



Trickey, A., May, M., & Sterne, J. (2017). Methodological and statistical issues related to analysis of survival – Authors' reply. *Lancet HIV*. https://doi.org/10.1016/s2352-3018(17)30136-4

Peer reviewed version

License (if available): CC BY-NC-ND

Link to published version (if available): 10.1016/s2352-3018(17)30136-4

Link to publication record in Explore Bristol Research PDF-document

This is the accepted author manuscript (AAM). The final published version (version of record) is available online via Elsevier at https://doi.org/10.1016/S2352-3018(17)30136-4. Please refer to any applicable terms of use of the publisher.

University of Bristol - Explore Bristol Research General rights

This document is made available in accordance with publisher policies. Please cite only the published version using the reference above. Full terms of use are available: http://www.bristol.ac.uk/pure/about/ebr-terms

We are grateful for the opportunity to respond to the points raised by Alizadeh and colleagues. First, we addressed between-cohort heterogeneity (clustering) by stratifying all Cox models on cohort. This allows the baseline mortality hazard to vary between cohorts, while assuming a common effect of covariates across cohorts(1). We have found previously that effects of important prognostic factors such as CD4 count are consistent across cohorts. Webtable 1 of our paper shows that calendar time effects were consistent across subgroups defined by values of important prognostic factors.

For the analyses of prognosis from 1 year after starting ART, we presented analyses (see Figure 2) in which we controlled for CD4 count and viral load measured at both start of ART and at one year after starting ART. These measurements were all made before start of follow up in those analyses. We do not agree that it would have been appropriate to address the effects of these time-dependent variables through joint modelling of time-to-event and longitudinal outcomes: our analysis appropriately addressed the extent to which controlling for one-year measurements attenuated associations with their baseline values.

We agree that we cannot exclude selection bias due to informative censoring. As noted by Alizadeh and colleagues, we reported that some patient characteristics predicted loss to follow up. However, this finding does not imply that censoring was informative, since our analyses conditioned on the variables that predicted loss to follow up. Informative censoring is unlikely to have substantially biased our results because cohorts have good recording of deaths and linkage to death registries. Sensitivity analyses such as those proposed by Kaciroti et al(2) would be of interest but were outside the scope of our paper.

Adam Trickey, Margaret T May, and Jonathan AC Sterne

School of Social and Community Medicine, University of Bristol

- 1. Cleves, M. A., W. W. Gould, and Y. V. Marchenko. 2016. An Introduction to Survival Analysis Using Stata. Rev. 3 ed. College Station, TX: Stata Press
- 2. Kaciroti NA, Raghunathan TE, Taylor JM and Julius S. A Bayesian model for time-to-event data with informative censoring. *Biostatistics (Oxford, England)*. 2012; 13: 341-54.