**Supplementary Material**

The expansion of a variable *X* using restricted cubic spline with *k* knots (i.e., *k–*1degrees of freedom, for *k*) at locations can be written as,

+…+

where *X*1=*X* and for *i=*1,…*k* – 2,

with if otherwise The knot locations, , can be specified by the user or placed at standard default software locations that usually correspond to percentiles of *X*.

In Cox regression, the hazard at time is modeled as , where is the “baseline hazard” (i.e., the hazard if all covariates *X* are set to 0) and is the linear predictor; here *X* denotes potentially multiple predictor variables and is a vector of coefficients. A hazard ratio is simply the hazard at a particular value of *X* (e.g., age=50) divided by the hazard at a different value of *X* (e.g., age=30), holding all other predictor variables constant. Note that the baseline hazard is not needed for computing the hazard ratio because it is in both the numerator and the denominator of the hazard ratio, and therefore cancels out. If *X* includes more than one term derived from the same variable (e.g., *X=*(*X*1,*X*2,*X*3)=(age, age2,sex)), then it is not sensible to hold one term derived from the same variable constant while varying the others (e.g., it is not possible to set age=30 without also setting age2=302), and therefore it becomes difficult to interpret in isolation the coefficients corresponding to the terms derived from the same variable (e.g., does not have a good interpretation without also considering ). However, it is still easy to compute and interpret the hazard ratio using combinations of variables (e.g., is the hazard ratio comparing age=50 vs. age=30 adjusting for sex). When a variable is expanded using restricted cubic splines, it is similarly difficult to interpret the individual coefficients in isolation, but hazard ratios for specific comparisons are similarly easy to compute and interpret. For example, the hazard ratio comparing age=50 versus age=30 would be , where the spline function, , is given above.

As with any Cox model, unbiased estimation requires that the censoring times are independent of the failure times conditional on *X*; this assumption may be more realistic with *X* expanded using splines. Unbiased estimation also requires that the model is properly specified; i.e., the hazards truly are proportional and the form of the linear predictor is correct. Simple linear relationships are a special case of splines, and therefore, splines are more robust to model misspecification than traditional regression models.

**Supplementary Figure.** Association between predictors and estimated 5-year survival probability after starting ART at 7 sites in Latin America and the Caribbean. The model is adjusted for the other variables at representative levels (given in Figure 1 legend). A similar figure, except using multiply imputed data, was published previously [13].

