

Maternal Mortality and HIV: Examining Research through a Programmatic Lens

Day 1 Recap

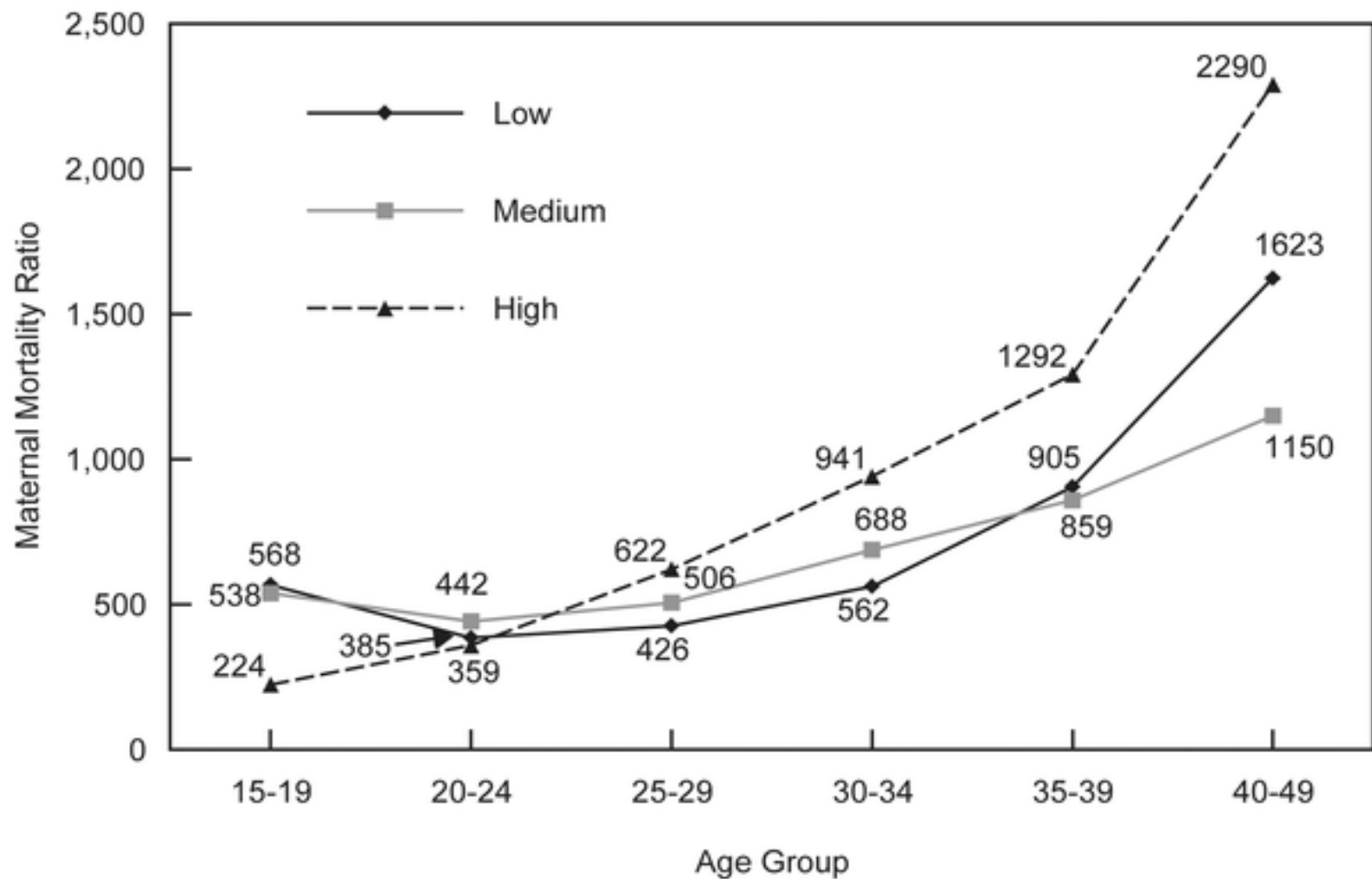
Introduction

- Every day, approximately 800 women die from preventable causes related to pregnancy and childbirth.
- 99% of all maternal deaths occur in developing countries. (50% in SSA and 30% in Southern Asia)
- A woman's lifetime risk of maternal death – the probability that a 15 year old woman will eventually die from a maternal cause – is 1 in 3800 in developed countries, versus 1 in 150 in developing countries.
- A WHO analysis estimated that worldwide in 2008, 61 400 maternal deaths **(18% of all maternal deaths) were attributable to HIV**







Maternal Mortality and HIV

- Purpose: evaluate evidence to develop programs to implement in high burden countries to reduce maternal mortality in HIV+ women.
- Remember the four prongs to PMTCT include prevention of HIV infection in women, prevention of unintended pregnancies as well as testing and treatment of HIV+ women.

Maternal mortality ratios, sub-Saharan African countries by HIV prevalence.

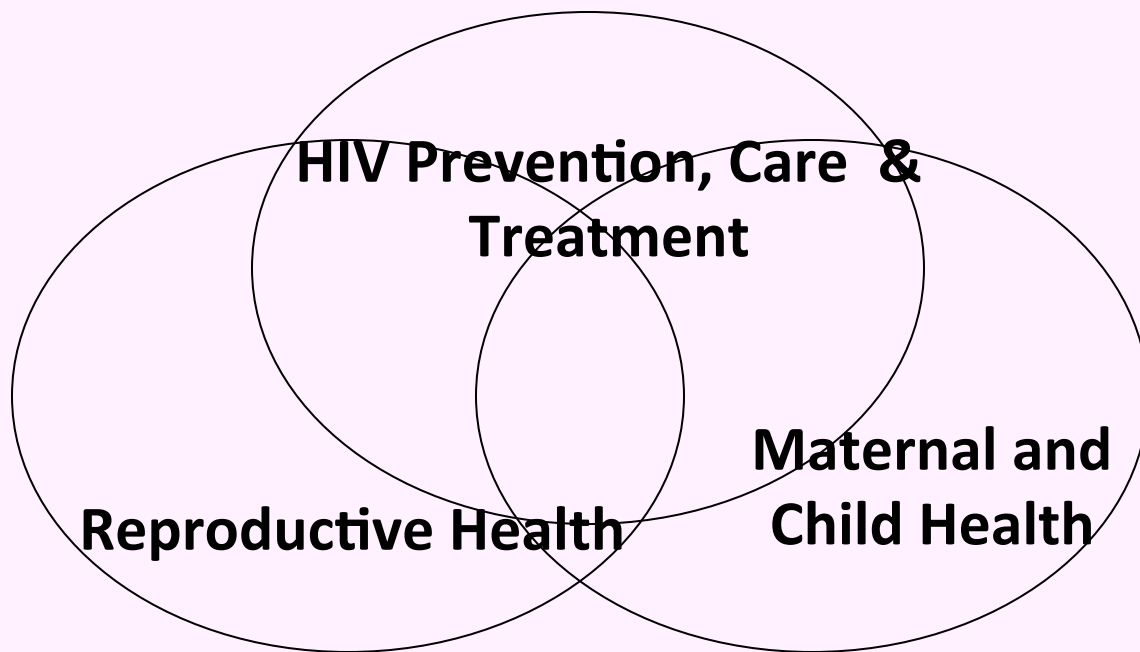


HIV Disease Motivates Challenge to Usual Paradigms

Characteristics of HIV Disease	Systems Required
 Impact throughout lifecycle	Programs for adults (including pregnant women and children)
 Asymptomatic periods, acute illness, chronic symptoms	Chronic disease model (health maintenance, continuity care, linkage within and between facilities)
 Multiplicity of clinical & psychosocial needs, stigma	Multidisciplinary teams, community linkages
 Importance of adherence & retention	Outreach & tracking, community engagement, provide-patient relationship
 Need for clinical & laboratory monitoring, secure supply of drugs	Infrastructure enhancements, laboratory facilities, procurement systems
 Transmissible infection	Prevention methods, counseling

Common Challenges

Health System Barriers	Maternal Mortality	Child Health	TB	Diabetes	HIV/AIDS
Demand for services	✓	✓	✓	✓	✓
Access to services	✓	✓	✓	✓	✓
Health care workers	✓	✓	✓	✓	✓
Support for follow-up & adherence	✓	✓	✓	✓	✓
Infrastructure and equipment	✓	✓	✓	✓	✓
Program management	✓	✓	✓	✓	✓
Drug and laboratory supplies	✓	✓	✓	✓	✓
Referral and linkages	✓	✓	✓	✓	✓
Community involvement	✓	✓	✓	✓	✓



Review of Studies of HIV and Maternal Mortality

- 22/23 studies showed increased risk of MM in HIV+ women, pooled RR 7.74 (5.37-11.?)
- Population attributable fraction
 - West Africa: HIV prev 1%, PAF 6% of deaths
 - East Africa: HIV prev 3%, PAF 17% of deaths
 - Southern Africa: HIV prev 17%, PAF 53% of deaths
- Increased risk of sepsis, endometritis, post CS sepsis, wound infection in HIV+

Questions to be addressed

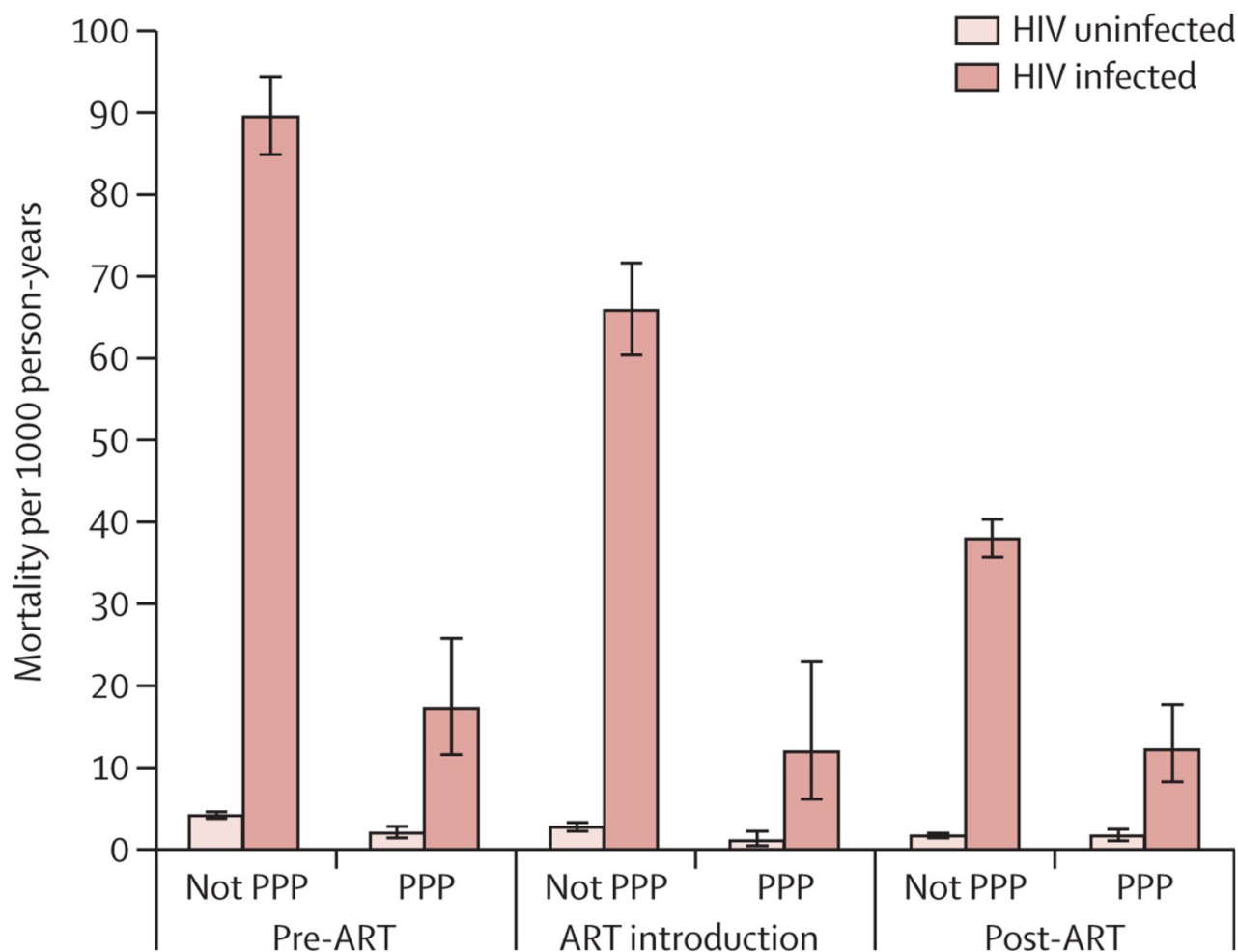
- What do we know about the major causes of death among HIV+ women during pregnancy and post-partum?
- Do we know if pregnancy worsens HIV progression?
- What do we know about the impact of treatment?

Summary

- Risk of mortality 2-10 x higher among HIV-infected pregnant women
- Increased mortality risk primarily due to indirect causes (TB, malaria, pneumonia, cerebral infections and HIV) as well as infections particularly post-C-section and post-abortion
- No evidence of increased HIV progression during pregnancy but questions remain, particularly in developing countries
- ART removed risk in developed countries but numbers are small
- To be seen whether in developing countries ART will bring mortality rates down to the level of HIV-negative women
- Data quality, completeness / representativeness an issue

Mortality rates in HIV-infected and HIV-uninfected women, by pregnancy status and availability of ART

Pooled Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA) network data, 1990—2012.



Source: [The Lancet 2013; 381:1763-1771](https://doi.org/10.1016/S0140-6736(13)60803-X); DOI:10.1016/S0140-6736(13)60803-X (Zaba B et.al.)



Implications for Cause of Death Determination

- In developing countries CoD investigation is restricted to **verbal autopsies**
 - Identification of CoD by **analysis of data derived from structured interviews** of family, friends, and caretakers, and available medical records
 - Interpreted by clinicians: large demands on limited resources
 - High degree of misclassification errors, specially for conditions with poor diagnostic specificity such as maternal and peri-neonatal deaths
- Clinical records
 - Many deaths occur outside health facilities
 - They may contain substantial inaccuracies

Conclusions

High rate of clinico-pathological discrepancies

- Impact on maternal mortality– a change in clinical management could have modified the prognosis
- **High rate of false negative diagnosis for infectious diseases**
 - Underestimation of prevalence
 - Low sensitivities (<40%) for frequent infectious categories (HIV/AIDS; pyogenic bronchopneumonia, meningitis, TB)
 - **Significant reductions in MM could be reached through improvements in their diagnosis**

Eclampsia main source of false positive diagnosis (57.1%)

- Can not ruled out that it was a true diagnosis
- A different cause of death was found
- Overestimation of prevalence
- **No pathological lesions related to eclampsia were found**

Conclusions

Infectious diseases are a significant cause of MM in Mozambique

Urgent need to implement effective and available tools . Minimally invasive autopsy being piloted.

Deaths due to obstetric causes require urgent improvements

Research Issues in Preconception Care

- How to motivate availability, uptake, and sustained use of longer acting, less user-dependent contraception for women who do not desire pregnancy
- How to implement and integrate preconception care interventions into HIV care
- The role of PrEP/ART in safe conception-implementation, supporting adherence
- Outcomes research re: PCC effectiveness for maternal health

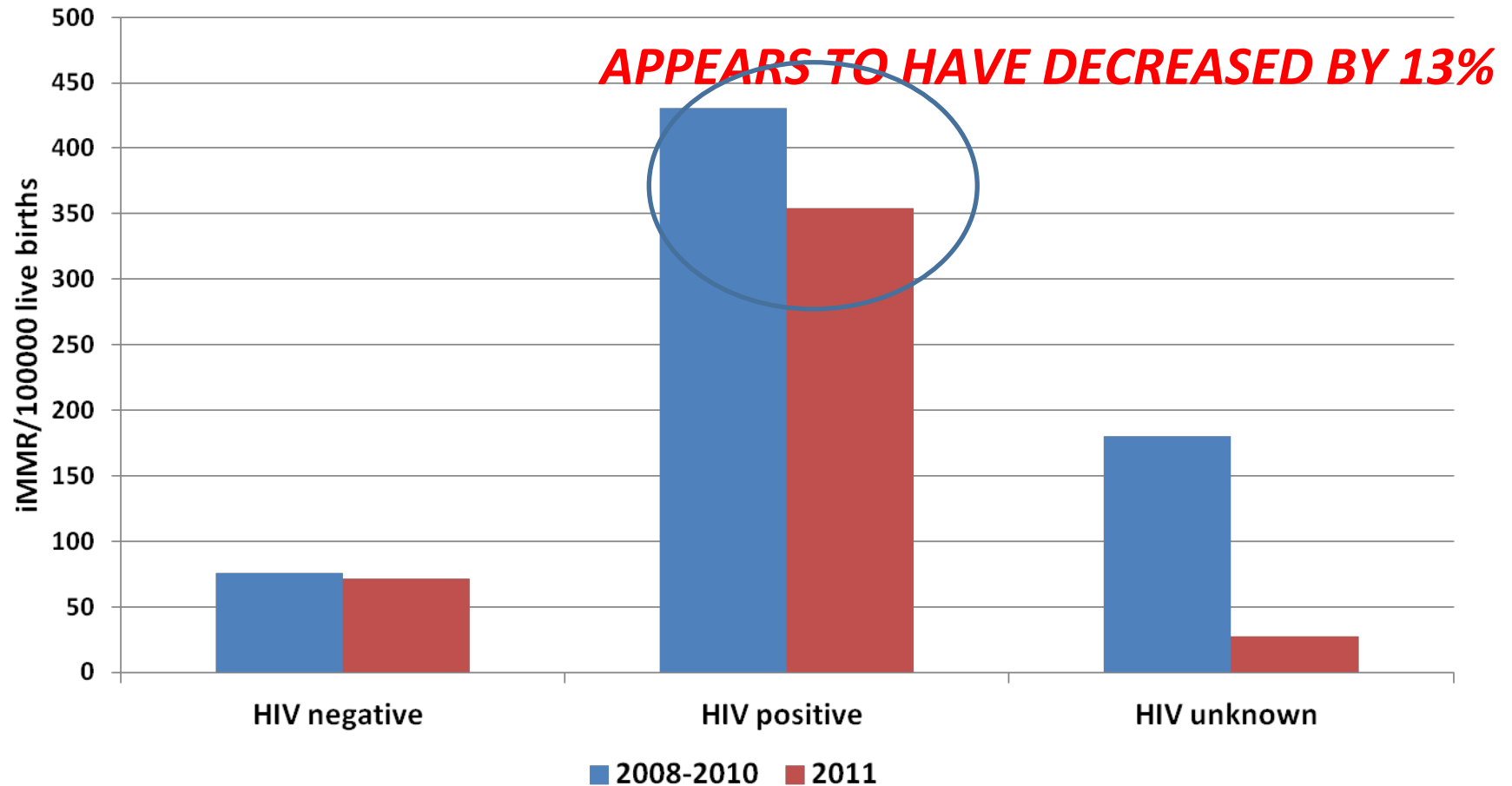
Comparison of HIV status and causes of maternal death (using estimated IMMR per 100 000 live births)

Cause of death*	HIV-negative	HIV-positive	Unknown
Medical and surgical disorders	11.5	24.2	16.7
NPRIs	6.6	267.3	25.6
Ectopic pregnancy	0.3	3.0	9.1
Miscarriage	1.4	9.9	17.6
Hyperemesis gravidarum	0.2	0.2	0.0
Pregnancy-related sepsis	4.1	24.2	6.8
Obstetric haemorrhage	17.2	38.4	30.5
Hypertension	18.8	27.4	37.0
Anaesthetic complications	4.1	4.8	4.5
Embolism	3.2	4.0	3.0
Acute collapse, cause unknown	3.2	9.2	6.8
Unknown	3.7	15.7	10.1
Total	74.4	428.3	167.8

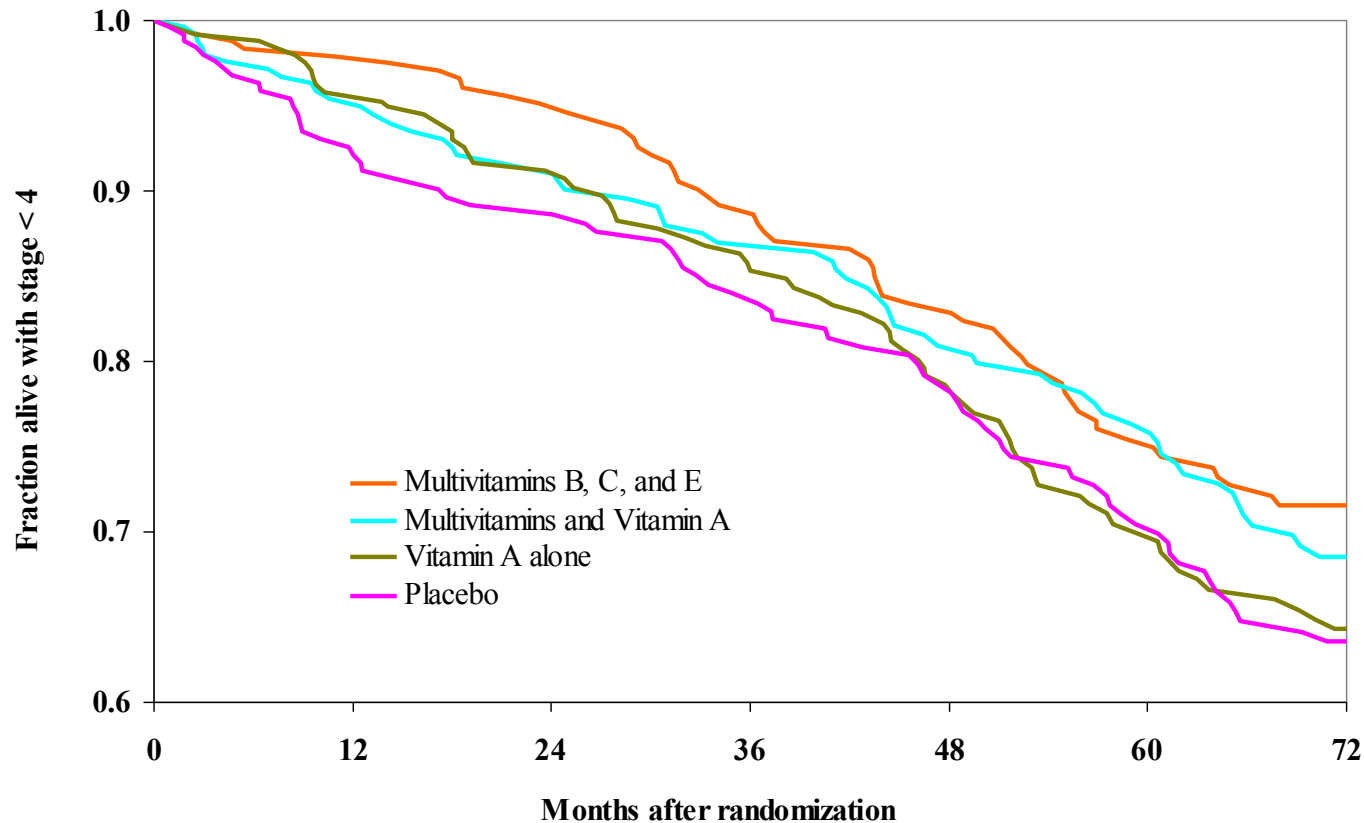
What Can Be Done to Reduce Mortality Associated with HIV?

- Prevention
- Early identification and initiation of treatment
- Use of regimen safe in pregnancy
- Screening for TB and prophylaxis
- Prevent unwanted pregnancies in HIV infected women (which result in septic abortions)

iMMR and HIV status (? Effect of HAART)



Nutrition and HIV: Kaplan-Meier curves of progression to WHO stage 4 or death, by regimen

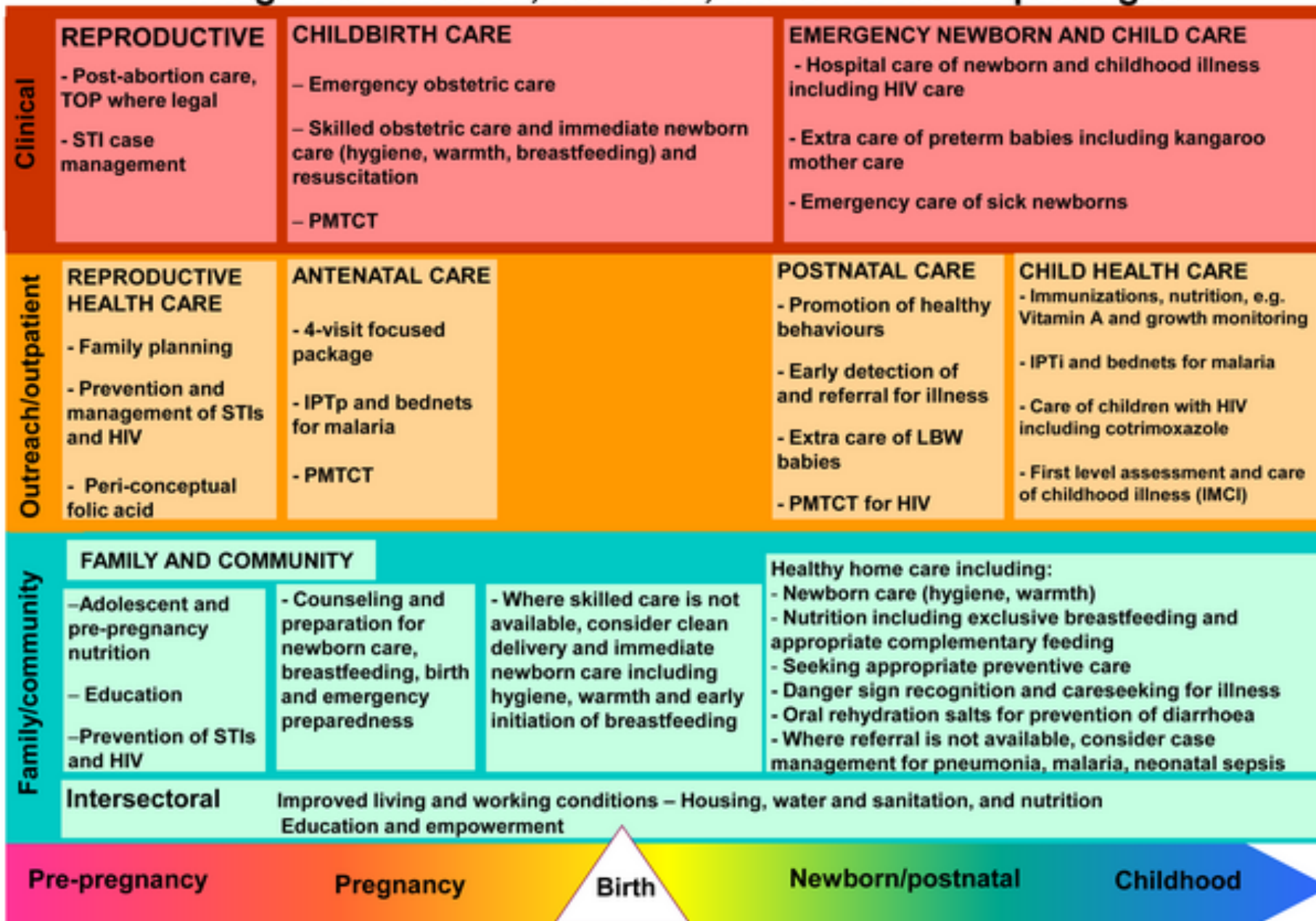


No. at risk				
Multivitamins B, C, and E	271	195	157	119
Multivitamins and Vitamin A	267	181	143	102
Vitamin A alone	272	190	147	104
Placebo	267	173	145	101

Multivitamins and HIV-related complications

Complication	Episodes†	Relative Risk in Placebo Group	Multivitamins		Vitamin A Alone	
			Relative Risk (95% CI)	P Value	Relative Risk (95% CI)	P Value
Thrush	0.14±0.48	1.0	0.47 (0.30–0.73)	<0.001	0.69 (0.44–1.07)	0.10
Gingival erythema	0.02±0.14	1.0	0.22 (0.06–0.83)	0.02	1.00 (0.40–2.46)	0.99
Angular cheilitis	0.11±0.48	1.0	0.45 (0.25–0.79)	0.006	1.54 (0.95–2.51)	0.08
Oral ulcer	0.10±0.30	1.0	0.44 (0.28–0.68)	<0.001	0.94 (0.59–1.48)	0.78
Reported mouth and throat ulcers	0.28±0.93	1.0	0.47 (0.33–0.66)	<0.001	1.01 (0.74–1.38)	0.93
Painful tongue or mouth	0.31±0.98	1.0	0.46 (0.33–0.66)	<0.001	1.03 (0.76–1.40)	0.85
Difficult or painful swallowing	0.16±0.55	1.0	0.41 (0.26–0.63)	<0.001	1.25 (0.88–1.77)	0.21
Nausea and vomiting	0.38±1.14	1.0	0.69 (0.50–0.97)	0.03	0.98 (0.71–1.35)	0.91
Diarrhea	0.55±1.25	1.0	0.83 (0.63–1.09)	0.18	0.95 (0.72–1.25)	0.71
Dysentery	0.19±0.71	1.0	0.66 (0.45–0.95)	0.03	0.90 (0.62–1.28)	0.54
Fatigue	0.59±1.43	1.0	0.64 (0.49–0.86)	0.003	1.04 (0.79–1.35)	0.79
Rash	0.96±1.76	1.0	0.74 (0.57–0.96)	0.02	0.83 (0.64–1.06)	0.13
Acute upper respiratory tract infection	0.83±1.13	1.0	0.79 (0.66–0.96)	0.02	0.96 (0.80–1.14)	0.62

Integrated maternal, newborn, and child health packages



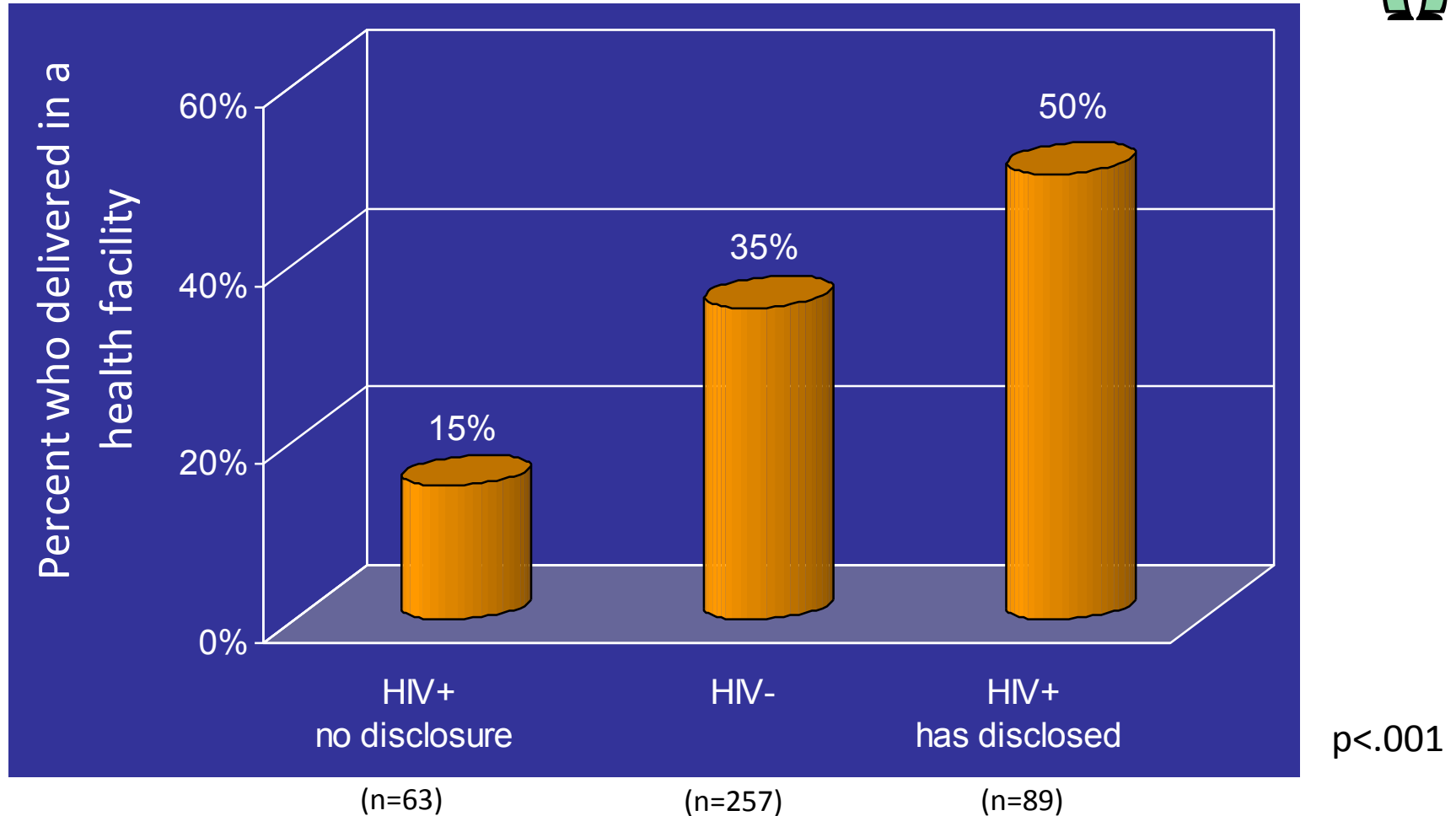
Maternal Health in the ARV Era: Gaps and Opportunities

1. Lack of evidence about non-clinical and clinical interventions other than ART
2. Question of why women on ART continue to have increased risk of mortality from TB remains unanswered
3. Insufficient evidence about effects of ART on birth outcomes and its long term effects on women
4. Option B+ for PMTCT offers opportunities to test more women/mother-centered and integrated models of care to improve initiation, adherence and long term retention

Maternal Health in the ARV Era: Gaps and Opportunities

5. Lack of information about women who do not use services so insufficient information is an impediment to designing effective interventions to address their needs and support them in accessing and using services
6. No consistent definition of adherence vs. retention, nor indicators to measure adherence

Effects of Disclosure on Use of Skilled Delivery Services*



* Turan et al., manuscript in preparation

Impact of Stigma on PMTCT, Maternal Mortality

- Unlikely that the global commitments to virtual elimination of new HIV infections in children and reduced HIV- related maternal mortality by 2015 will be met unless major efforts are made to identify and counter HIV-related stigma facing pregnant women*
- Existing stigma-reduction tools and interventions, as well as measures to evaluate progress, can be modified for the specific needs of pregnant women
- *While it has yet to be fully recognized, reducing stigma is an essential piece of delivering care for all women, men, and children*

* Turan and Nyblade, JAIDS, forthcoming

RH decision-making along a continuum

- Desire for children
- Sexual and reproductive rights
- Major challenges:
 - Testing
 - Retention in care
 - ART initiation
 - ART adherence
- Many behavioral, social, structural, and health system factors can act as barriers or facilitators of care for HIV+ women.

PREVENTING GENDER EQUALITY BARRIERS IN MATERNAL HEALTH PROGRAMMES

Aim is to promote gender equality

- Requires equitable distribution of resources, opportunities, benefits according to sex
- Requires to include needs, experiences and visions of women and men in defining the programme

QUESTIONS:

1. Does the programme take into account men & women different roles and responsibilities & their differential access to and control of resources?
2. Does the programme challenge existing gender and social relations?
3. Have you considered the potentially different impacts of the programme both to men and women:
 - not to worsen position of women or favoring advantaged women than disadvantaged women
 - Gender specific indicators for monitoring the programme performance?

Summary

- HIV increases the risk of maternal death through several mechanisms, especially infectious complications. Better ascertainment of deaths and causes needed.
- Wider availability of ARV therapy appears to decrease but not eliminate increased risk.
- Creative, multidisciplinary programs are needed to encourage testing and uptake and retention in care.
- Stigma, depression, IPV, and gender inequality contribute to adverse outcomes.

