

Supplemental Digital Content

Technical details on multiple imputation

The multiple imputation was carried out using the mi suite of Stata 12 (Stata Corporation, College Station, Texas, USA) under the assumption that observations were missing at random. While most countries had no or only few non-missing measurements of CD4%, in some countries like Zambia and South Africa a substantial proportion of patients had only CD4% measurements available. For this reason we also included CD4% in the multiple imputation. We imputed the logarithms of CD4 counts and CD4% simultaneously using predictive mean matching and chained equations with a burn in period of 10. Diagnostic plots showed that this burn in period was sufficient. To allow for interaction terms in the analyses, we stratified the multiple imputation by age, gender and income groups. We included the variables country, year, continent, income group and coverage group. We coded the variable year and all the other variables as categorical variables. To minimize multiple imputation variability, we created 20 imputed datasets.

Table S1. Derivation of weights used in weighted regression analyses.

| Country | Study patients n (%) | | Patients on cART* n (%) | | Weighting factor |
|---------------------|-------------------------|--------|----------------------------|--------|---------------------|
| Low income | | | | | |
| Benin | 854 | (1%) | 15401 | (1%) | 0.81 |
| DR Congo | 4122 | (5%) | 34967 | (3%) | 0.38 |
| Kenya | 34389 | (43%) | 336980 | (26%) | 0.44 |
| Malawi | 17304 | (22%) | 198846 | (15%) | 0.51 |
| Mali | 2214 | (3%) | 21100 | (2%) | 0.43 |
| Rwanda | 2794 | (4%) | 76726 | (6%) | 1.23 |
| Tanzania | 4107 | (5%) | 199413 | (15%) | 2.17 |
| Uganda | 8566 | (11%) | 200413 | (15%) | 1.05 |
| Zimbabwe | 4938 | (6%) | 218589 | (17%) | 1.98 |
| Total | 79288 | (100%) | 1302435 | (100%) | |
| Lower middle income | | | | | |
| Cameroon | 3485 | (2%) | 76228 | (10%) | 1.50 |
| Côte d'Ivoire | 15271 | (10%) | 72011 | (10%) | 0.32 |
| Nigeria | 10307 | (7%) | 302973 | (41%) | 2.02 |
| Zambia | 124177 | (81%) | 283863 | (39%) | 0.16 |
| Total | 153240 | (100%) | 735075 | (100%) | |
| Upper middle income | | | | | |
| Botswana | 1431 | (2%) | 145190 | (10%) | 0.87 |
| Brazil | 946 | (1%) | 185982 | (12%) | 1.69 |
| South Africa | 77160 | (95%) | 971556 | (64%) | 0.11 |
| Thailand | 1389 | (2%) | 216118 | (14%) | 1.33 |
| Total | 80926 | (100%) | 1518846 | (100%) | |
| High income | | | | | |
| Australia | 522 | (2%) | 9933 | (2%) | 0.68 |
| Canada | 2357 | (7%) | 27000 | (5%) | 0.41 |
| France | 15735 | (46%) | 79680 | (14%) | 0.18 |
| Italy | 1097 | (3%) | 95000 | (17%) | 3.11 |
| Spain | 6621 | (19%) | 79500 | (14%) | 0.43 |
| USA | 8133 | (24%) | 268000 | (48%) | 1.18 |
| Total | 34465 | (100%) | 559113 | (100%) | |

* World Health Organization (WHO) estimates for 2009 [5].

Table S2. Comparison of patients starting cART with and without documented CD4 cell count.

| Variable | CD4 cell count at start of cART available (n=309 564) | CD4 cell count at start of cART missing (n=127 666) |
|-------------------------------------|--|--|
| Median age (years) | 36.6 (IQR 31 - 43) | 35.7 (IQR 30 - 42) |
| Sex | | |
| Men | 146 511 (47%) | 48 697 (38%) |
| Women | 163 053 (53%) | 78 969 (62%) |
| Clinical stage | | |
| WHO stage I/II or CDC stage A/B | 143 732 (46%) | 38 717 (30%) |
| WHO stage III/IV or CDC stage C | 135 295 (44%) | 68 061 (53%) |
| Missing | 33 217 (11%) | 20 959 (16%) |
| Country income level | | |
| Low | 63 240 (20%) | 30 041 (24%) |
| Lower middle | 107 198 (35%) | 72 379 (57%) |
| Upper middle | 61 509 (20%) | 25 235 (20%) |
| High | 77 617 (25%) | 11 (0%) |
| Median year of starting cART | 2006 (IQR 2004 - 2008) | 2007 (IQR 2006 - 2008) |

IQR, interquartile range

Table S3. Annual change between 2002 and 2009 in median CD4 cell count at the start of cART in low income, lower middle income, upper middle income and high income countries, by gender.

| Country | Women | | Men | |
|----------------------------|--------------------|--------------|--------------------|--------------|
| | CD4 cells/ μ l | (95% CI) | CD4 cells/ μ l | (95% CI) |
| Low income | | | | |
| Benin | +8 | (-24 to +40) | +5 | (-11 to +22) |
| DR Congo | -6 | (-42 to +29) | +7 | (+2 to +13) |
| Kenya | +15 | (+12 to +18) | +12 | (+8 to +15) |
| Malawi | +8 | (+4 to +12) | +8 | (-1 to +17) |
| Mali | +11 | (-6 to +28) | +4 | (-0 to +8) |
| Rwanda | +32 | (+14 to +49) | +31 | (-4 to +65) |
| Tanzania | +7 | (-5 to +20) | +2 | (-3 to +8) |
| Uganda | +24 | (+9 to +40) | +18 | (-1 to +38) |
| Zimbabwe | +10 | (-0 to +19) | +6 | (-2 to +13) |
| <i>Pooled crude</i> | +12 | (+7 to +18) | +10 | (+6 to +14) |
| <i>weighted*</i> | +11 | (+4 to +17) | +8 | (+3 to +13) |
| Lower middle income | | | | |
| Cameroon | -3 | (-34 to +28) | +7 | (-29 to +42) |
| Côte d'Ivoire | +14 | (+7 to +21) | +11 | (-2 to +23) |
| Nigeria | -2 | (-36 to +32) | -4 | (-31 to +23) |
| Zambia | +11 | (+9 to +14) | +8 | (+4 to +12) |
| <i>Pooled crude</i> | +9 | (+5 to +13) | +7 | (+4 to +10) |
| <i>weighted*</i> | +4 | (-1 to +9) | +5 | (+1 to +8) |
| Upper middle income | | | | |
| Botswana | +12 | (-2 to +27) | +2 | (-19 to +22) |
| Brazil | +10 | (-8 to +27) | +16 | (-2 to +34) |
| South Africa | +9 | (+7 to +12) | +3 | (-1 to +7) |
| Thailand | +9 | (-0 to +19) | +6 | (-8 to +20) |
| <i>Pooled crude</i> | +9 | (+6 to +12) | +4 | (+0 to +7) |
| <i>weighted*</i> | +8 | (+2 to +14) | +7 | (-0 to +14) |
| High income | | | | |
| Australia | +10 | (-24 to +44) | -3 | (-14 to +9) |
| Canada | +7 | (-2 to +17) | +16 | (+11 to +21) |
| France | +11 | (+8 to +13) | +9 | (+1 to +16) |
| Italy | +4 | (-6 to +13) | +6 | (-5 to +17) |
| Spain | +3 | (-2 to +8) | +6 | (+1 to +11) |
| USA | +9 | (-0 to +18) | +13 | (+4 to +21) |
| <i>Pooled crude</i> | +9 | (+6 to +11) | +9 | (+6 to +12) |
| <i>weighted*</i> | +7 | (+4 to +11) | +9 | (+6 to +13) |

Complete case analysis (model 1) based on 240,322 patients.

* Weighted by the number of patients on cART in the respective country, as estimated by WHO [5].

Table S4. Individual-level and country-level predictors of the median CD4 cell count at the start of cART in 2009.

| Variable | Median CD4 cell count (cells/μl) |
|------------------------------------|--|
| Sex | |
| Male | 160 (intercept, 131 to 179) |
| Female | 24 (18 to 29) |
| Income group | |
| Low | 160 (intercept, 131 to 179) |
| Lower middle | -11 (-51 to 31) |
| Upper middle | -19 (-54 to 20) |
| High | 114 (82 to 152) |
| Age group (years) | |
| < 30 | 160 (intercept, 131 to 179) |
| 30 to <40 | -15 (-21 to -9) |
| 40 to <50 | -16 (-23 to -9) |
| ≥ 50 | 0 (-11 to 9) |
| National cART coverage (%)* | |
| < 40 | 138 (intercept, 99 to 176) |
| 40 to < 60 | 11 (-35 to 54) |
| 60 to < 80 | -4 (-48 to 45) |
| ≥ 80 | 90 (32 to 130) |

Complete case analysis (model 2) based on 31,512 patients starting cART in 2009. Intercepts and coefficients (95% confidence intervals) are shown. All models include calendar year, age, gender and income group. The intercept of 160 cells/ μ l corresponds to men in low income countries.

* Separate analysis based on 29,245 patients starting cART in 2009 in low income and middle income countries (model 2). The intercept of 138 cells/ μ l corresponds to men in low income countries. Estimates of national cART coverage in 2009, based on WHO 2006 guidelines were as follows [25]: Benin 72%, Democratic Republic of the Congo 26%, Kenya 65%, Malawi 63%, Mali 65%, Rwanda >95%, Tanzania 44%, Uganda 53%, Zimbabwe 49%, Cameroon 41%, Côte d'Ivoire 39%, Nigeria 31%, Zambia 85%, Botswana >95%, Brazil 80%, South Africa 56%, Thailand 76%.

Figure S1. Map of countries contributing patients to the collaborative analysis.

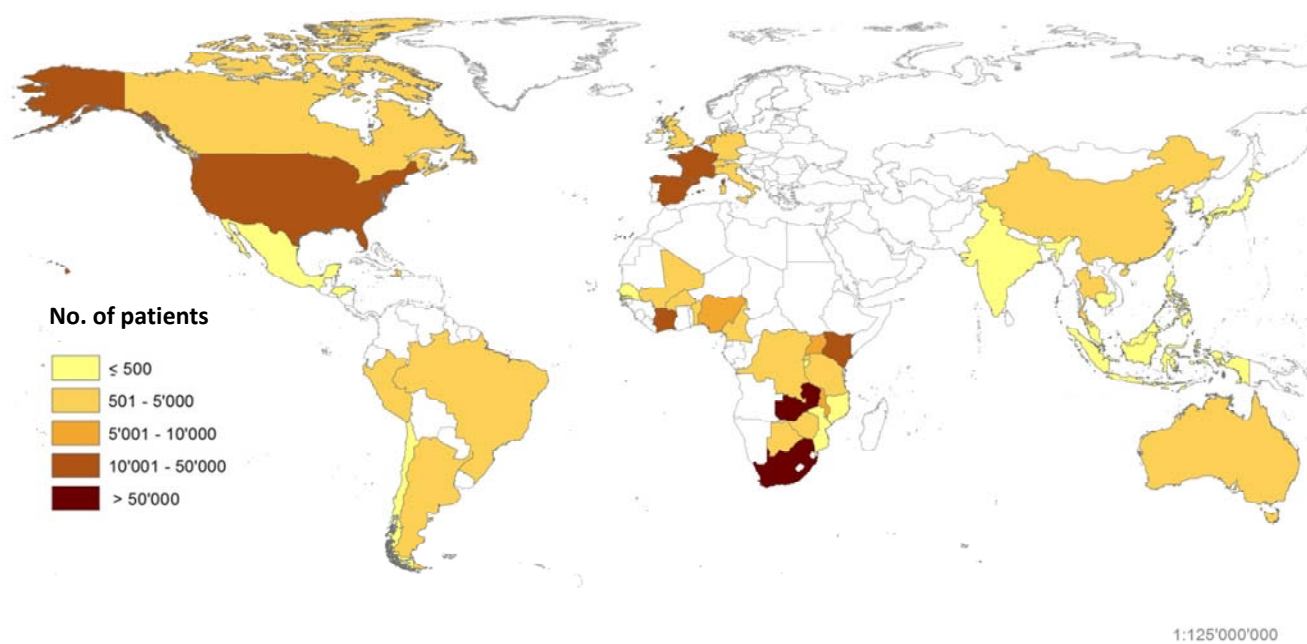
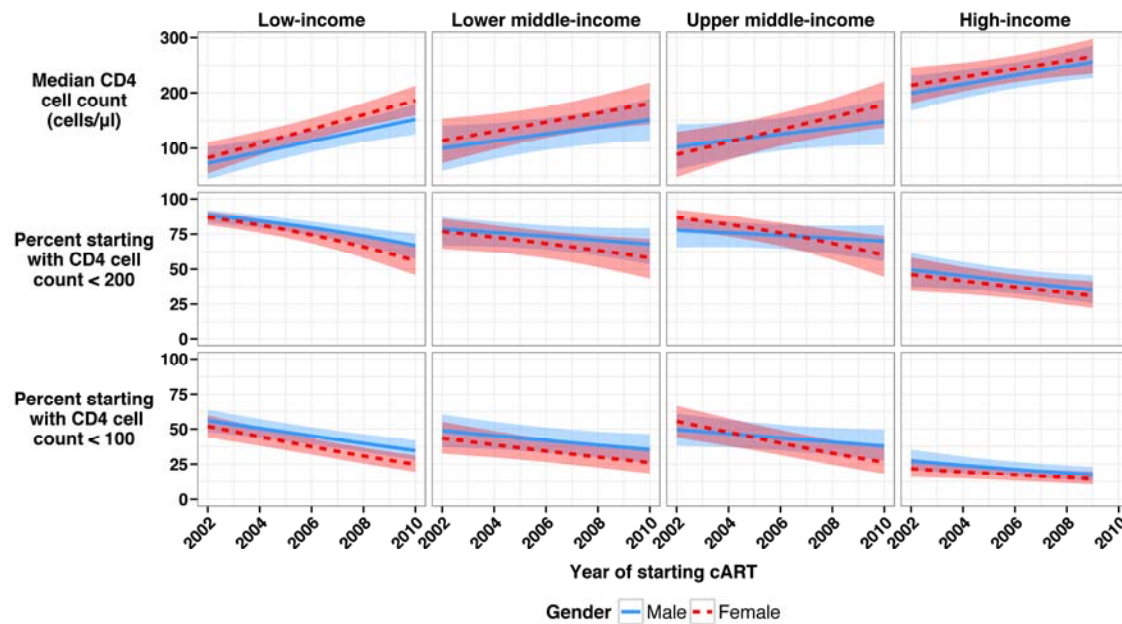


Figure S2. Trends of median CD4 cell counts at the start of cART (upper panel) and in proportions of men and women starting cART below 200 cells/ μ l (middle panel) or below 100 cells/ μ l (lower panel) in low, middle and high income countries, 2002 to 2010.



The shaded areas represent the 95% confidence intervals for each year. Complete case analysis (model 3) based on 256,601 patients.