

Trends in maternal deaths in HIV-infected women, on a background of changing HIV management guidelines in South Africa: 1997 to 2015

1,2,3CN Mnyani, 1EJ Buchmann, 4,5MF Chersich, 1KA Frank, 6,7JA McIntyre

¹Department of Obstetrics and Gynaecology, University of the Witwatersrand, Johannesburg, South Africa

²School of Public Health, University of the Witwatersrand, Johannesburg, South Africa

³SACEMA (DST/NRF Centre of Excellence in Epidemiological Modelling and Analysis), Stellenbosch University, Stellenbosch, South Africa

⁴Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

⁵International Centre for Reproductive Health, Department of Obstetrics and Gynaecology, University of Ghent, Ghent, Belgium

⁶Anova Health Institute, Johannesburg, South Africa

⁷School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa



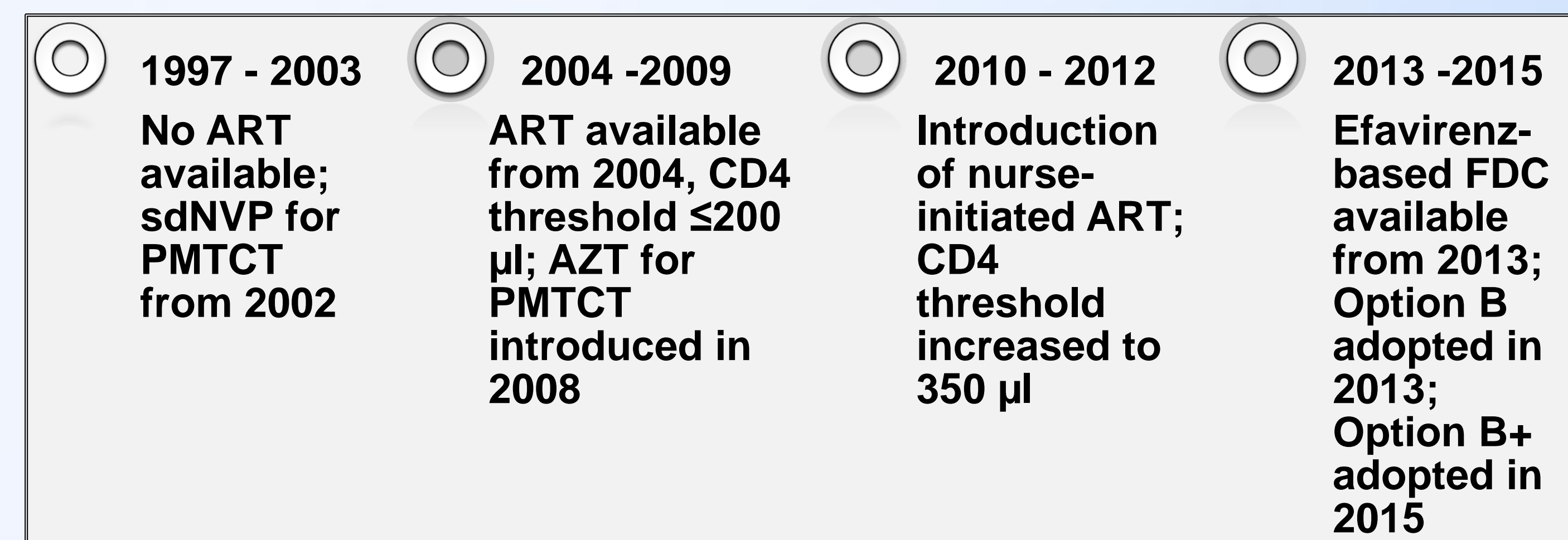
Background: South Africa made no progress towards the MDG 5 target of decreasing the maternal mortality ratio (MMR) by 75% between 1990 and 2015. The country saw a reversal in gains made, largely to the HIV epidemic. The HIV prevalence among women accessing antenatal care in South Africa increased dramatically from less than 1% in 1990 to 22.8% by 1998, and the prevalence has plateaued at around 29%.

The estimated MMR in 1990 was **108** per 100 000 live births, and for 2015, it was estimated to be **138** per 100 000 live births. Hence, the aim of the study was to assess trends in maternal mortality and leading causes of death in HIV-infected women, at Chris Hani Baragwanath Academic Hospital (CHBAH), a large referral hospital in Johannesburg, South Africa, with over 20 000 deliveries per annum.

Method: This was a retrospective record review of maternal deaths at CHBAH, from 1997 to 2015. Data were extracted on timing of HIV diagnosis and management during pregnancy; antenatal and admission details; and details about the death. Classification for causes of maternal deaths used was the same used in the South African Confidential Enquiries into Maternal Deaths. The analysis time periods for the study coincide with major prevention of mother-to-child transmission of HIV (PMTCT) and antiretroviral therapy (ART) guideline changes in South Africa – Figure 1.

Results: From January 1997 to December 2015, 692 women died at CHBAH; 490 (70.8%) had a documented HIV status, and 335 (68.4%) were HIV-infected. The HIV testing rate increased from 48.4% (101/208) in 1997-2003, to 84.3% (86/102) in 2013-2015 ($p < 0.001$). Overall, **83.8% (281/335) were diagnosed as HIV-infected during pregnancy.**

The iMMR in HIV-infected women peaked in the period 2004-2009 at 379 (95% CI 319-446) per 100 000 live births, with a decline to 267 (95% CI 198-353) per 100 000 live births in 2013-2015, $p < 0.05$ – Figure 2. Non-pregnancy related infections were the leading cause of death throughout the review period, accounting for 61.5% (206/355) of maternal deaths in HIV-infected women. The other leading causes of death were obstetric haemorrhage, pregnancy-related sepsis, hypertensive disorders, and medical and surgical disorders – Table 1.



sdNVP=single dose nevirapine; PMTCT= prevention of mother-to-child infection of HIV; AZT=zidovudine; FDC= fixed dose combination; Option B and B+ =triple ART for all HIV-infected pregnant and breastfeeding women, and with Option B+, treatment is for life

Figure 1: Analysis time periods and major changes in South African PMTCT and ART guidelines

Table 1: Leading causes of maternal death among HIV-infected women

| Causes of death, n (%) | 1997-2003 (n=71) | 2004-2009 (n=144) | 2010-2012 (n=71) | 2013-2015 (n=49) |
|---|------------------|-------------------|------------------|------------------|
| Non-pregnancy related infections | 49 (69.0) | 93 (64.6) | 42 (59.2) | 22 (44.9) |
| Obstetric haemorrhage | 3 (4.2) | 16 (11.1) | 7 (9.9) | 4 (8.2) |
| Pregnancy-related sepsis | 3 (4.2) | 11 (7.6) | 5 (7.0) | 6 (12.2) |
| Hypertensive disorders | 2 (2.8) | 9 (6.3) | 2 (2.8) | 9 (18.4) |
| Medical and surgical disorders | 2 (2.8) | 3 (2.1) | 10 (14.1) | 4 (8.2) |

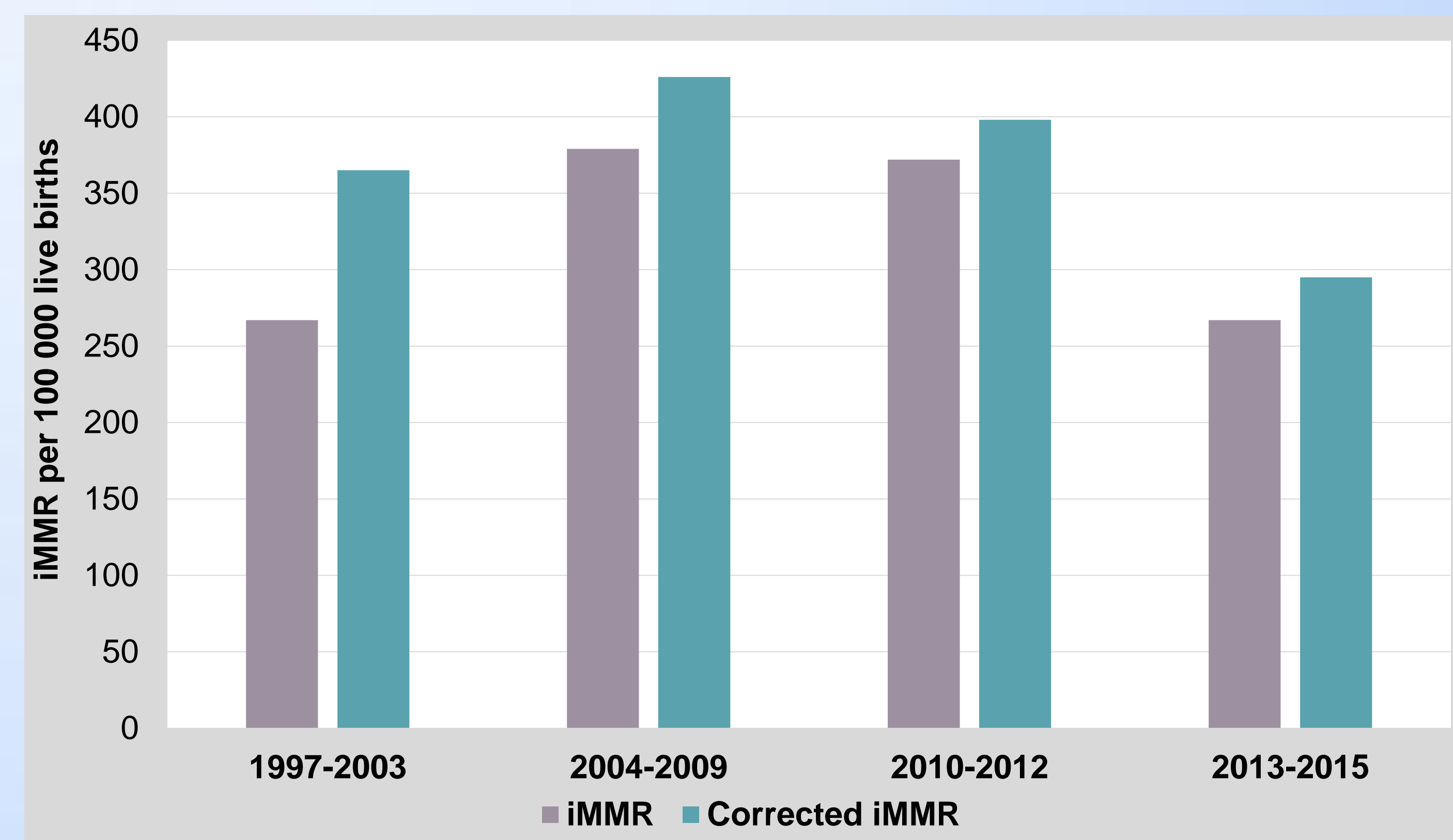


Figure 2: Institutional maternal mortality ratio (iMMR) – 1997-2015

Among the non-pregnancy related infections, the leading cause of deaths were respiratory infections, accounting for 56.3% of maternal deaths due to non-pregnancy related infections. Only 22.3% (46/206) of the women who died of non-pregnancy related infections were on ART at the time of death, despite advanced immune suppression. Of those assessed for ART, 79.3% (65/82) had a CD4 count ≤ 200 cells/ μ l. Overall, only 23.3% (78/335) were on antiretroviral therapy (ART) at the time of death, despite a median CD4 count of 136 cells/ μ l (IQR 45-301). In 2013-2015, 38.8% of women who died were not on ART, despite widespread availability of ART and recommendations for triple therapy for all HIV-infected pregnant women. There was a fall-off at all stages of the HIV diagnosis and treatment cascade – Figure 3.

The majority of deaths, 60.9%, occurred in the age group 25-35 years. In women with antenatal details (309), the median gestational age at booking was 21 weeks, and 19.1% of the HIV-infected women who died did not access any antenatal care. The majority, 75.2%, of women were still pregnant at the time of admission, but most deaths, 79.1%, occurred postpartum.

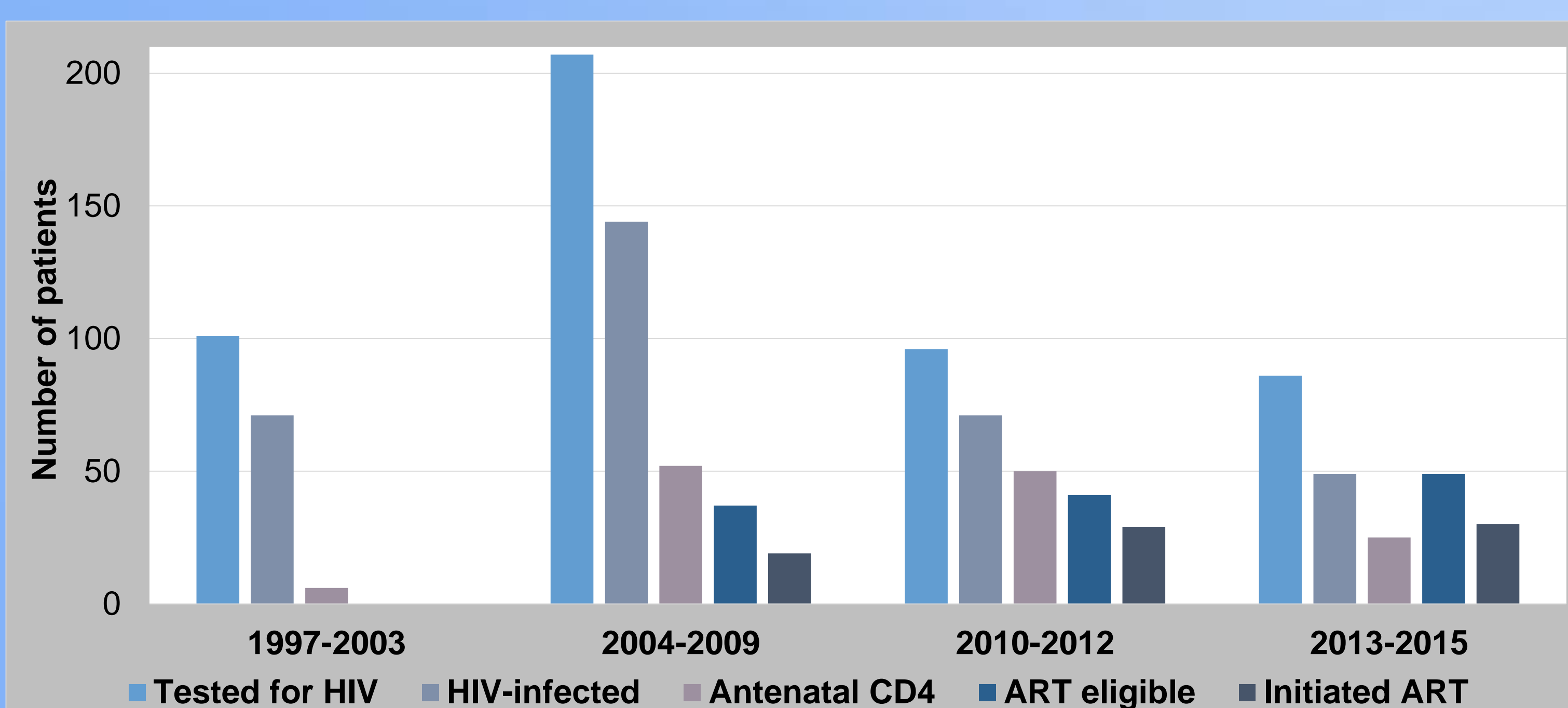


Figure 3: HIV diagnosis and management cascade – 1997-2015

Discussion: There was a cascade of events that ultimately led to maternal deaths in HIV-infected women. This started with delayed access or no antenatal care, leading to delayed HIV diagnosis and ART initiation, and delayed diagnosis and inappropriate management of underlying HIV-related comorbidities. In those initiated on ART during pregnancy, the duration of ART prior to delivery was short, not enough to reverse advanced immune suppression.

Conclusion: The iMMR in HIV-infected women remains unacceptably high. Drivers of mortality and barriers to accessing antenatal care and ART early need to be addressed if we are to achieve the Sustainable Development Goal target of a MMR of 70 per 100 000 live births by 2030.

