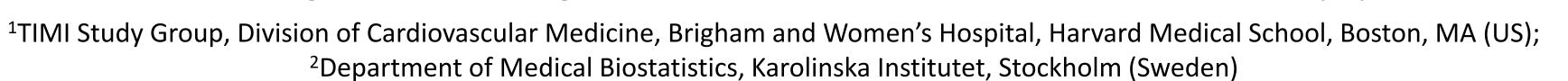


Flexible Splines Modeling of Absolute Risks in Survival Analysis with R and SAS

Michael G. Palazzolo¹, Jeong-Gun Park¹, Giorgio EM. Melloni¹, Andrea Discacciati², Sabina A. Murphy¹, Andrea Bellavia¹





INTRODUCTION

- Absolute Risks (AR, or event probabilities), represent a clinically relevant measure in survival analysis that should complement HRs in regular practice
- Splines transformations are recommended to incorporate potential non-linearities when evaluating continuous covariates in regression models
- We reviewed current approaches for estimating timespecific ARs from statistical models, and extended SAS and R material to flexibly account for non-linearities

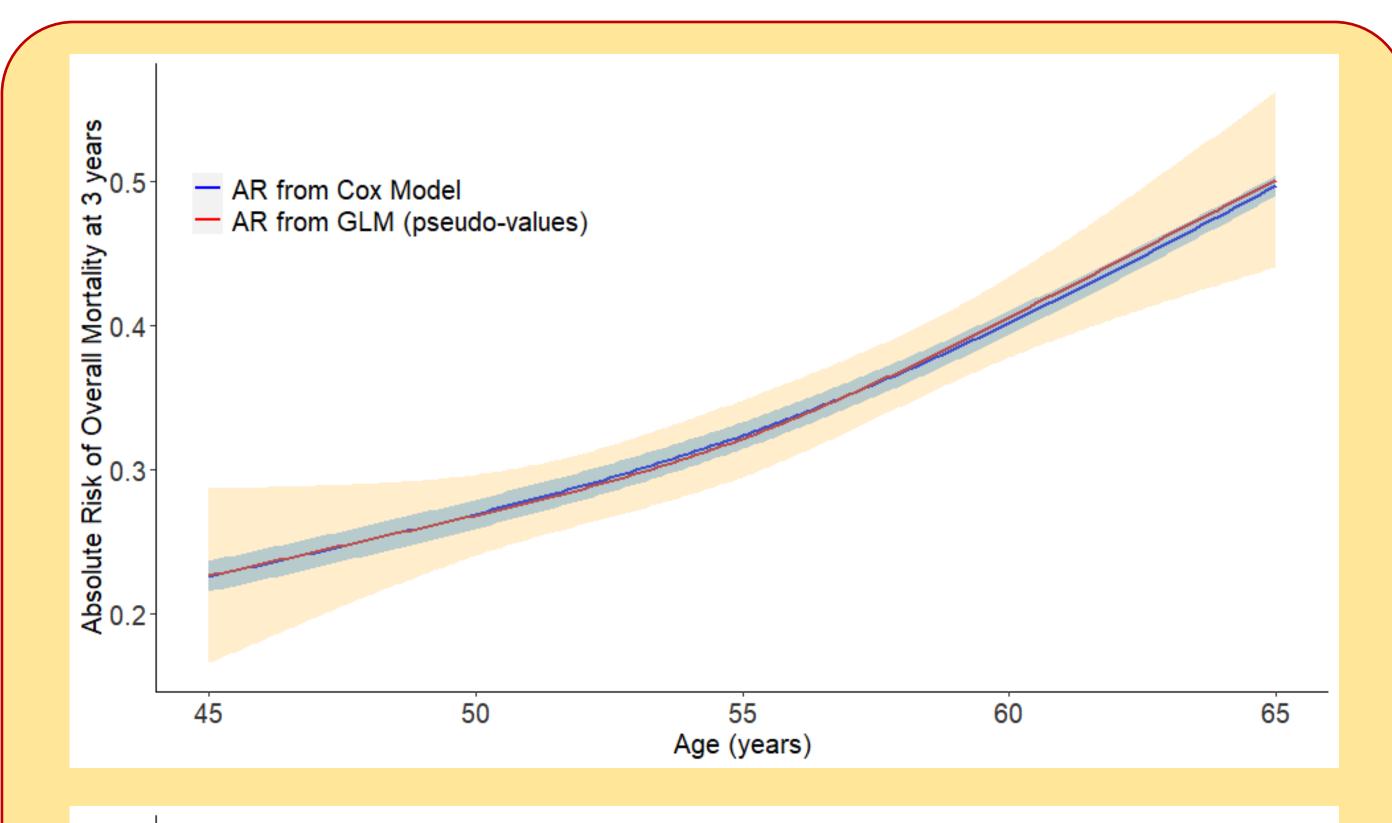
STATISTICAL MODELING OF ABSOLUTE RISKS

- Statistical models for the hazard (eg: Cox, parametric survival) followed by absolute risk derivation through:
 - Inverse Probability Weights
 - Regression Standardization
 - Conditional estimation
- Generalized Linear Models using pseudo-values
- Binomial regression (or Risk Regression)

ILLUSTRATIVE EXAMPLE

- Simulated data on 10,000 individuals with 3 years of follow-up. The figure show an example of splines modeled using a flexible display of time-specific AR for both a linear (panel A) and non-linear (panel B) example. Scan QR code for simulation details
- SAS macro and R code for flexible estimation of ARs available online (scan QR code)

Contact: mgpalazzolo@bwh.harvard.edu timi.org/biostatistics



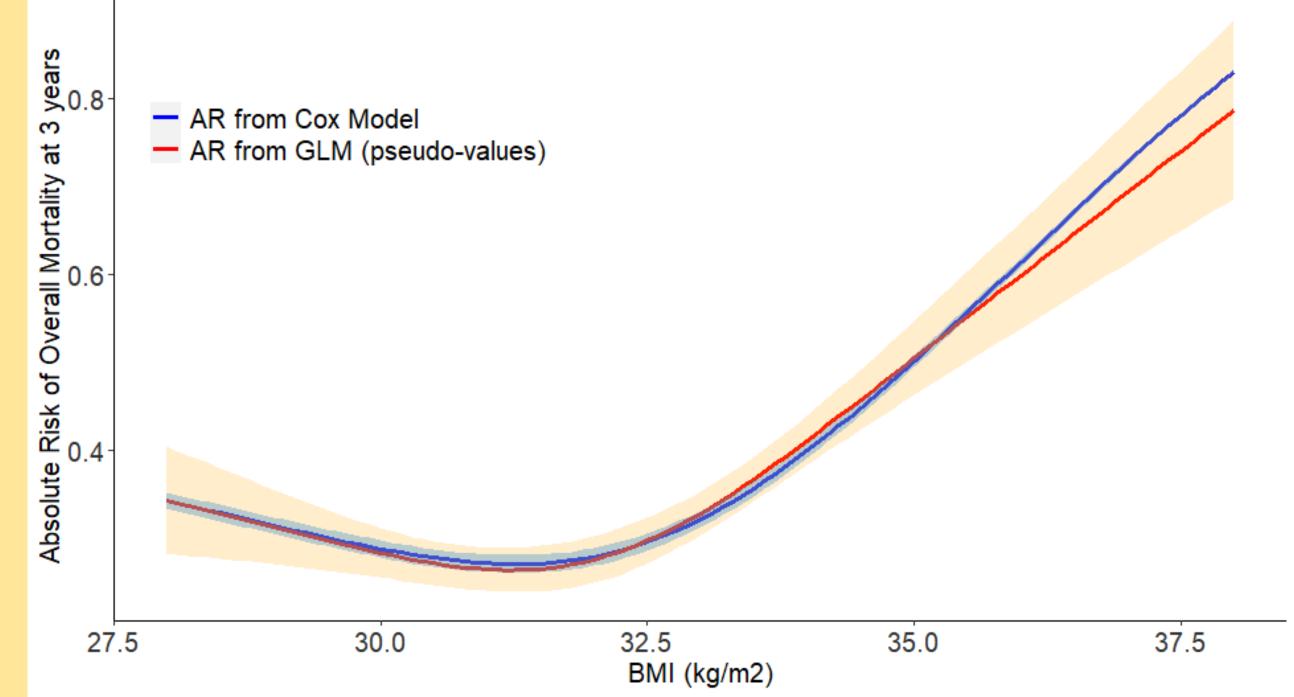


Figure. Absolute Risk of Overall Mortality at 3 years over levels of age (upper panel) and BMI (lower panel), modeled with restricted cubic splines in a Cox model (blue lines) and GLM model with pseudo-values (red line), in a simulated population.

Table: R and SAS function to estimate Absolute Risks from statistical models

Prediction after regression modeling	R: predict.survreg (survival) predict.coxph (survival) Predict (rms) predictrms (rms) predictSurvProb (pec) stdReg SAS: PROC PHREG (BASELINE) ANALY_PHREG_RCS (see QR code)
Generalized Linear Models using pseudo- values	 R: cuminglm (eventglm) SAS: Klein et al. 2008 ANALY_PSEUDO_RCS (see QR code)
Binomial Regression	R: • riskRegression

CONCLUSIONS

- Several R packages are available to estimate AR with different modeling techniques
- We extended some of the available software to include splines modeling and flexible display of AR, and developed a new set of SAS macros
- Future work will include incorporating interactions with flexible transformation and their estimation on the risk scale

References:

- 1Sjölander A. Estimation of causal effect measures with the R-package stdReg. EJE. 2018.
- **2** Gerds TA et al. Absolute risk regression for competing risks: interpretation, link functions, and prediction. Stat in medicine. 2012.
- **3** Sachs MC, Gabriel EE. Event history regression with pseudo-observations. Journal of Statistical Software. 2022