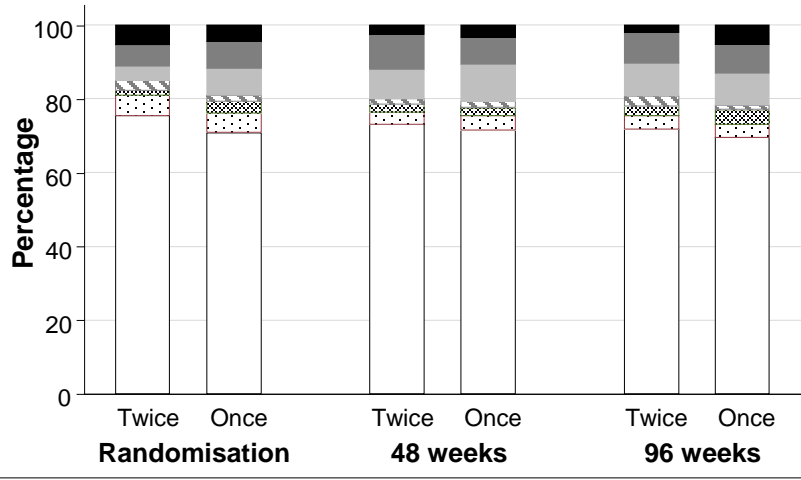


**Figure 1: Virologic suppression on twice-daily vs once-daily lamivudine+abacavir**

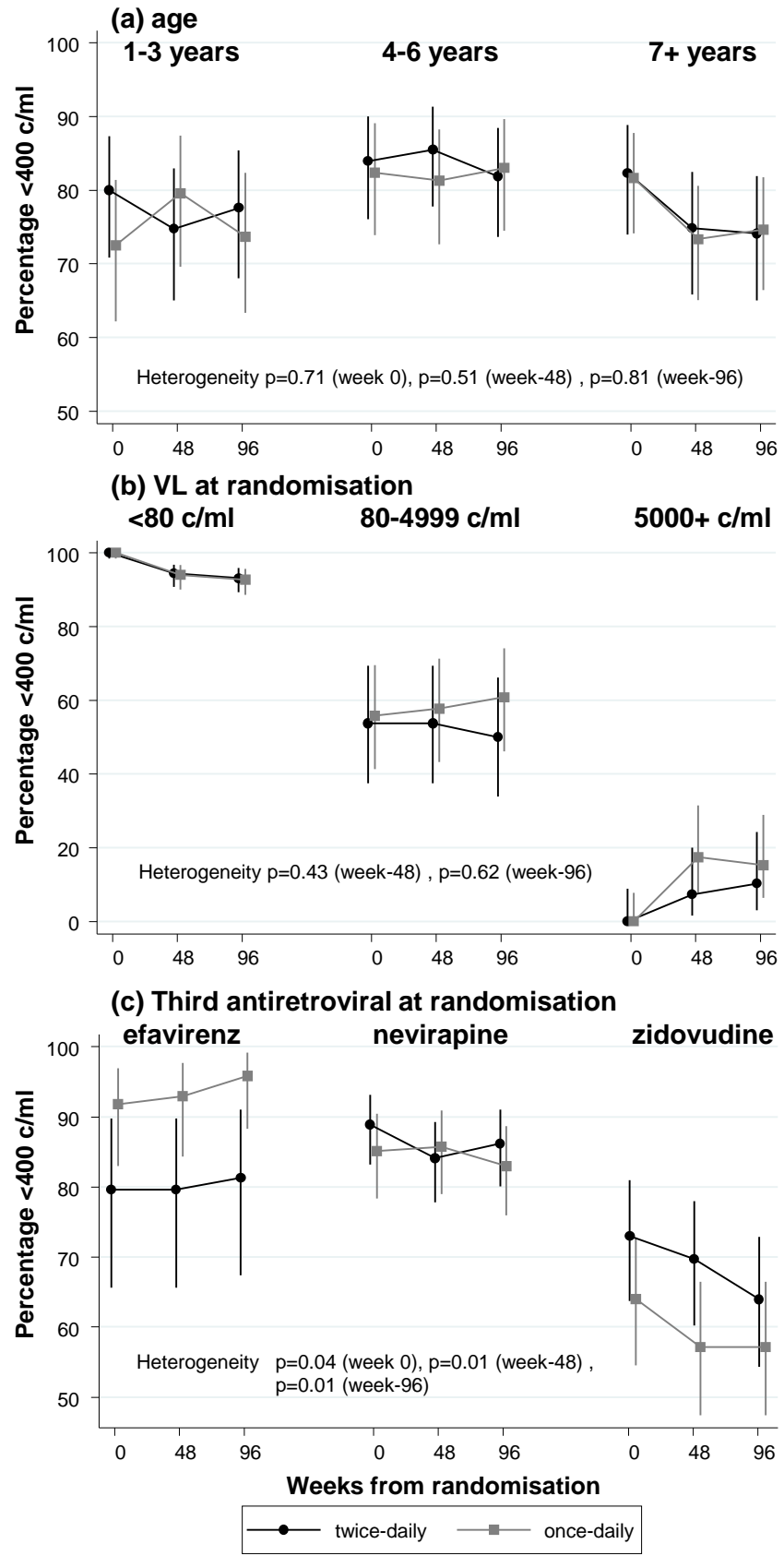


**Absolute difference once minus twice daily (95% CI)**

|                    | <80 c/ml                           | <400 c/ml                         | <1000 c/ml                        |
|--------------------|------------------------------------|-----------------------------------|-----------------------------------|
| Week 0<br>(n=666)  | -4.8%<br>(-11.5%, +1.9%)<br>p=0.16 | -2.8%<br>(-8.8%, +3.2%)<br>p=0.36 | -4.0%<br>(-9.7%, +1.7%)<br>p=0.17 |
| Week 48<br>(n=661) | -1.6%<br>(-8.4%, +5.2%)<br>p=0.65  | -1.0%<br>(-7.3%, +5.3%)<br>p=0.76 | -0.7%<br>(-6.8%, +5.5%)<br>p=0.83 |
| Week 96<br>(n=657) | -2.3%<br>(-9.3%, +4.7%)<br>p=0.52  | -0.9%<br>(-7.3%, +5.5%)<br>p=0.79 | -2.4%<br>(-8.6%, +3.7%)<br>p=0.44 |

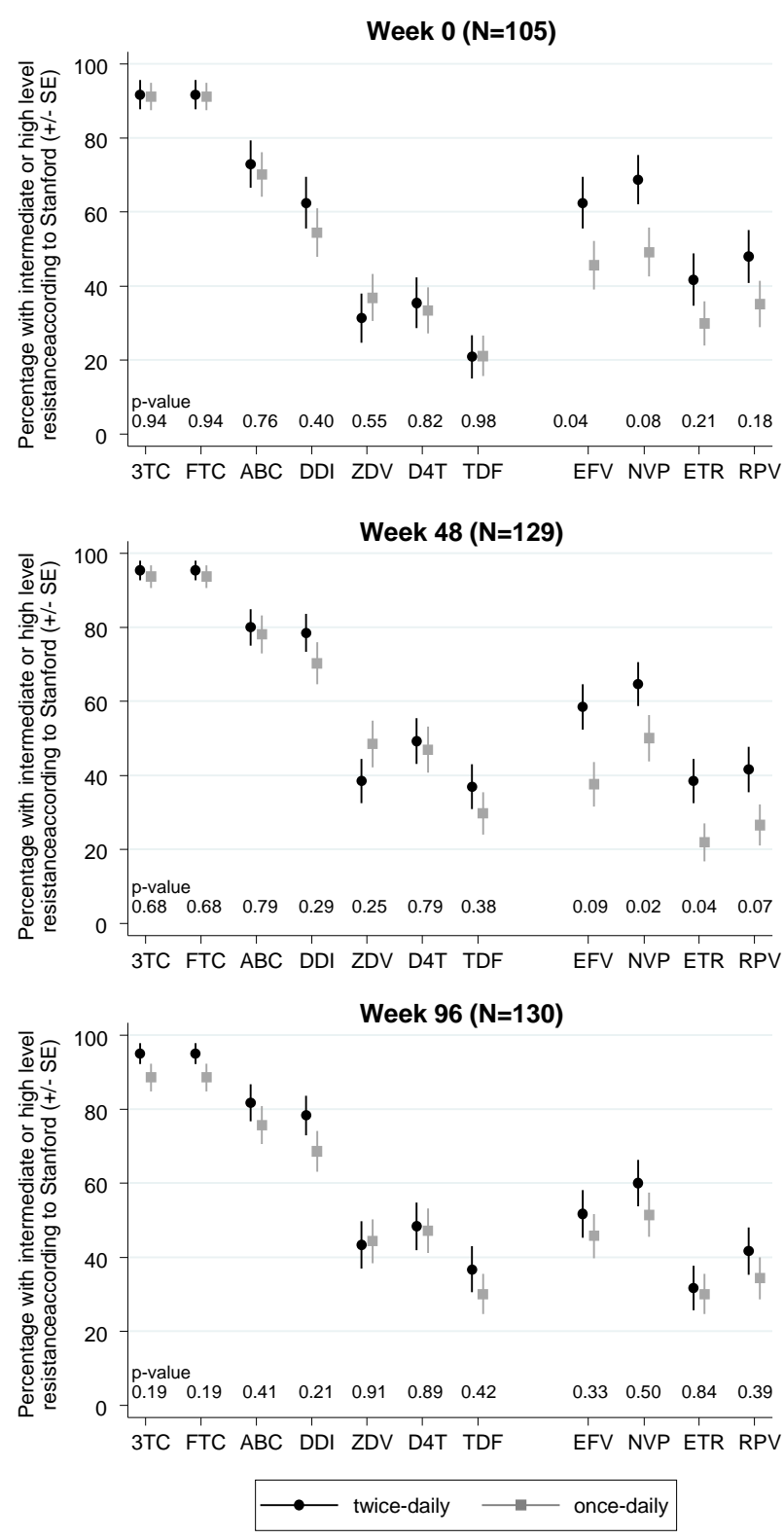
Note: excluding missing VLs at week-0 (2 twice-daily, 1 once-daily), week-48 (2 twice-daily, 6 once-daily), and week-96 (7 twice-daily, 5 once-daily) due to assay failure or died/lost before week 96.

**Figure 2: <400 c/ml on twice-daily vs once-daily lamivudine+ abacavir by (a) age (b) baseline VL and (c) third antiretroviral**



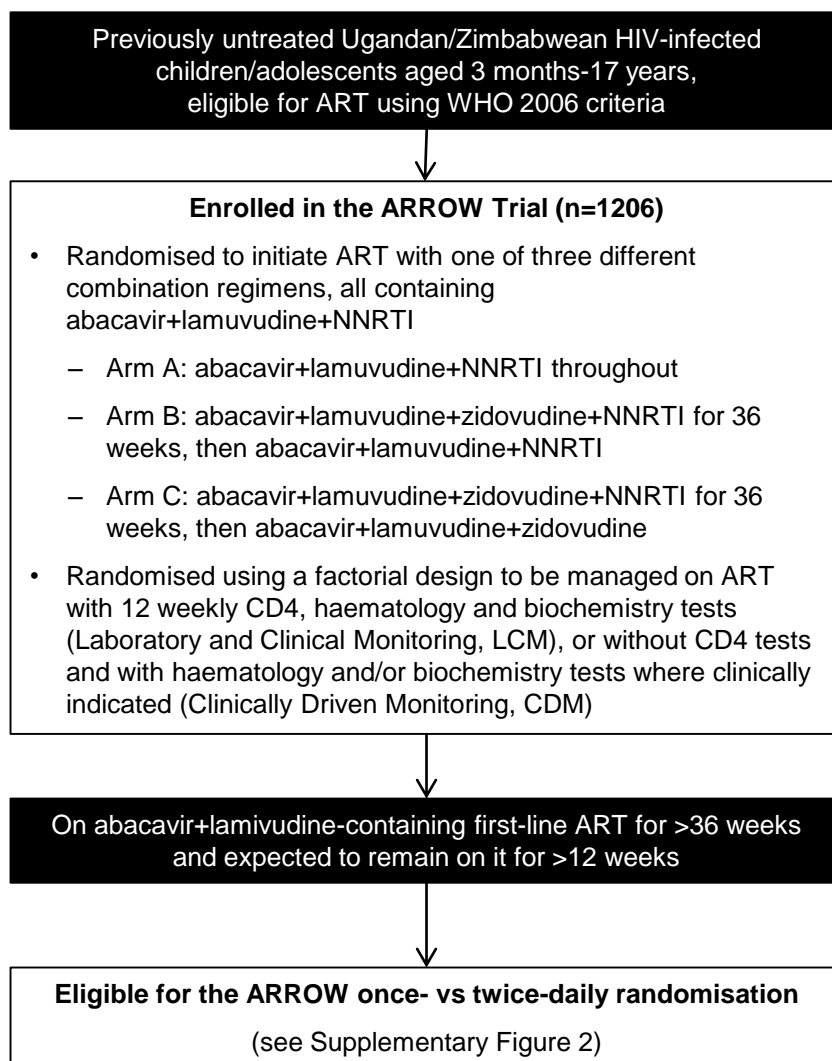
Note: Each panel shows VL suppression <400 c/ml in children randomised to twice-daily (black circles) vs once-daily (gray squares), according to different subgroups of age (a), VL at randomisation (b) and third drug (c). In each subgroup, VL suppression at randomisation (week 0), and 48 and 96 weeks later are connected by lines. Similar responses to once- and twice-daily lamivudine+abacavir are reflected in parallel lines. Heterogeneity (interaction) in response to once- and twice-daily lamivudine+abacavir is reflected by different relative positions of black and gray lines in the different subgroups. Overall effect of the subgroup factor is reflected by different average suppression levels in the different subgroups

**Figure 3: Predicted drug susceptibility**

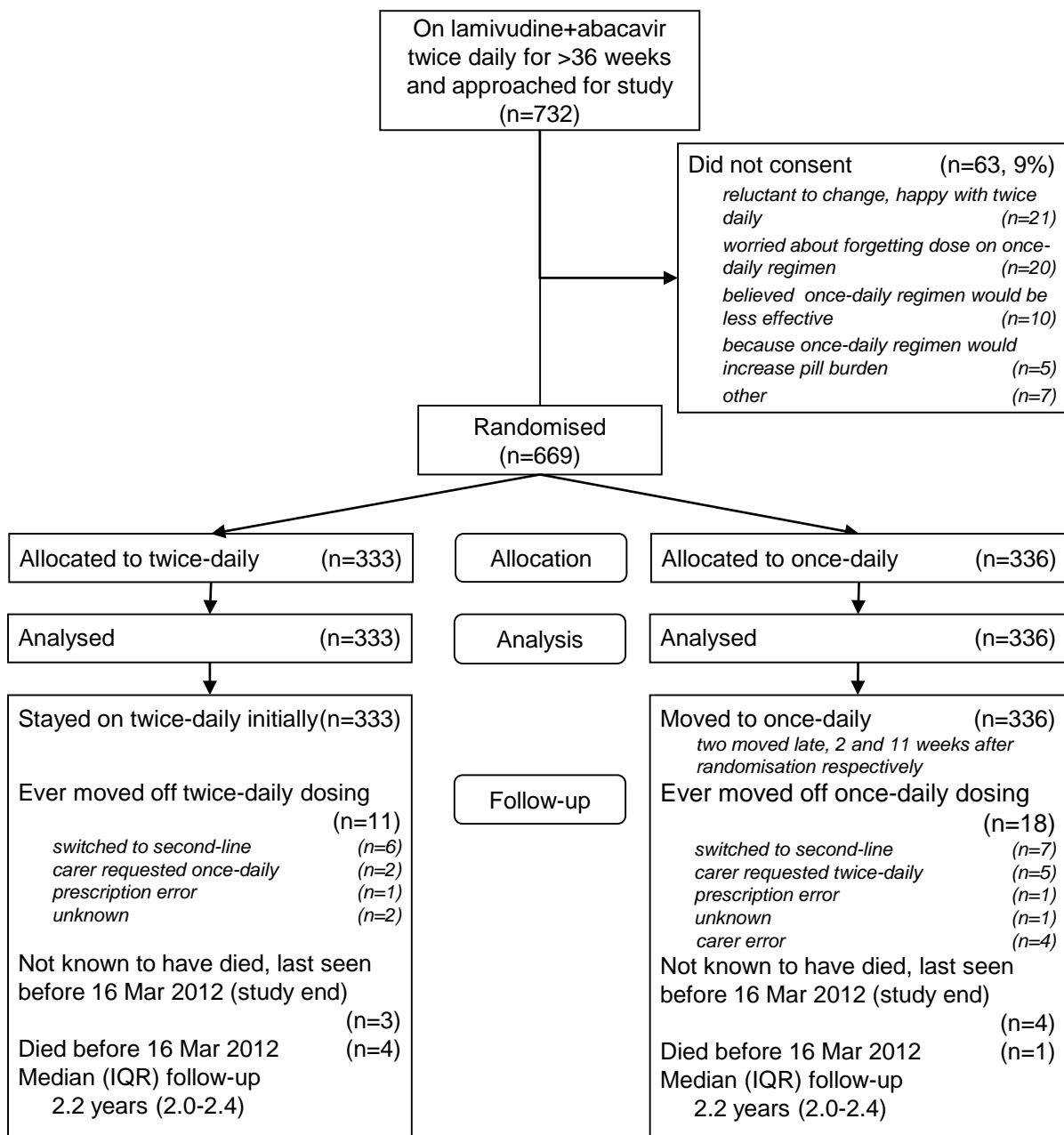


Note: Approximately one-half of children with genotypes were receiving triple NRTI (no NNRTI). 3TC=lamivudine, FTC=emtricitabine, ABC=abacavir, DDI=didanosine, ZDV=zidovudine, D4T=stavudine, TDF=tenofovir, EFV=efavirenz, NVP=nevirapine, ETR=etravirine, RPV=rilpivirine.

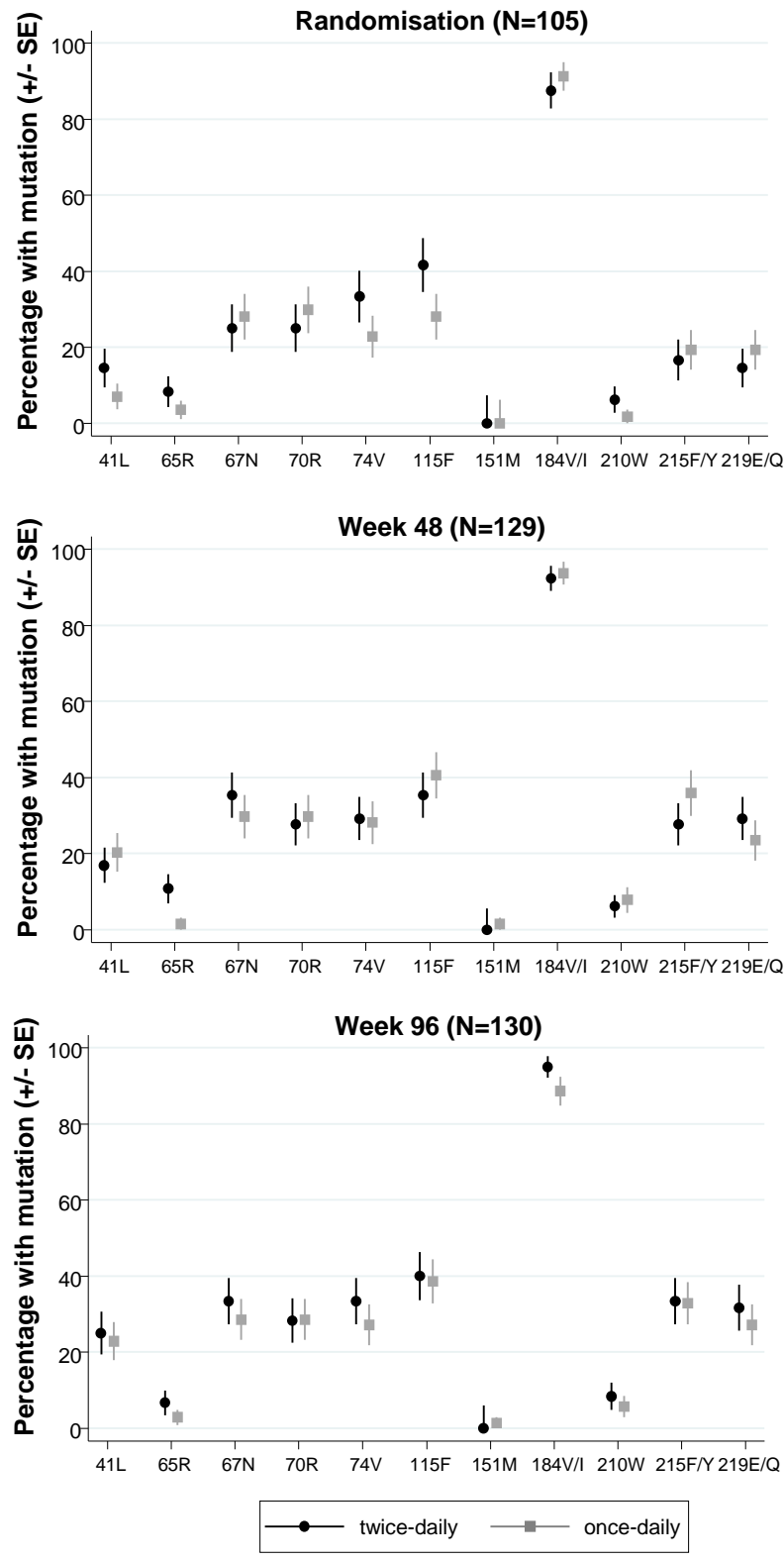
## Supplementary Figure 1. ARROW trial design



# Supplementary Figure 2. CONSORT flow diagram



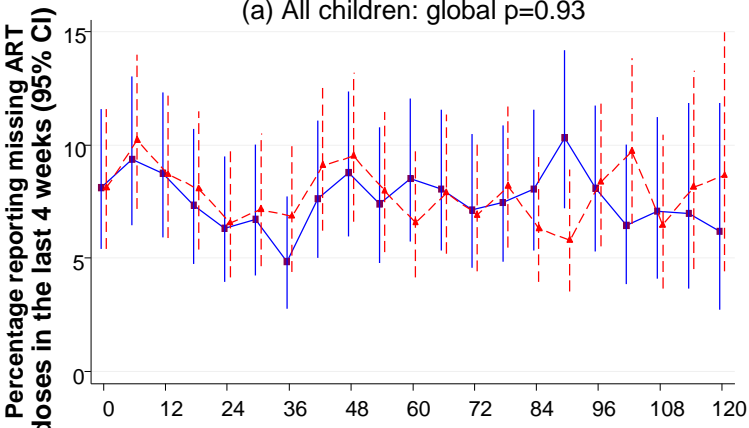
### Supplementary Figure 3: IAS NRTI mutations



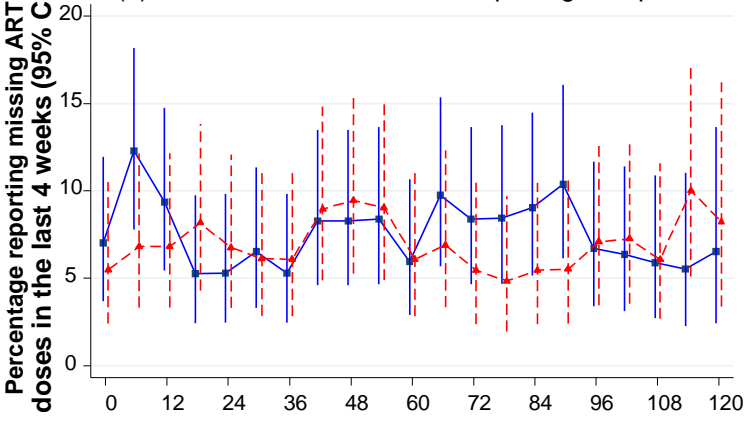
Note: Approximately one-half of children with genotypes were receiving triple NRTI (no NNRTI).  
 p>0.05 comparing twice- vs once-daily.  
 Randomisation occurred after at least 36 weeks on first-line ART.

# Supplementary Figure 4: Self-reported missing any ART pills in the last 4 weeks

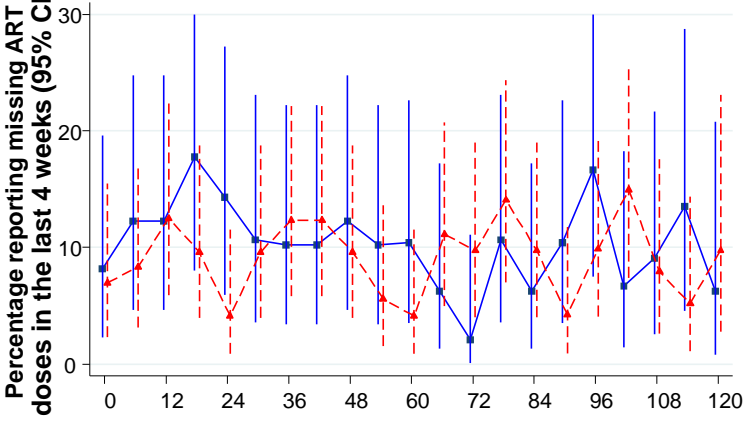
(a) All children: global p=0.93



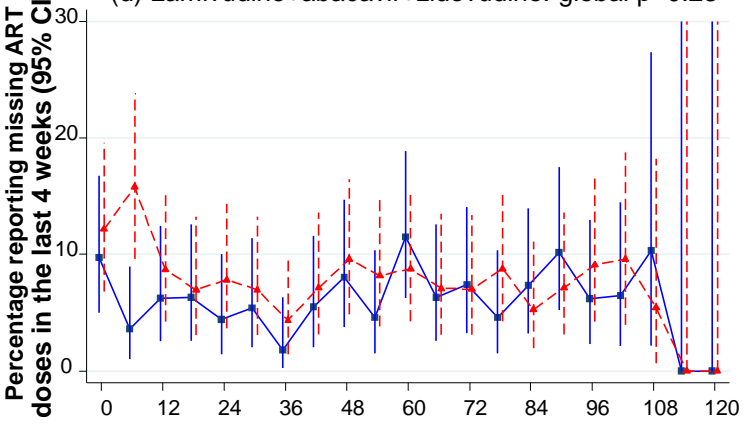
(b) Lamivudine+abacavir+nevirapine: global p=0.59



(c) Lamivudine+abacavir+efavirenz: global p=0.62



(d) Lamivudine+abacavir+zidovudine: global p=0.23



—■— Twice daily    - - - ▲ - - - Once daily