

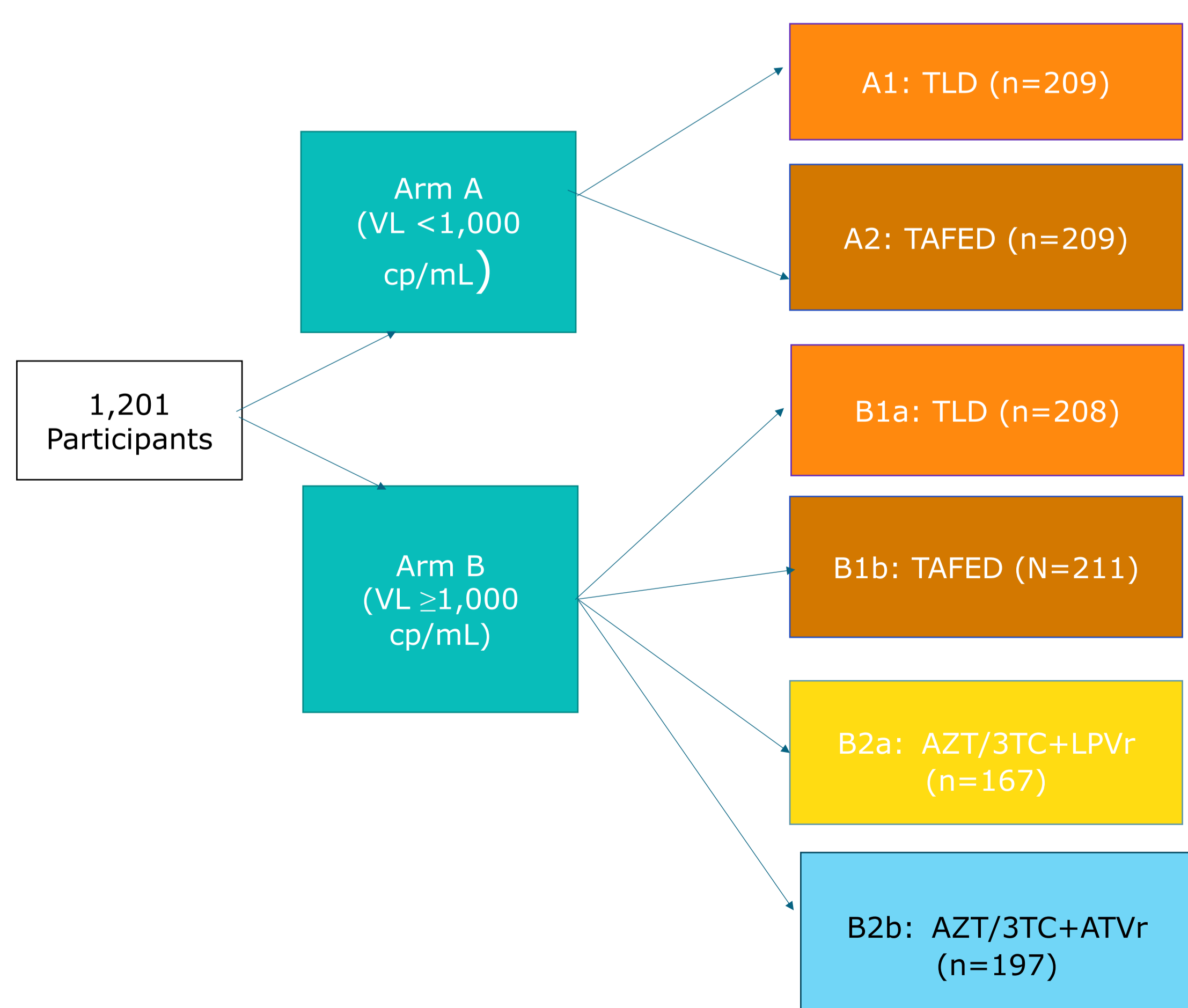
## BACKGROUND

- Tenofovir disoproxil fumarate (TDF) is associated with higher risks of kidney and bone adverse events, a reason why WHO had recommended the use of Tenofovir alafenamide (TAF) as a favorable alternative, especially in those with pre-existing kidney or bone abnormalities.
- However, there has been limited use of TAF in resource-constrained settings with a paucity of data on its safety, especially among pregnant women.
- We therefore evaluated safety/tolerability among ART-treated Zambian adults living with HIV receiving TDF/lamivudine(3TC)/dolutegravir (DTG) or TAF/emtricitabine (FTC)/DTG after being switched from non-nucleoside reverse transcriptase inhibitors (NNRTI)-based ART.

## METHODS

- The VISEND trial is a 144 week, randomized, open label, phase 3 non-inferiority study.
- Individuals on TDF/3TC/efavirenz 400(EFV<sub>400</sub>) [TLE<sub>400</sub>] or TDF/3TC/ nevirapine (NVP) with baseline HIV-1 RNA <1,000 copies/mL were randomized to TDF/3TC/DTG [TLD] (**Arm A1**) or TAF/FTC/DTG [TAFED] (**Arm A2**)
- Individuals on TLE<sub>400</sub> and or TDF/3TC/NVP with baseline HIV-1 RNA ≥1,000 copies/mL were randomized to either TLD (**Arm B1a**) or TAFED (Arm B1b) or Zidovudine (AZT)/3TC/ Lopinavir-ritonavir (LPV-r (Arm B2a) or AZT/3TC/Atazanavir-r (ATV-r) (**Arm B2b**) (**Figure 1**).
- Safety was monitored using serum creatinine. Creatinine clearance (CrCl) < 50 mL/min/1.73m<sup>2</sup> (Grade 3) and <30 mL/min/1.73m<sup>2</sup> (Grade 4) warranted TDF and TAF discontinuations, respectively. Dual-energy X-ray absorptiometry (DEXA scans) were performed among individuals with bone pain or fracture or suspected osteoporosis.
- Participants who became pregnant after randomization were maintained on their randomized ART regimens, referred to antenatal care, and given folic acid supplementation.
- Current analysis only concentrates on Arms A, B1a, and B1b.

**Figure 1: VISEND Study Design**

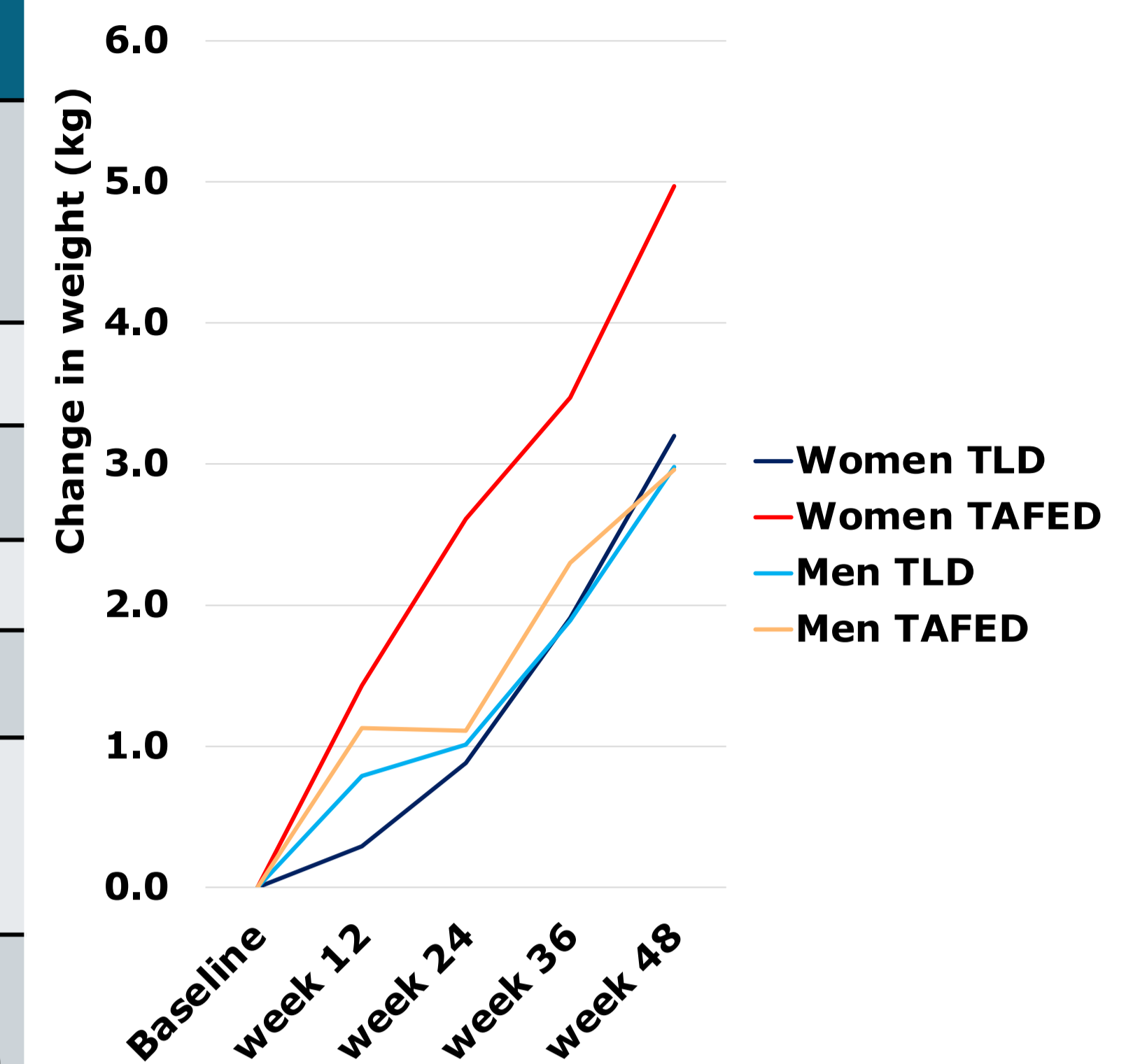


## RESULTS

**Table 1: Baseline Characteristics**

	Baseline VL <1,000 cp/mL		Baseline VL ≥ 1,000 cp/mL			TOTALS (n=1,201)
	Arm A1: TLD (n=209)	Arm A2: TAFED (n=209)	Arm B1a: TLD (n=208)	Arm B1b: TAFED (n=211)	Arm B2: AZT/3TC/boosted PI (n=364)	
Age(years)	44 (37-51)	44 (37-49)	38 (31-44)	39 (31-46)	37 (30-44)	40 (33-47)
Female n (%)	135 (65)	118 (56)	123 (59)	134 (64)	226 (62)	736 (61)
Weight (kg)	65 (55-76)	61 (55-76)	59 (51-67)	56 (51-66)	58 (53-67)	59 (53-69)
Creatinine (umol/L)	59 (51-72)	65 (53-76)	59 (51-69)	54 (47-68)	62 (53-74)	60 (51-73)
HIV-1 RNA (viral load) (log <sub>10</sub> copies/mL)	1.3 (1.3-1.6)	1.3 (1.3-1.6)	4.5 (3.9-5.1)	4.5 (4.0-4.9)	4.6 (4.0-5.1)	3.9 (1.5-4.7)
CD4 cell count (cells/mm <sup>3</sup> )	454 (298-661)	414 (277-589)	155 (71-277)	174 (85-303)	174 (93-303)	250 (126-425)

**Figure 4: Mean Change in body weight (kg) by Sex**



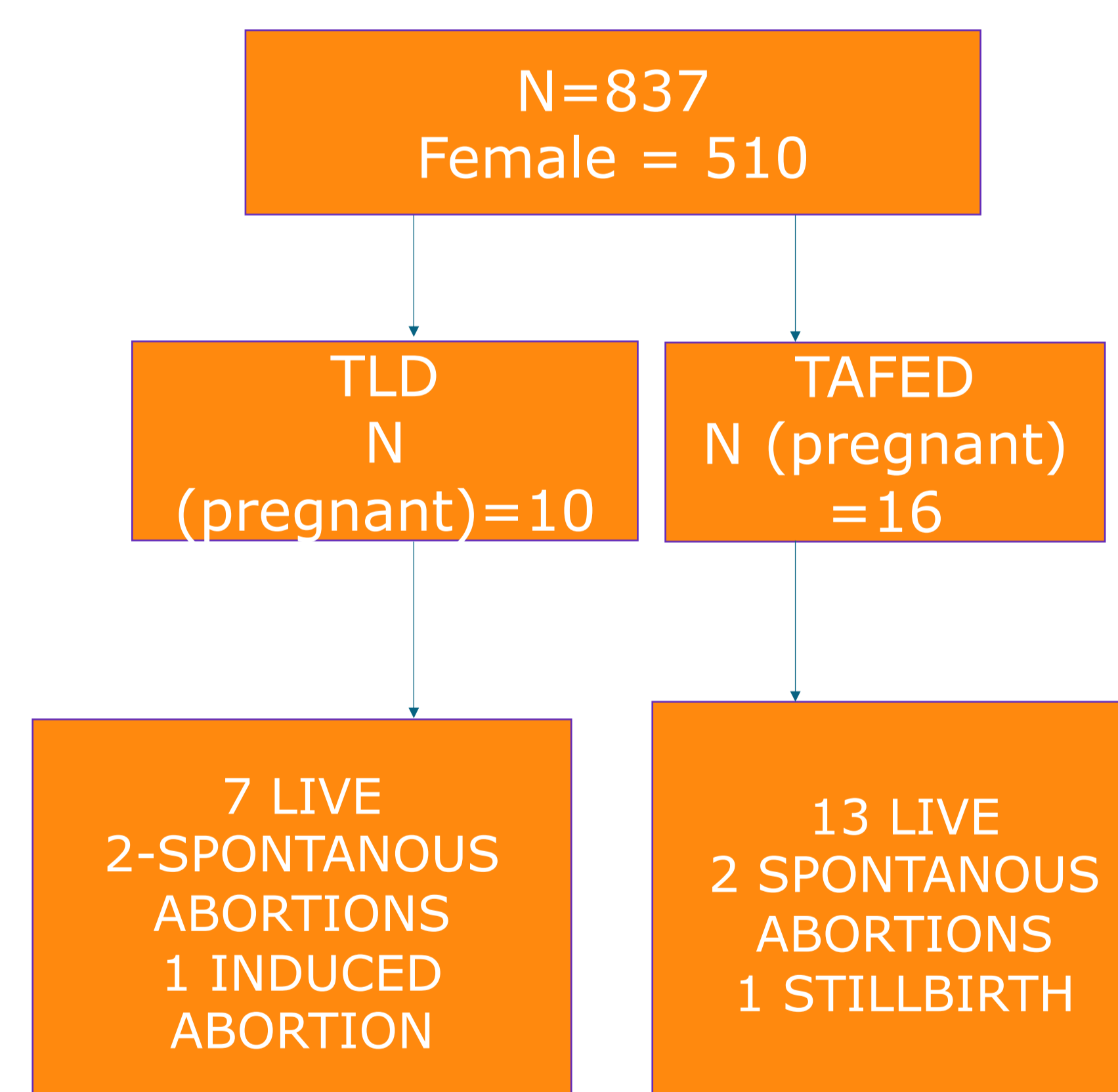
## Safety/tolerability (48-week results)

- 1.9% (8/417) individuals receiving tenofovir (TDF)-containing ART had their regimens discontinued due to kidney events.
- 0.5% (2/417) participants receiving tenofovir (TDF)-containing ART had their regimens discontinued due to bone demineralization events.
- There were zero (0) discontinuations among individuals receiving tenofovir alafenamide (TAF)-containing ART.

## CONCLUSIONS

- TAF provides an efficacious and well-tolerated alternative ARV option to TDF, especially among persons with kidney and bone disease/abnormalities, as well as pregnant women.
- However, due to its association with increased weight gain, longer term follow up is needed to ascertain metabolic complications, especially in women.

**Figure 2: Pregnancy Outcomes**



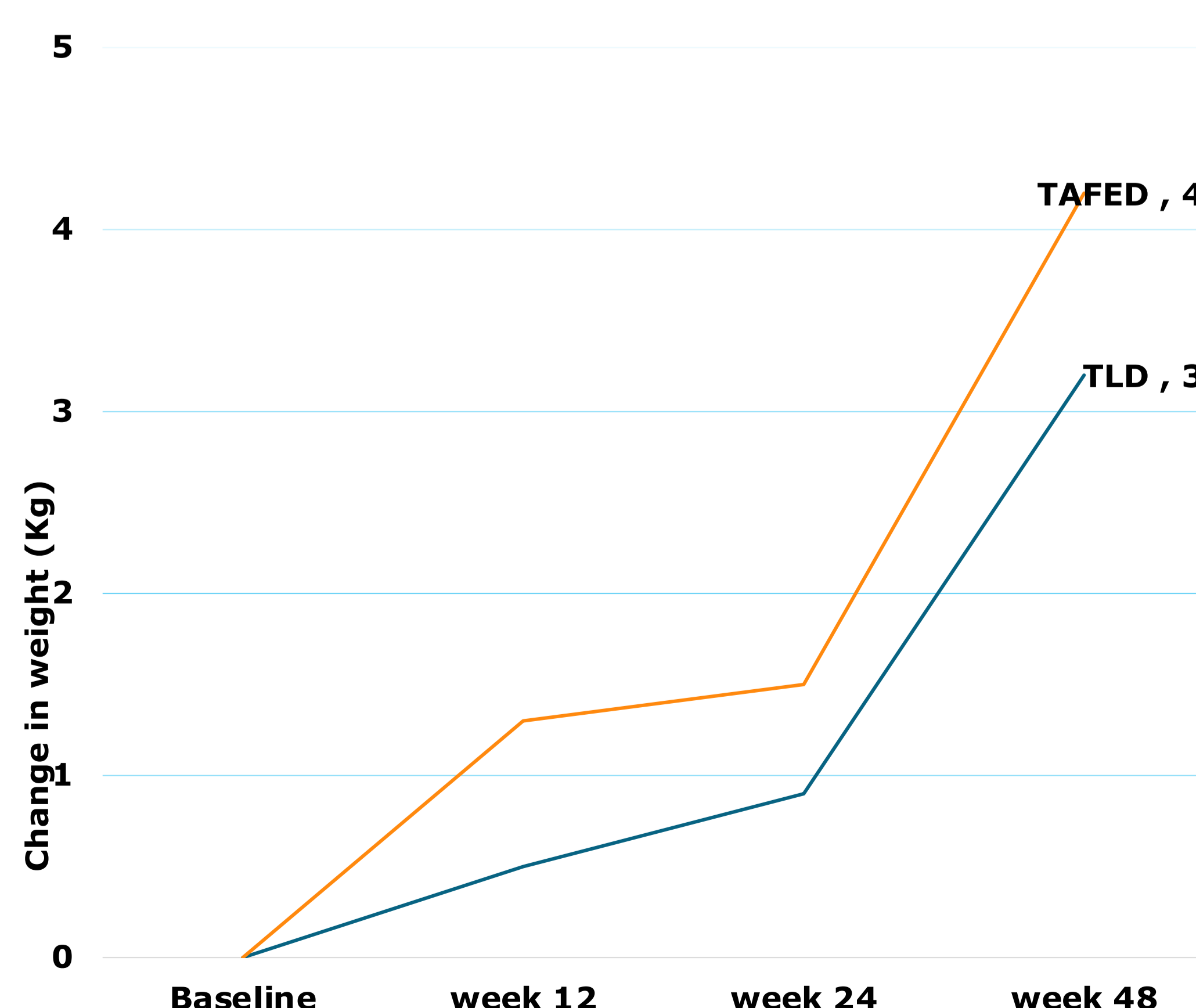
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**Figure 3: Mean Changes in body weight (kg)**



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