PMTCT GUIDELINES
RATIONALE AND GOING FORWARD

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SA Background

- Population: 48m
- Annual number of deliveries:1,2m
- 97% of women attend the first ANC
- 71% of women attend 5th ANC visit
- 97% of pregnant women accessing syphilis testing
- 95%have access annual skilled attendance at birth
- 95% deliver at health facilities

Source: Health of our Children,HSRC 2008

Epidemiological data

- HIV prevalence in the general population: 12%
- HIV prevalence among pregnant women: 29.1%
- Uptake of PMTCT >85%

Timing of transmission

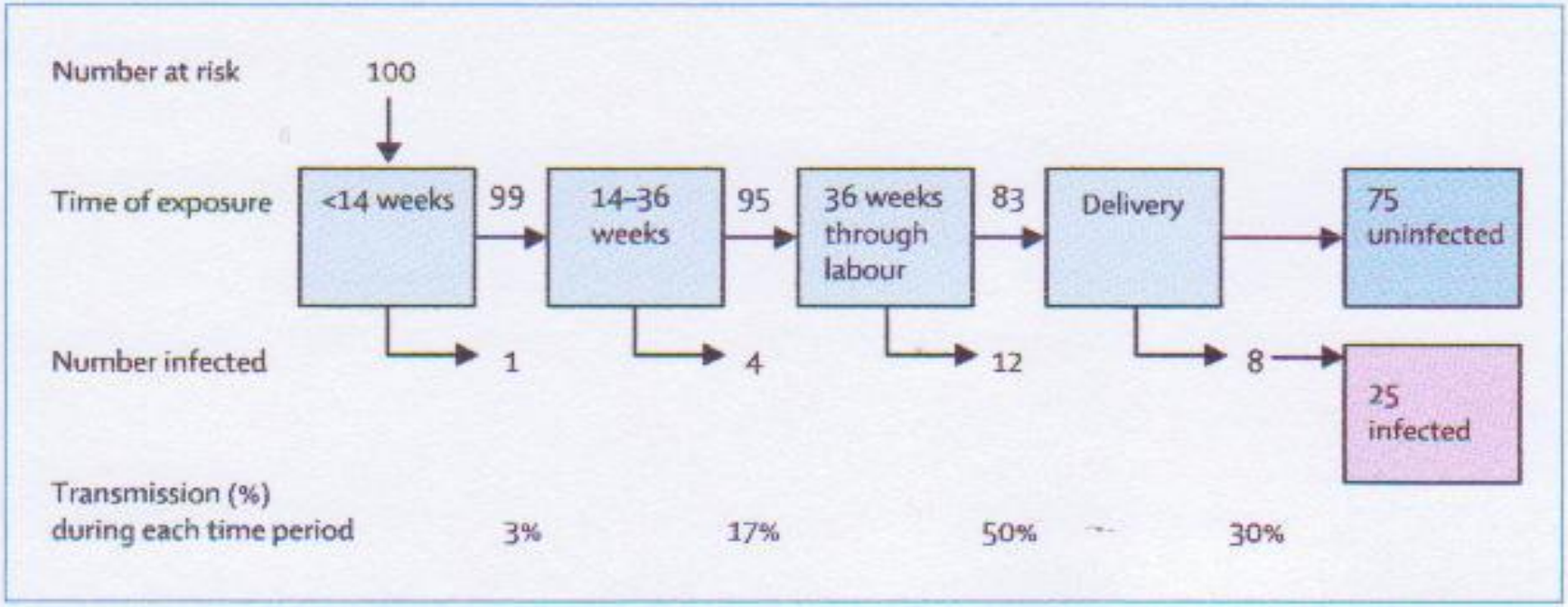
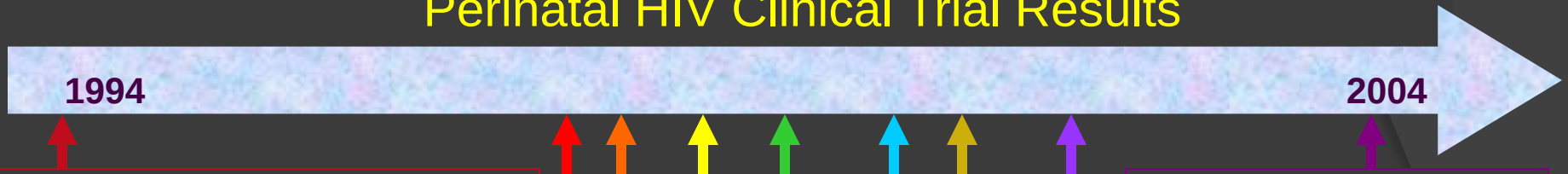


Figure 2: **Estimation of timing of mother-to-child HIV-1 transmission in a non-breastfeeding population**
Estimates are based on a hypothetical cohort of 100 children born to HIV-infected women without any interventions. Upper line numbers indicate number of children at risk for infection. Adapted from reference 6.

What did we know and when did we know it?
Perinatal HIV Clinical Trial Results



1994 U.S. AZT Trial ACTG 076
- **67% reduction in transmission**

1998 Thai Bangkok short AP/IP AZT trial
- 50% reduction in transmission

1998 Cote d'Ivoire short AP/IP AZT trials
- 37% reduction in transmission (breastfeeding)

1999 PETRA AZT/3TC trial (6 wk results)
- 50% reduction with longest arm.
- 38% reduction with the IP/PP arm

2000 Thailand
Long vs short AZT regimens
- 4% TR in LL (non BF)

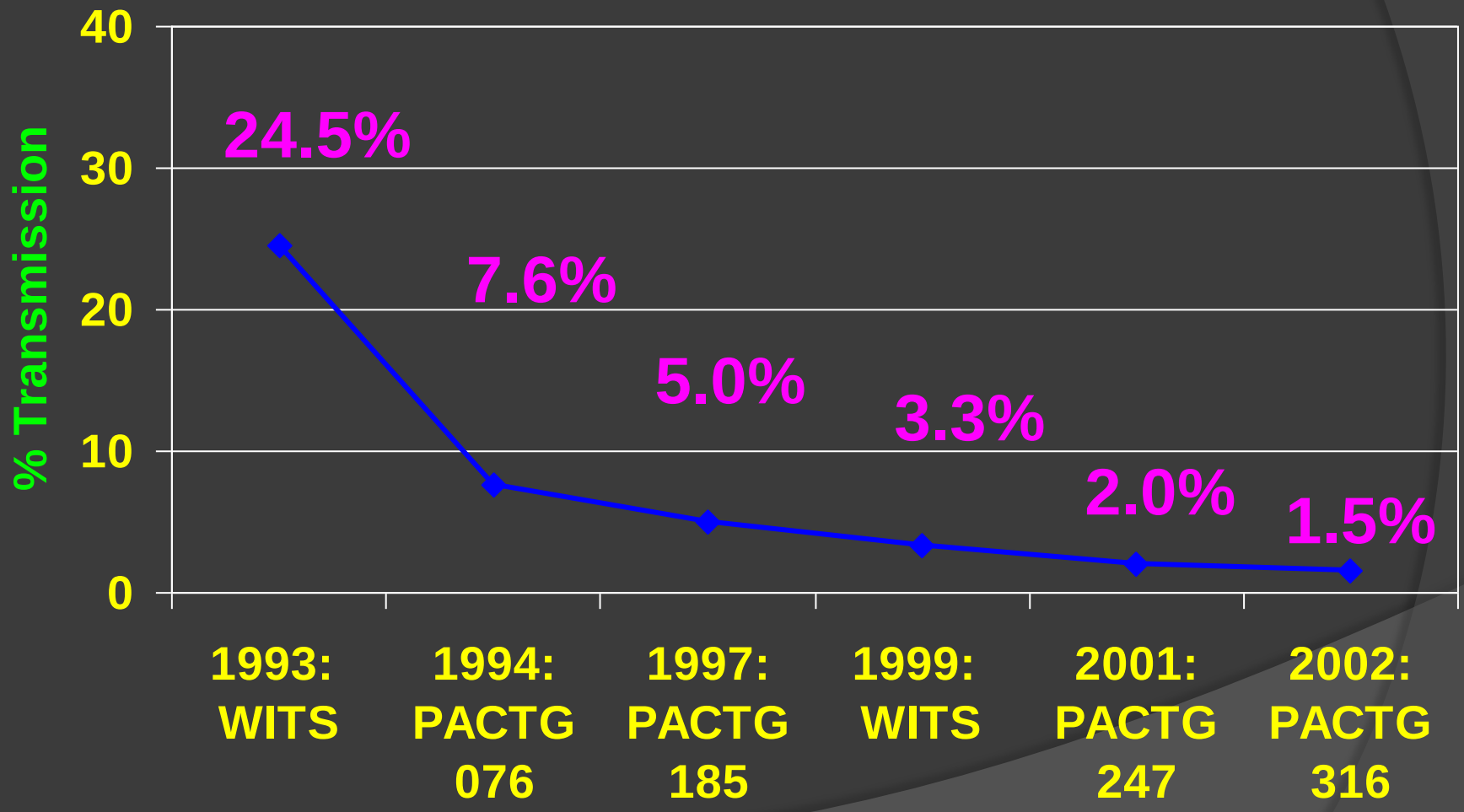
2002 Cote d'Ivoire DITRAME +
- 6.2% TR with AZT & IP/PP NVP

2003 DITRAME + 1201.1
- 4.7% TR with AZT/3TC & IP/PP NVP

2004 Thailand PHPT
- **<2% AZT + NVP**

1999 Uganda 2-dose IP/PP NVP trial (HIVNET 012)
- **47% reduction in transmission (breastfeeding)**

Prevention of MTCT in the US



History of SA PMTCT program

1999 HIVNET 012 (13-14%)	**2001 – pilot sites (PETRA and SAINT)**
2004 – Thai regimen – AZT +sd NVP	**2003 – PMTCT regimen of sd-NVP (20%)**
WHO guidelines in 2006	2008 – guidelines to include AZT frm 28wks and HAART for <200
Rapid advice 2009 / implemented 2010	2010– HAART for <350, Dual for >350 frm 14wks AZT for infant x4wks (<5%)

2006	2009/2010
ART eligible – CD 4 <200 or ≤200 or <350 with WHO stages 3 or 4	ART eligible – CD 4 ≤350 or WHO stage 3 or 4
If not, for AZT from 28wks +sd-NVP during labour	Maternal 3 drug regimen seen as equivalent to AZT (+sd-NVP) Start earlier at 14wks
Infant = AZT syrup for 1wk or 4 wks if maternal therapy <28wks	Infant – 4 wks of AZT for all – regardless of maternal therapy
No recommendation for mom or infant ARV's if mom breastfeeding	Maternal and infant ARV's if mom breastfeeding

WHO eligibility criteria for pregnant women

- CD 4 ≤350 regardless of clinical stage
- CD 4 > 350 – if sympt (WHO 3 or 4)
- Start asap irrespective of GA
- Preferred regimen –
  - AZT +3TC +NVP or
  - AZT +3TC +EFV (not 1st trimester)
  - Alternative – TDF +3TC (FTC) +NVP (EFV)

Those not qualifying

Option A:

- AZT 300mg bd from 14wks
- AZT 300hr'ly in labour +sd NVP
- Tail cover (?maintained from 2006)

Option B:

triple therapy in pregn +BF

Infant – AZT or NVP daily for 4 - 6wks or until 1wk after cessation of BF

Rationale behind changes

- **Optimal timing** and **eligibility** for ART initiation in non-pregnant adults
- **Timing of transmission** (with or without b/feeding) and benefits of **early initiation** of ARV during pregn
- **Safety** of 3drug regimen for use during pregnancy
- More countries ready to expand more effective PMTCT services

Why 350

- Sufficient data from non-pregn adults of benefits of earlier initiation
- Accounts for 40% of pregn HIV infected women
- Accounts for >75% of MTCT risk and >80% of pp transmission
- Account for 85% of maternal deaths within 2yrs of delivery

Efficacy of ARV in reducing MTCT

- HAART for PMTCT - <2% in developed / developing countries
  - 2.4% in Thai study (20% of women with CD 4 <200)
  - AZT from 28wks +sd-NVP (mom not eligible) – 2% in PHPT-2
- Kesho Bora – women CD 4 200 – 500, btwn 28 - 36wks
  - **– HAART =1.8% vs dual =2.2% (NS)**

What to start

Start one of the following regimens in ART-naïve individuals (for maternal HAART or for PMTCT)

Preferred	Alternative
AZT + 3TC + EFV AZT + 3TC + NVP	TDF + 3TC or FTC + EFV TDF + 3TC or FTC + NVP

- EFV – no convincing evidence of teratogenencity
- No superiority of AZT over TDF / no concerns of TDF from RCT's

Drug safety during pregnancy

- NVP associated with hepato-toxicity when initiated at >250
- EFV or alternatively LPV/r
  - Use of PI to avoid this in women >250
  - Side effects –dislipidaemia / N/V/loose stools /Hyperglycemia
  - No concern of drug resistance after discontinuation
  - LPV/r levels reduced during 3rd trimester but no need to adjust dosage

NVP @ higher CD 4

"The review of NVP safety in pregnant women with CD4 count 250–350 cells/mm3 did not confirm an increased risk of serious adverse events and the panel concluded that the benefits of using NVP in this situation outweigh the risks of not initiating ART.

The panel was unable to conclude from the evidence reviewed whether there are benefits associated with the use of EFV vis a vis NVP in pregnant women after the first trimester and with higher or unknown CD4 cell counts, although more than half of the panel members preferred EFV in these situations."

EFV during pregnancy

- Rash and hepatitis can occur
- 5 retrospective cases and 1 prospective case of NTD in humans exposed to EFV in 1st/3
- Meta analysis of 11 prospective and 5 retrospective cases with 1st /3 exposure – 1132 exposed to EFV vs 7163 non exposed – RR=0.87 (0.61-1.24) (Ford, 2010)
- 2.9% overall birth defects

OCTANE (A5208)

- Octane 1 – women with prev exposure to sd-NVP
  - TDF/FTC/NVP (n=120) – VF or death=26%
  - TDF/FTC/LPVr (n=120) VF or death =8% (p=0.0004)
- Octane 2 – women with no prev exposure
  - TDF/FTC/NVP (n=249) – VF or death=17%
  - TDF/FTC/LPVr (n=251) VF or death =20% (NS even with ITT)

Tail therapy

- NVP has long half life and low genetic barrier
- NNRTI resistance ff sd exposeure to sd-NVP up to 60%
- Resistance can be detected up to 12m ff exposure in plasma and cellular provirus
- 1wk combivir reduced NVP resistance from 60 – 10% but risk not eliminated (TOPS study, McIntyre)
- NNRTI based HAART in women with prev exposure to sd-NVP impaired optimal viral suppression (Octane study)

Truvada

A5207 7 vs 21days

- AZT /3TC
- Kaletra
- Truvada (TDF +FTC/emtricitabine)

- All equivalent, less resistant mutations if taken for 21days
- Has long half life, already used in PrEP
- trials of stat dose vs combivir x7d almost completed

infant

There are two choices for HIV-positive women who breastfeed and are not taking ART:

- **If a woman received zidovudine during pregnancy, daily nevirapine is recommended for her child from birth until the end of the breastfeeding period.**

Or

- If a woman received a three-drug regimen during pregnancy, a continued regimen of three-drug prophylaxis is recommended for the mother until the end of the breastfeeding period.

6. REGIMENS

Table 1: Standardised national ART and ARV regimens for women who are HIV positive and pregnant and their infants

Maternal regimens		
Woman	**Regimen**	**Comment**
Eligible for lifelong ART (i.e. CD4 ≤ 350 or WHO clinical stage 3 or 4)	TDF + 3TC/FTC + NVP	Start lifelong ART within 2 weeks
Currently on lifelong ART	Continue ART	Substitute EFV with NVP if in first 12 weeks of pregnancy
Contraindication to TDF (renal disease)	AZT+ 3TC + NVP	
Not eligible for ART i.e. CD4 > 350 and WHO stage 1 or 2	AZT from 14 weeks sdNVP + AZT 3hrly in labour TDF + FTC single dose (stat) after delivery	
Unbooked and presents in labour	sdNVP + AZT 3hrly in labour TDF + FTC single dose after delivery	Assess maternal ART eligibility before discharge

Success??

- Evaluation of current PMTCT program done last year, (6th IAS, 2011)
- Good coverage of 6 wks immunization
- DBS from565 facilities – 30% HIV exposed (vs 31% from national data)
- 34% were on HAART and 20% exclusive BF; 62% no BF
- Exclusive BF and HAART both beneficial

TR

- Nationally – 3.5%
- Provinces
  - NC – 1.7% (15.6%)
  - FS – 6% (31.1%)
  - KZN – 2.8%(43.9%)

(c/section not helpful)

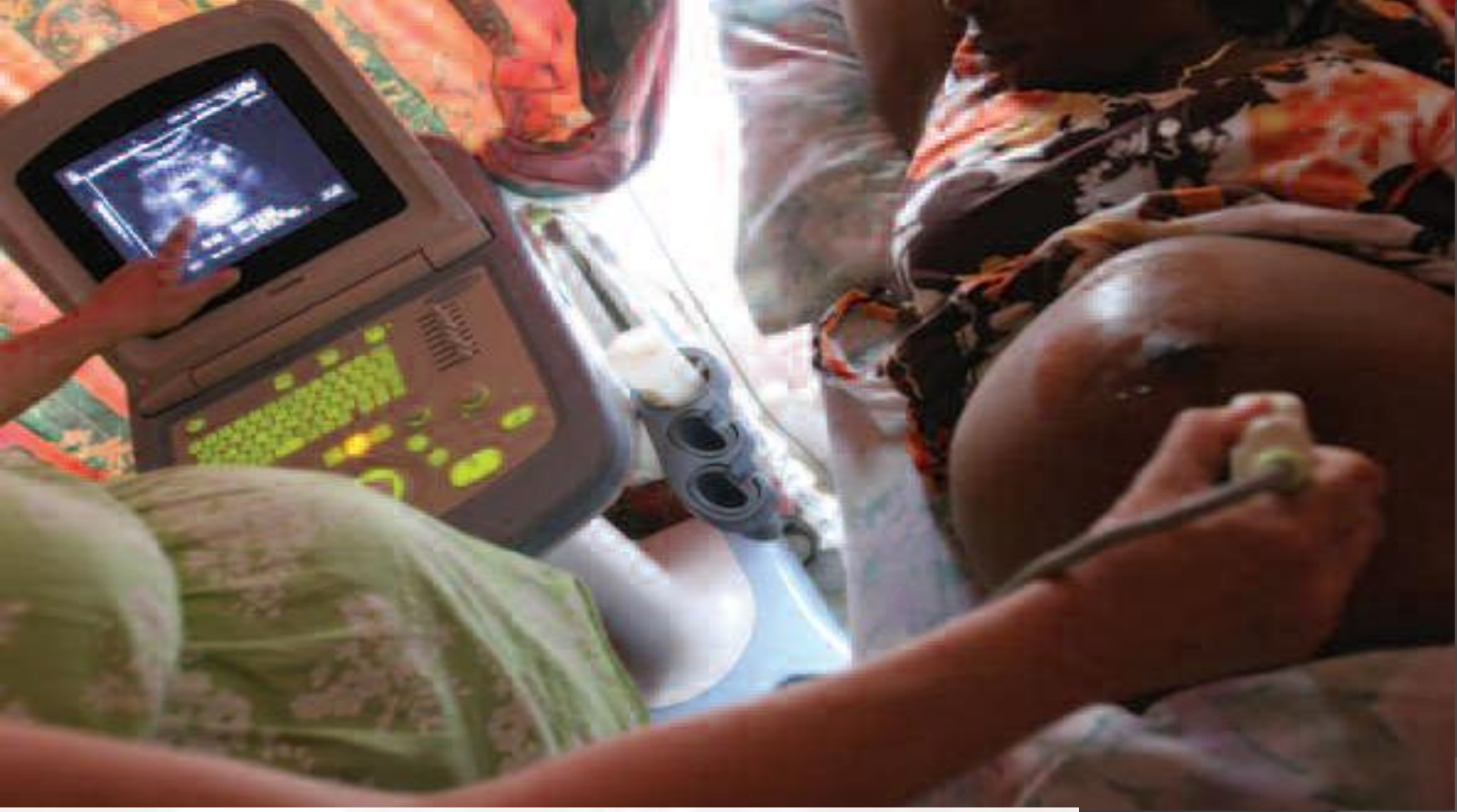
Challenges

- Increase dual therapy uptake in ANC (still 5% unbooked)
- Early initiation of HAART in 40% of pt CD 4<350
  - Contributes to 90% of maternal deaths
- Increased testing for infants

SA and MDG's

1. To eradicate extreme poverty and hunger
2. To achieve universal primary education
3. **To promote gender equality and empower women**
4. **To reduce child mortality**
5. **To improve maternal health**
6. **To combat HIV/AIDS**, malaria and other diseases
7. To ensure environmental sustainability
8. To develop a global partnership for development

between 1998 and 2007, the maternal mortality rate leapt from 150 to 625 deaths for each 100,000 live births. That means South Africa, sub-Saharan African's economic powerhouse, has no hope of meeting the U.N. MDG that require 38 deaths per 100,000 births by 2015



South Africa

“Stop Making Excuses”

Accountability for Maternal Health Care in South Africa

HUMAN RIGHTS WATCH

“Quotes”

- “While many sub-Saharan African countries are not on track to meet their MDG targets, South Africa is one of only six countries in sub-Saharan Africa that made no progress in reducing maternal deaths by 2008, and one of five (together with Botswana, Lesotho, Swaziland, and Zimbabwe) that experienced the largest percentage increases”

Ke a leboga