

POSTER PRESENTATION

Open Access

# Assessing violations of the proportional hazards assumption in Cox regression: does the chosen method matter?

Louise Hiller\*, Andrea Marshall, Janet Dunn

From 3rd International Clinical Trials Methodology Conference  
Glasgow, UK. 16-17 November 2015

## Objectives

The Cox proportional hazards (PH) model is commonly used in randomised clinical trials (RCTs) to assess a treatment effect after adjusting for known prognostic factors. However, the Cox model requires that a covariate effect is constant over time. Violation of this assumption invalidates the simple Cox model. Various PH checks exist, some in the form of statistical tests and some empirical ones involving graphical examination. We investigated if results vary from some of the different methods available.

## Methods

Individual patient data for the same five prognostic factors was collated from 6248 patients participating in four similar RCTs and a time to event analysis undertaken (median follow-up 6.2 years; 1335 events). The PH assumption was checked for each variable using four different methods:

- 1/ Plot of the log of the negative log of the estimated survival density function vs log(time)
- 2/ Cumulative Sums of Martingale Residuals and the Kolmogorov-type Supremum Test
- 3/ Fitting time dependent covariates
- 4/ Schoenfeld's residuals

## Results

For two variables, all four PH assessment methods agreed. For the other three variables, different results were found depending on the method used.

## Conclusion

Different conclusions were reached on PH violation of covariates depending on which PH assessment method

was used. With the requirement for upfront Statistical Analysis Plans (SAPs) specifying the exact statistical methodology for analysing RCTs, it is also recommended that the PH assessment technique to be used to determine the validity of the Cox PH model should be stated within RCT SAPs.

Published: 16 November 2015

doi:10.1186/1745-6215-16-S2-P134

**Cite this article as:** Hiller et al.: Assessing violations of the proportional hazards assumption in Cox regression: does the chosen method matter? *Trials* 2015 **16**(Suppl 2):P134.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at  
[www.biomedcentral.com/submit](http://www.biomedcentral.com/submit)



University of Warwick, Coventry, UK



© 2015 Hiller et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.