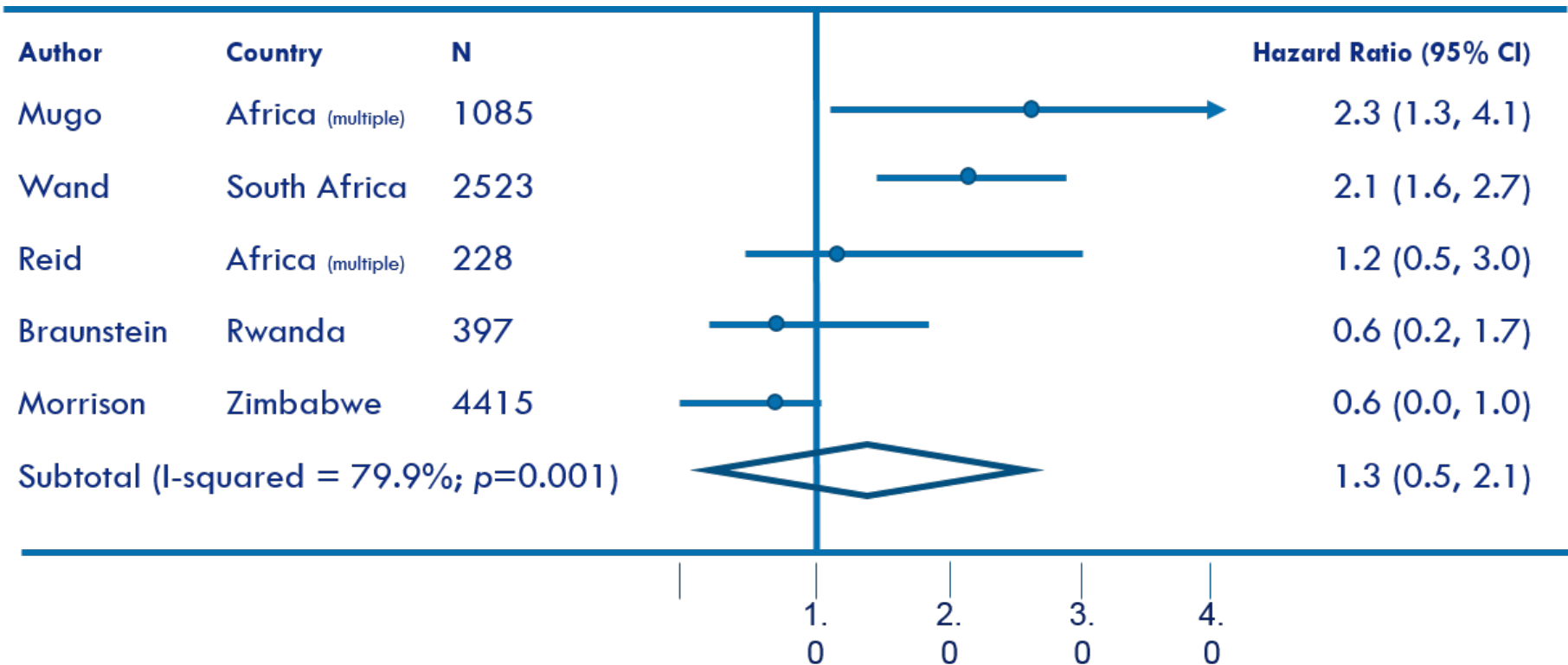
Leading causes of death for women 15-49 years worldwide



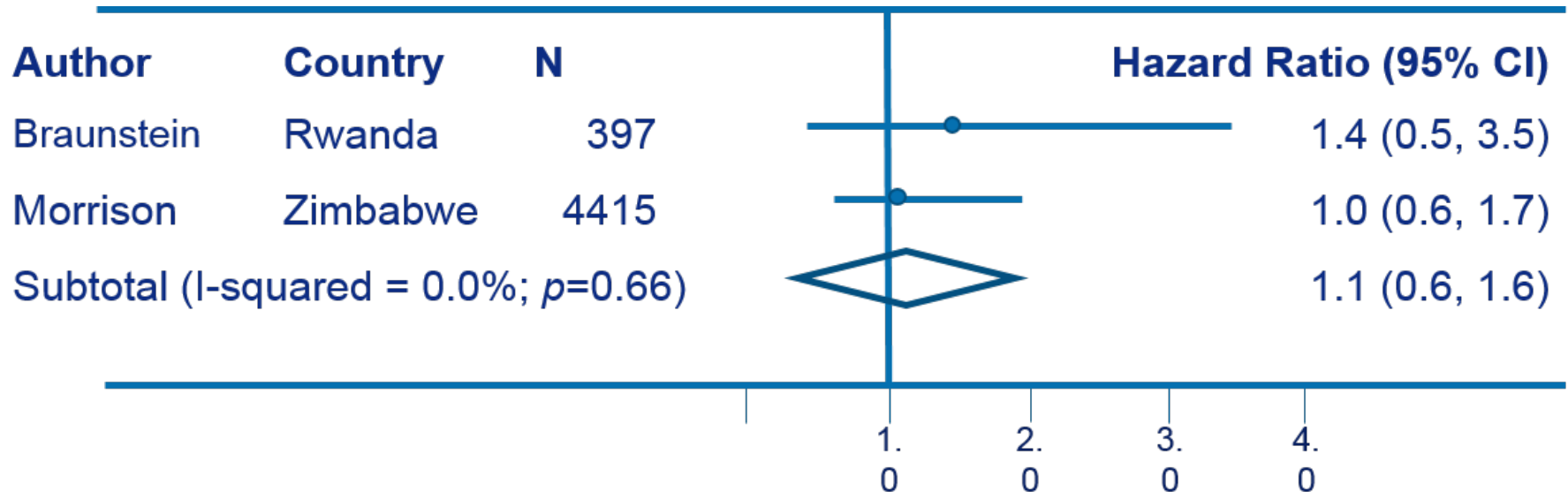
- High HIV incidence during pregnancy and postpartum



Studies of pregnancy as a risk factor for HIV acquisition



Studies of postpartum as a risk factor for HIV acquisition



New data – per coital act probabilities

- Prior studies calculated HIV incidence rates during pregnant and non-pregnant periods
- Include adjustment for sexual frequency and condom use
- New data calculate the probability of HIV acquisition with each sex act and adjust for condom use

Research objective

To estimate the probability of HIV acquisition per sex act during periods when women were pregnant and postpartum and compare these probabilities to time periods unrelated to pregnancy

Data sources

Two longitudinal HIV prevention studies

HIV serodiscordant couples, ART naïve

Frequent testing of HIV and pregnancy

Monthly reports of sexual behavior (sex acts and condom use)

Genetic linkage of incident infections

The Partners in Prevention HSV/HIV Transmission Study

2004 – 2007

Botswana, Kenya, Rwanda, South
Africa, Tanzania, Uganda, Zambia

3,408 couples for 24 months

No effect of acyclovir on HIV
incidence



The Partners PrEP Study

2008 - 2012

Kenya and Uganda

4,747 couples up to 36 months

Significant reduction in HIV
incidence from daily oral PrEP

Analytic approach

- HIV uninfected women ages 18-49
- Censoring
 - Study visits after male partner reported ART initiation
 - Seroconversions determined to be unlinked HIV infections (from partners with unknown sexual activity)
- Outcome: First evidence of an HIV infection linked to the male study partner
 - earliest visit with positive HIV EIA or RNA

Defining reproductive stages

- Exposures:

1. Pregnant/non-pregnant stage (time dependent)
 - Pregnancy testing: Monthly (Partners PrEP) or as clinically indicated (HSV-2)
 - Pregnancy start and stop dates defined using date of last menstrual period and pregnancy outcome
2. Number of sex acts within partnership (reported monthly)



**Early
Pregnancy**
0-13 wks gestation



Postpartum
Delivery –
6 months (less for losses)



**Late
Pregnancy**
14 wks – delivery/loss



Unrelated
Not pregnant
or postpartum

Postpartum definition for pregnancy loss ≥ 20 weeks or newborn death: 6 weeks; for pregnancy loss 6-19 weeks: 4 weeks; for pregnancy loss < 6 weeks: 0 weeks.

Statistical model

- Complementary log-log model
- Adjustment
 - HIV plasma viral load of male partner
 - Active PrEP use
 - Condom use
 - Age
 - Additional adjustment for STI/HSV-2 infection and parent study did not yield substantial changes
- Reference group for the absolute probability of HIV acquisition per condomless act:
 - 25 year old woman
 - not pregnant
 - not using PrEP
 - male partner viral load=10,000 copies/ml

Participant characteristics

2,751 HIV-Negative Women, Median (IQR) or N (%)

HIV Negative Women

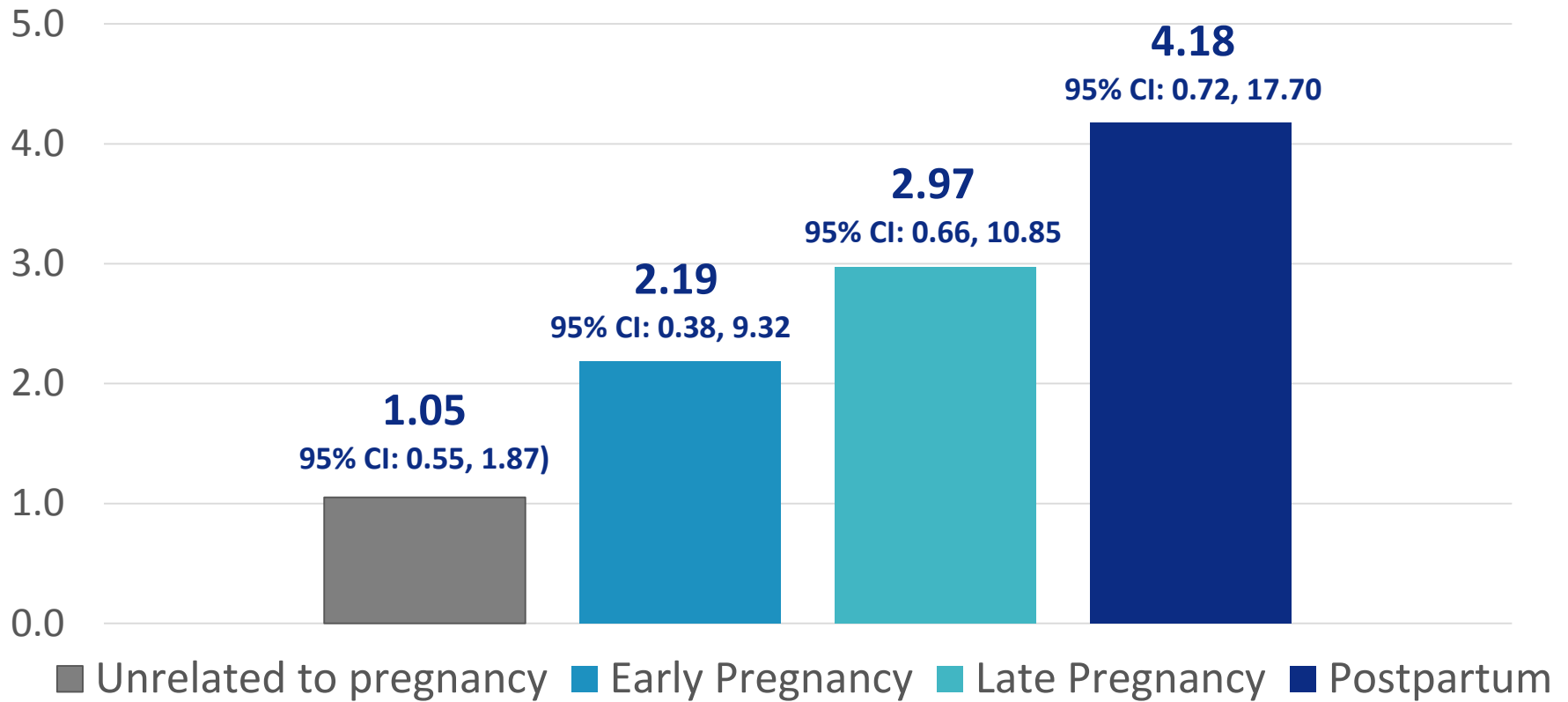
Characteristics at enrollment

Age (years)	32.0 (27.0-37.7)
Number sex acts with study partner, past month	4.0 (2.0-8.0)
Any condomless sex with study partner, past month	670 (24.4)

Pregnancies during follow-up

Ever pregnant during follow-up	615 (22.4)
Total pregnancies	686
Live birth	426 (62.1)
Loss	169 (24.6)
Ongoing at study exit	91 (13.3)

HIV infectivity per 1,000 sex acts



Calculated using a reference case of a 25-year old woman not pregnant, not using PrEP, with a partner with viral load of 10,000 copies/ml

Relative risk of HIV acquisition

Reproductive Stage	Base Model*		Adjusted Model**	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Non-pregnant/ postpartum	1.00	--	1.00	--
Early pregnancy through postpartum	4.97 (2.95, 8.38)	<0.001	2.76 (1.58, 4.81)	<0.001
Early pregnancy	3.20 (1.24, 8.25)	0.02	2.07 (0.78, 5.49)	0.14
Late pregnancy	5.54 (2.62, 11.69)	<0.001	2.82 (1.29, 6.15)	0.01
Postpartum	7.80 (3.04, 20.02)	<0.001	3.97 (1.50, 10.51)	0.01

*Adjusted for condom use, reproductive stage

**Adjusted for condom use, reproductive stage female age, active PrEP use, HIV RNA of male partner

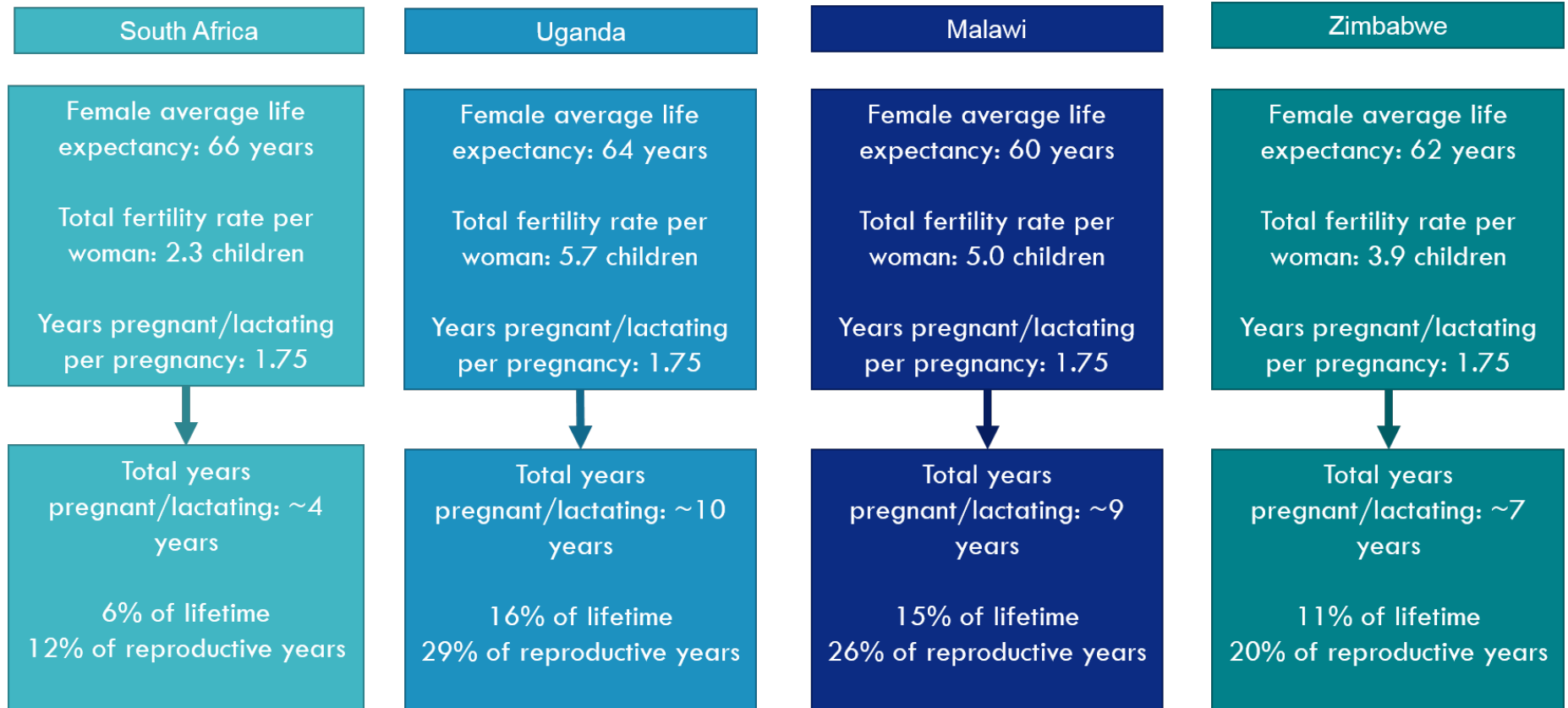
Additional analyses

- Similar results in sensitivity analyses
 - Used estimated date of HIV infection
 - Excluded women randomized to active PrEP arms
 - Excluded women who were never pregnant during follow-up
 - Included a longer postpartum period from 6-12 months

Results summary

- Increased risk of HIV acquisition per sex act
 - 3-fold increase in late pregnancy
 - 4-fold increase in postpartum
 - Similar results seen across multiple sensitivity analyses
- Results accounted for decreases in sexual frequency and condom use as pregnancy progressed
- Results of this per-coital act analysis suggest that biological changes associated with pregnancy and postpartum, contribute to increased HIV acquisition.
 - However, we did not directly assess any biological mechanisms for increased HIV susceptibility

Implications: Duration of risk is substantial



Implications: Many opportunities to intervene

- Antenatal care presents tremendous opportunities to promote HIV prevention and care
- These data highlight the importance of:
 - Counseling on increased HIV risk during pregnancy and postpartum
 - Promoting repeat HIV testing during maternal health visits
 - Identifying HIV infected male partners and linking to HIV care and ART initiation
 - Promoting woman-controlled HIV prevention strategies during pregnancy and postpartum, such as oral PrEP