

# ART and women The last decade Successes and Challenges



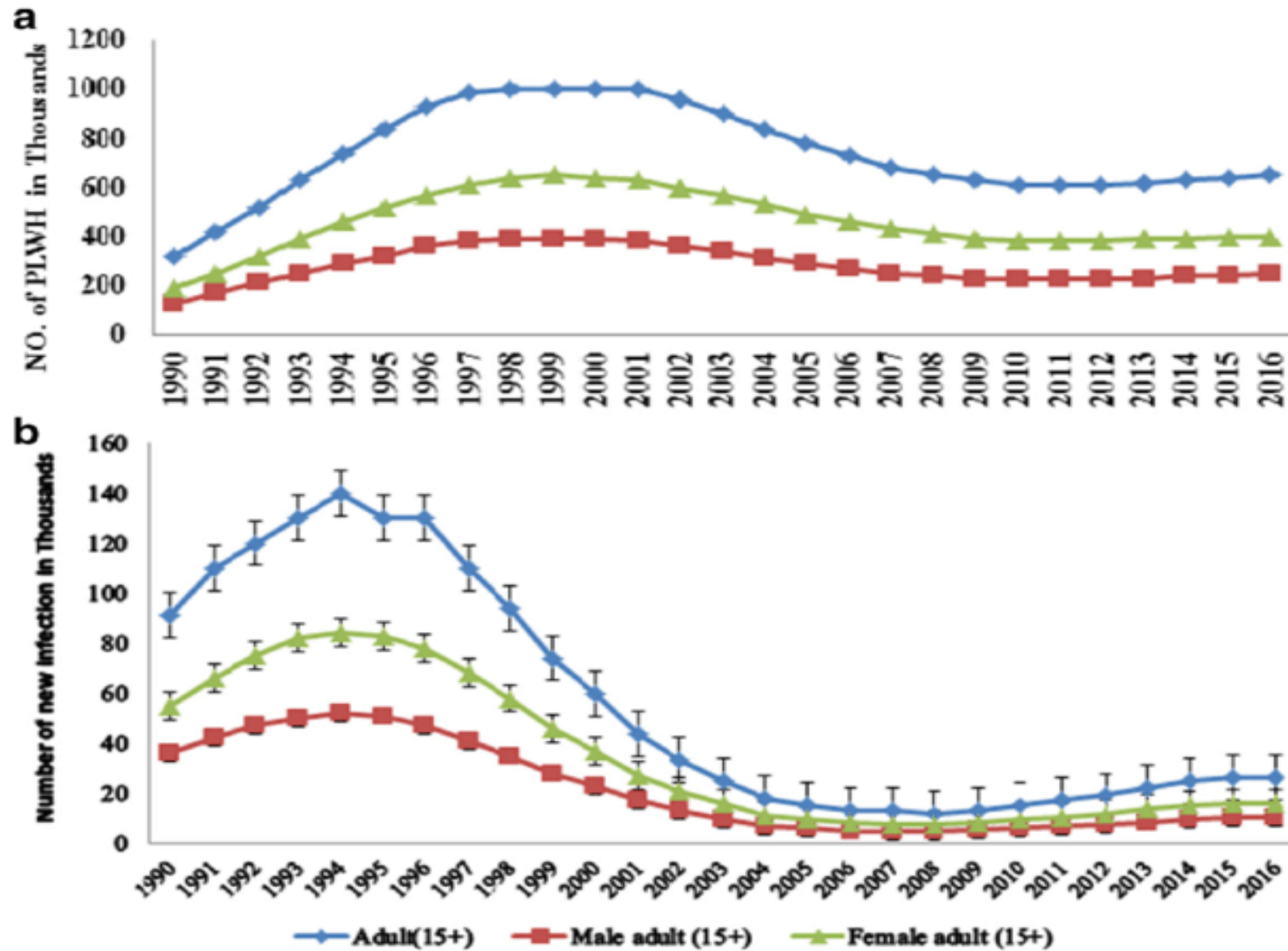
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Although rates are declining: Women represent more than half of incident and prevalent cases of HIV globally



# Summary of the global HIV epidemic (2018)

	People living with HIV in 2018	People newly infected with HIV in 2018	HIV-related deaths 2018
 Total	<b>37.9 million</b> [32.7 million – 44.0 million]	<b>1.7 million</b> [1.4 million – 2.3 million]	<b>770 000</b> [570 000 – 1.1 million]
 Adults	<b>36.2 million</b> [31.3 million – 42.0 million]	<b>1.6 million</b> [1.2 million – 2.1 million]	<b>670 000</b> [500 000 – 920 000]
 Women	<b>18.8 million</b> [16.4 million – 21.7 million]	–	–
 Men	<b>17.4 million</b> [14.8 million – 20.5 million]	–	–
 Children (<15 years)	<b>1.7 million</b> [1.3 million – 2.2 million]	<b>160 000</b> [110 000 – 260 000]	<b>100 000</b> [64 000 – 160 000]

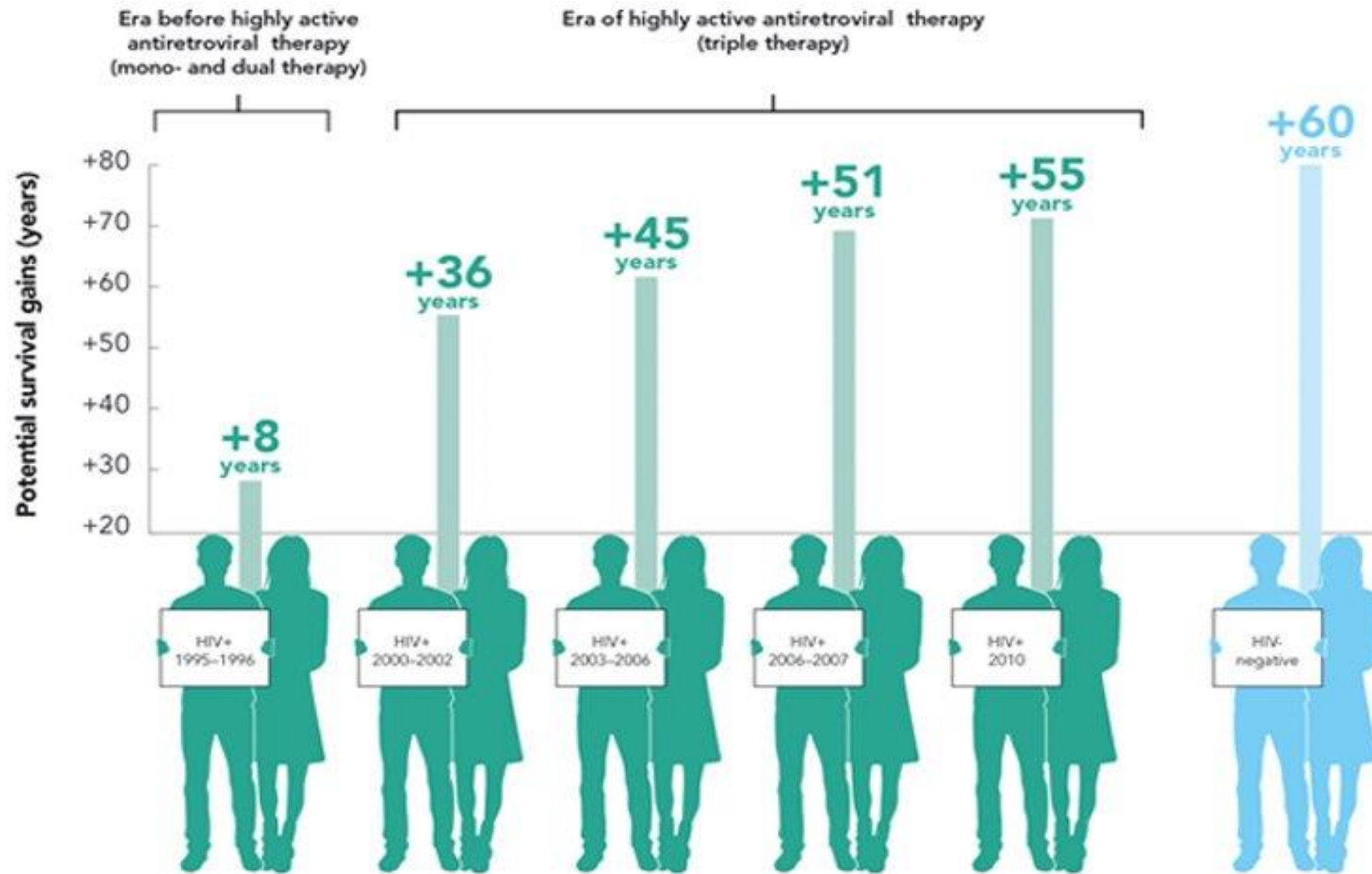
Source: UNAIDS/WHO estimates



World Health Organization

## Life expectancy has improved with the use of effective ART

Expected impact of HIV treatment on a survival of a 20-year-old person living with HIV in a high-income country

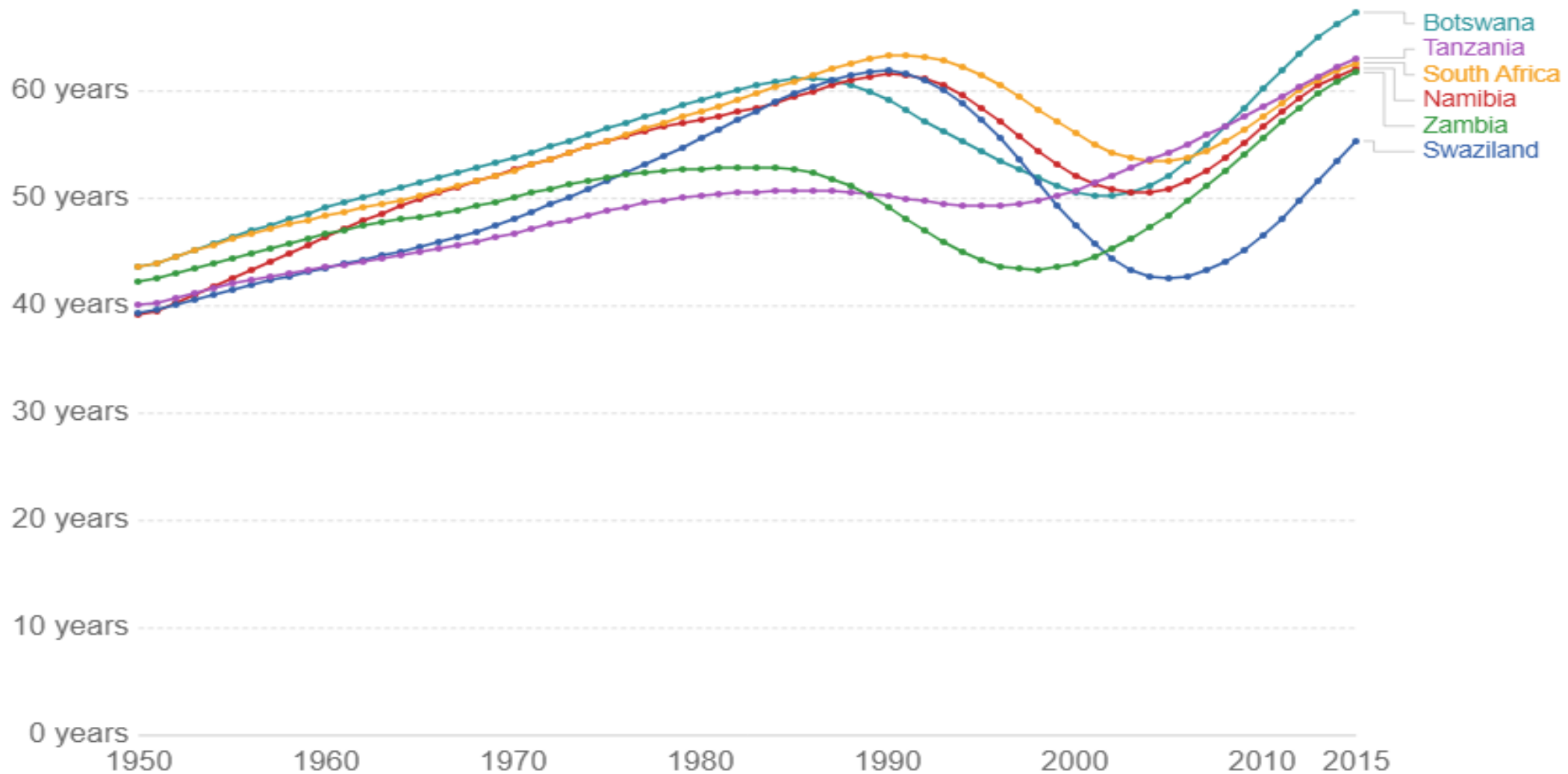


Source: Adapted from Lohse et al, 2007; Hoog et al, 2008, May et al, 2011 & Hogg et al, 2013.

# Life expectancy

Also improved in resource limited setting with ART

Our World  
in Data

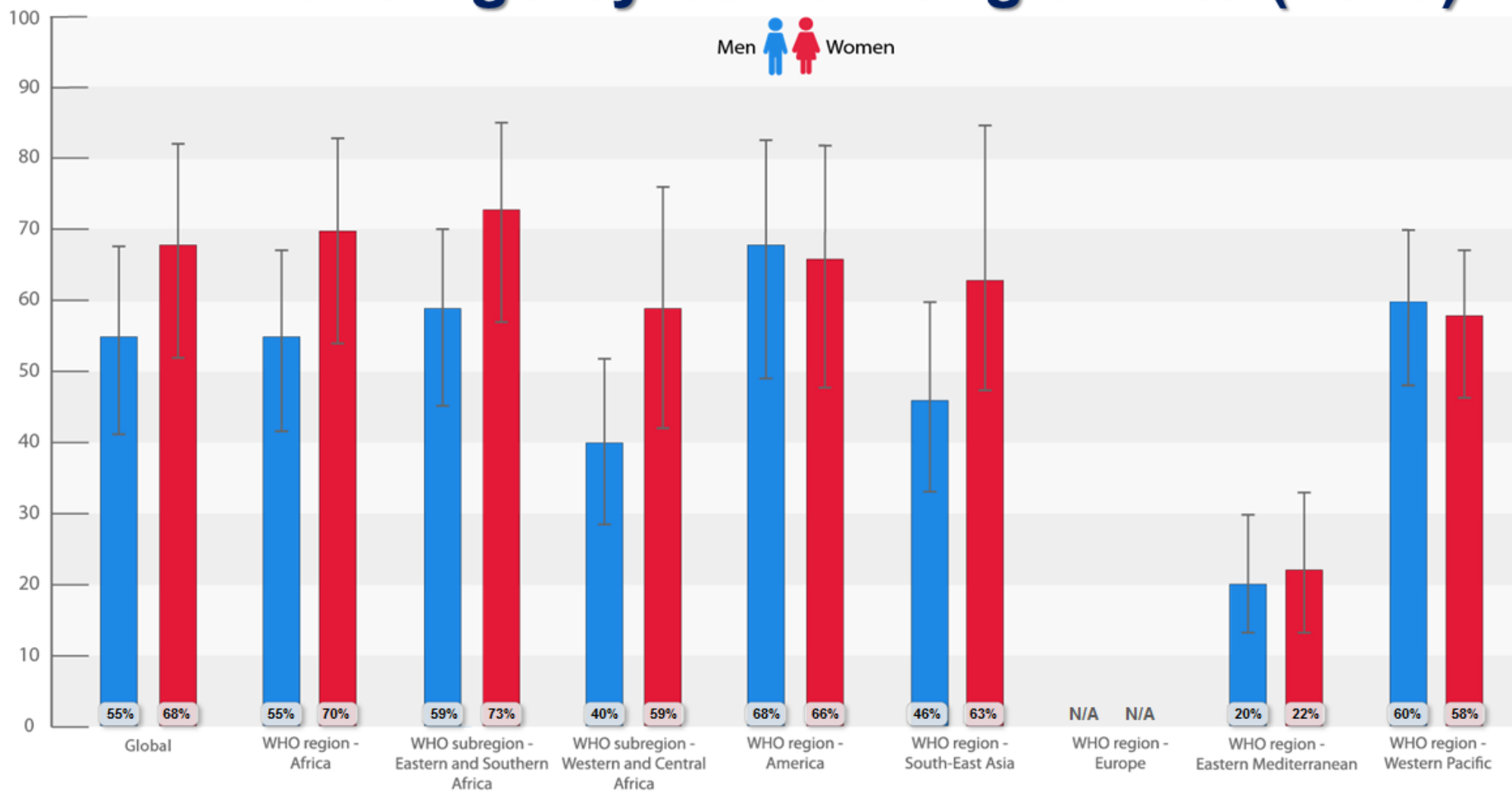


Source: Riley (2005), Clio Infra (2015), and UN Population Division (2019)

Note: Shown is period life expectancy at birth, the average number of years a newborn would live if the pattern of mortality in the given year were to stay the same throughout its life.

OurWorldInData.org/life-expectancy • CC BY

# ART coverage by sex among adults (2018)



Source: UNAIDS/WHO estimates



World Health Organization

# Is there an optimal ARV for women?

- Most pivotal trials of ARV largely in MSM
- Typically the proportion of women < 20%
- Even if sub-analysis by gender reported, underpowered to detect differences
- Most studies show no differences in efficacy although there may be differences in toxicity
- Most guidelines only comment on pregnancy as the only gender consideration

## And we aren't doing any better: Latest Pharmaceutical RCT for Naïve Patients

Study- Naive	(%) women
Gilead- Biktarvy studies	10%
Viiv- Gemini- Dovato (DTG)	14%
Drive forward /ahead Doravirine	15%
Janssen-Emerald-Symtuza	12%
Viiv- Atlas- cabotegravir/rilpivirine	25%



# Latest Pharmaceutical Switch Studies

Study	% women
Dolutegravir to Biktarvy	13% (separate study of 400 women)
CAR to Juluca	22%
Atlas- CAR to cabotegravir/rilpivirine	25%
Emerald- CAR to Symtuza	18%
DRIVE SHIFT-CAR to doravirine	15%
TANGO- CAR to Dovato	8%

# Barriers to enrollment of women

- Proportion of women in a clinical trial site
- Need for “multiple” methods of contraception
- Uncertain pregnancy intentions
- Accommodation for other demands- childcare, partner, etc- more women leave trials for “ other reasons”
- Not have a natural support group to encourage clinical trials
- “TRUST”

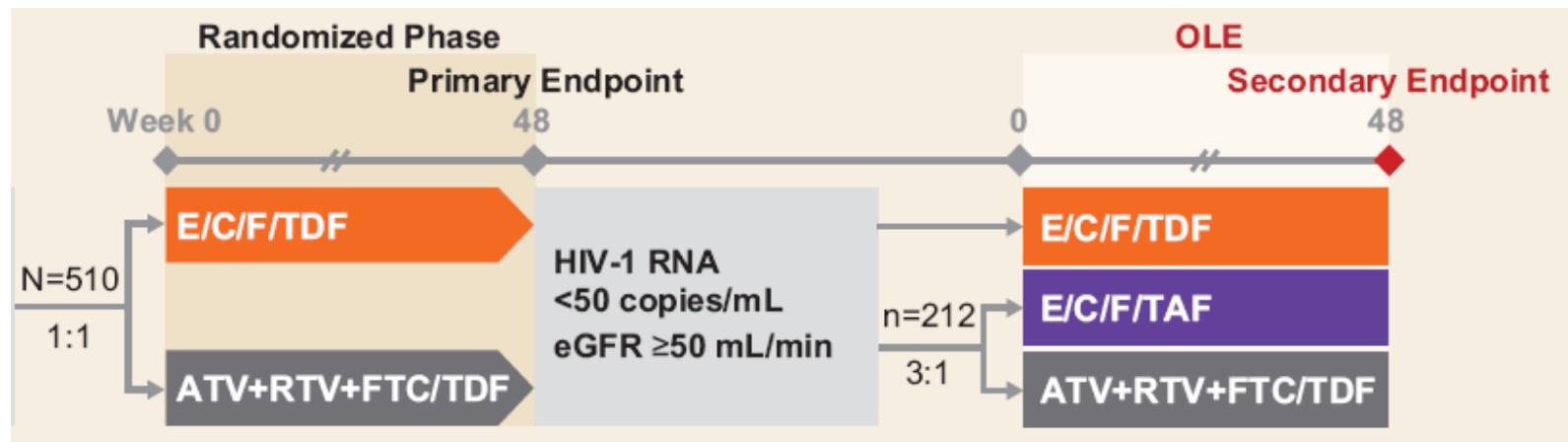
# Strategies to improve participation of women in clinical trials

- Choose centers and investigators with large female clinic populations
- Increasing involvement of centers from South Africa, Russia, South America
- Compensation for childcare
- Study participation linked to health care
- Quotas for women in RCT- but stick to it

But the good news

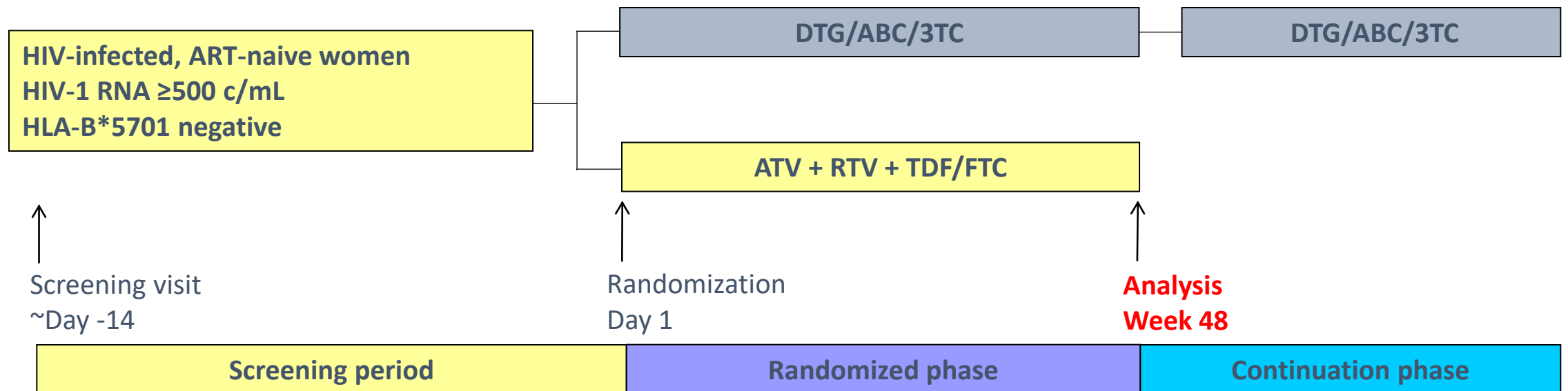
We have now seen women specific ARV studies

# Elvitegravir/c in women-WAVES



# Dolutegravir in women: ARIA Study

- Phase IIIb, parallel group, open-label, (N=474; 237 per arm)
- 1:1 randomized, regimen-to-regimen comparison
- Stratified by HIV-1 RNA and CD4+ cell count



# Are they important?

- Most studies show that viral efficacy is similar
- Over the years we have learned that there may be differences in toxicity
  - Rash and hepatitis with nevirapine
  - Lactic acidosis with DDI/d4T
  - Patterns of lipodystrophy
  - Different rates of diarrhea, nausea with the protease inhibitor
- And women may have different thresholds for tolerability of different adverse events

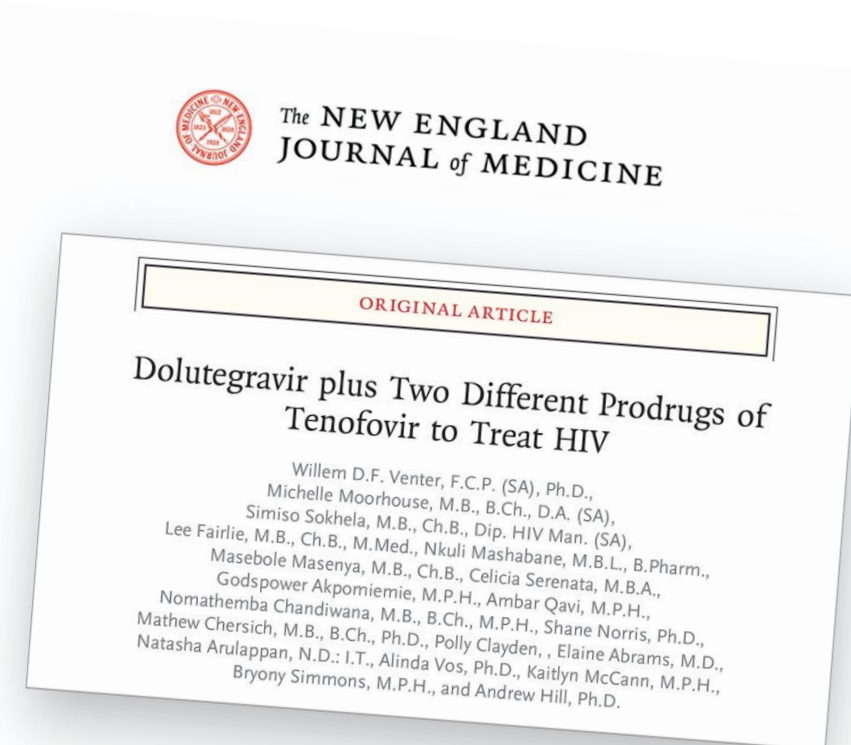
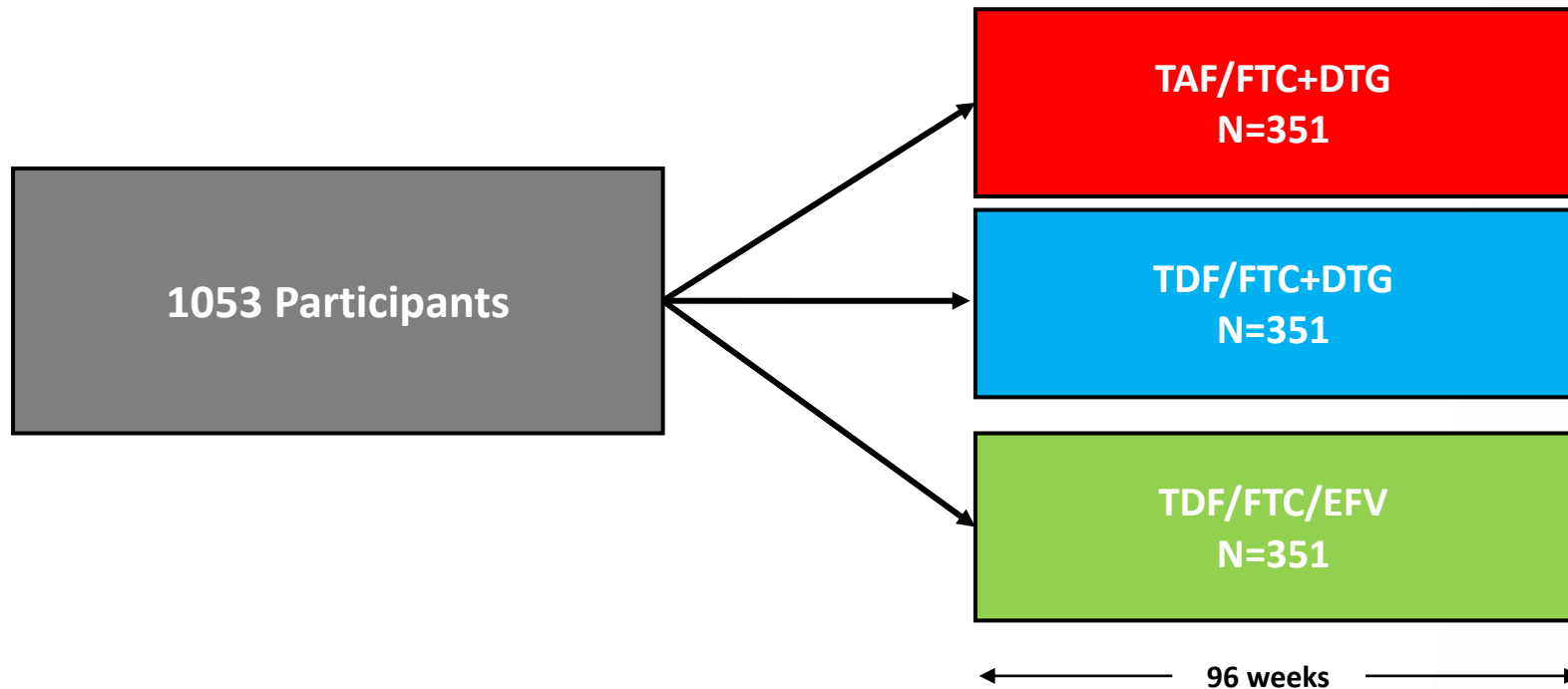
# What sample size is necessary to show an increase in adverse events?

- Would need 200 exposures to show a 2 X increased risk of an adverse event that occurs at 3% frequency
- Would need 2000 exposures to show a 3 x increased risk of an adverse event that occurs at 0.3% frequency



# ADVANCE: Study design

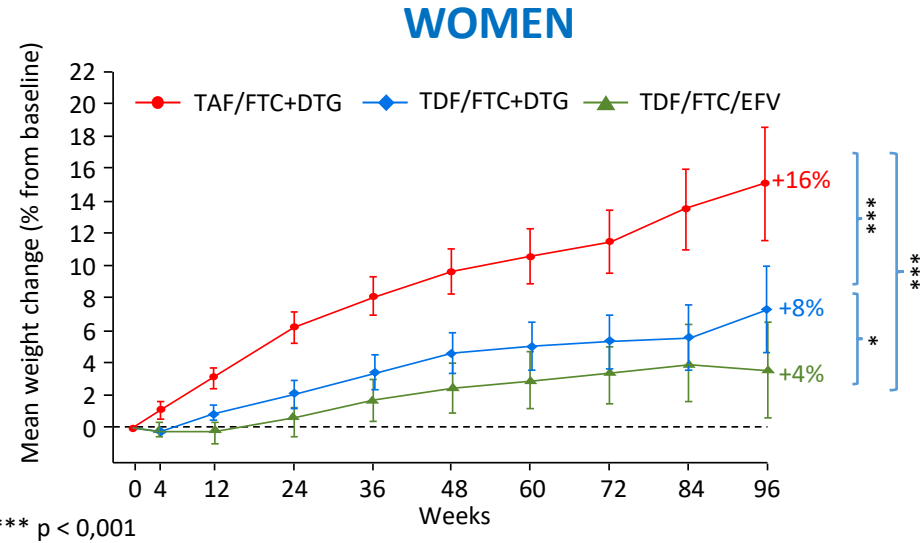
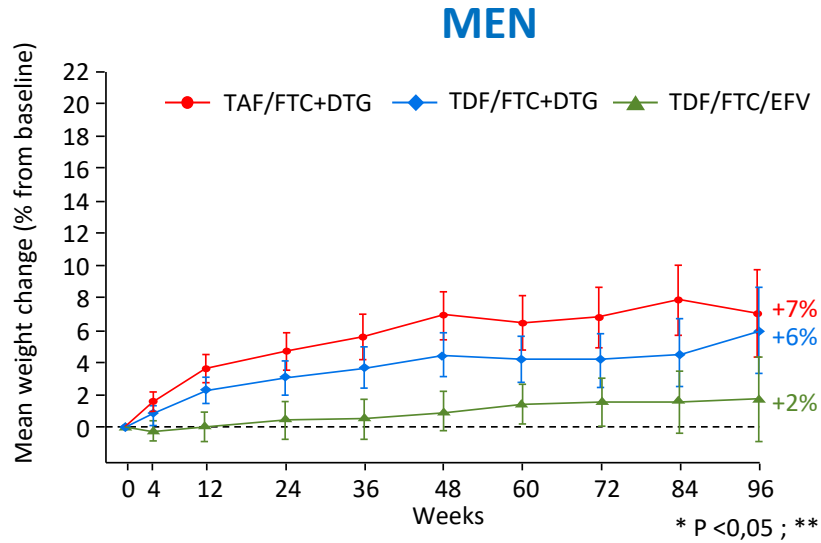
**Inclusion criteria:** treatment-naïve, HIV-1 RNA level  $\geq 500$  copies/mL, no TB or pregnancy, no baseline genotyping



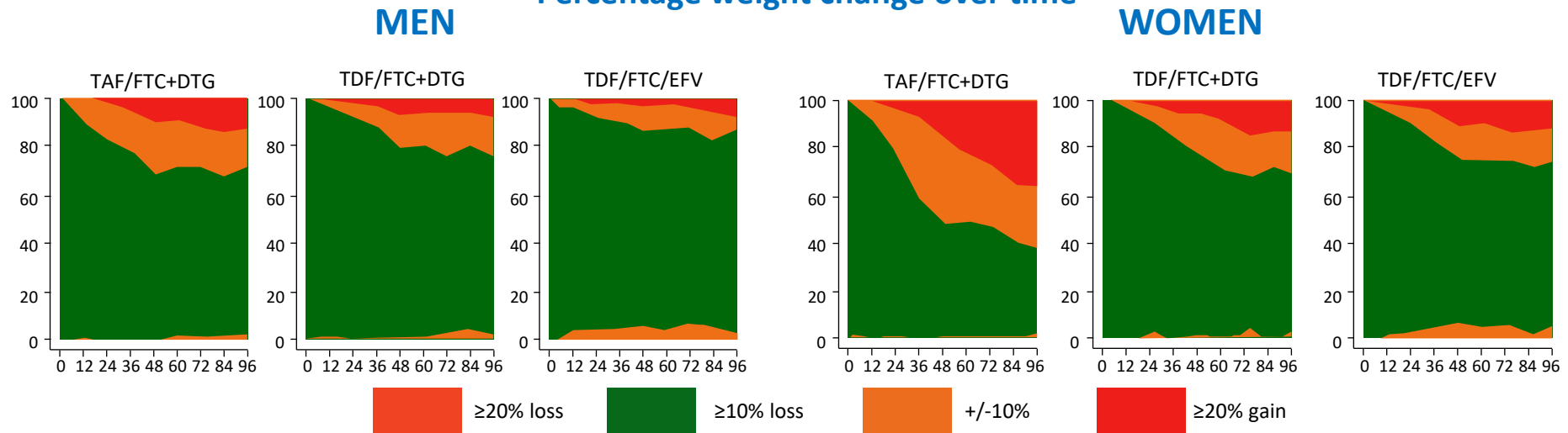
Open-label, 96-week study in Johannesburg, South Africa  
Study visits at Baseline, Week 4, 12, 24, 36, 48, 60, 72, 84, and 96

# ADVANCE study: 1<sup>st</sup> line open-label randomized ART in Johannesburg

## Percentage weight change (%) to w96



## Percentage weight change over time



# Issues for ART for aging women with HIV

- The menopausal period is a time when there is increased risk of comorbidity
- Menopause may occur earlier in HIV
- It is unknown whether we should change ART with age, declining renal function, or with menopause for safety
- There are challenges to using Hormone Replacement Therapy with ART
- And considerations with other drug interactions with medications for comorbidity

# Successes

- Effective ART prolongs the life of women with HIV
- Women have increasing access to life saving ART
- ART appears to be as effective in women as men
- We now have ART studies which only enrol women enabling us to compare the tolerability of these regimens for women
- There is starting to be a move to enable women living with HIV in clinical trials to stay in the trial should they become pregnant
- Companies are recognizing the need to enrol more women in RCT and are developing strategies to ensure that ( and stick to them)

# Gaps

- The number of women in pivotal clinical trials remains poor and is still < 25%
- We do not know what the optimal ART is for women
- As newer delivery systems evolve for ART, implementation science projects will be required to see which are best for women