



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

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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 time-specific 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 (e.g.: Cox, parametric survival) followed by absolute risk derivation through the survival-cumulative hazard relationship. Different approaches to handle covariates adjustment:
 - Inverse Probability Weights
 - Regression Standardization¹
 - Conditional estimation
- Direct modeling of the absolute risk
 - Generalized Linear Models using pseudo-values²
 - Risk Regression³

ILLUSTRATIVE EXAMPLE

- Simulated data on 10,000 individuals with 3 years of follow-up.
 Data based on Weibull distribution; age has a log-linear effect while BMI has a quadratic effect on overall mortality.
- 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)

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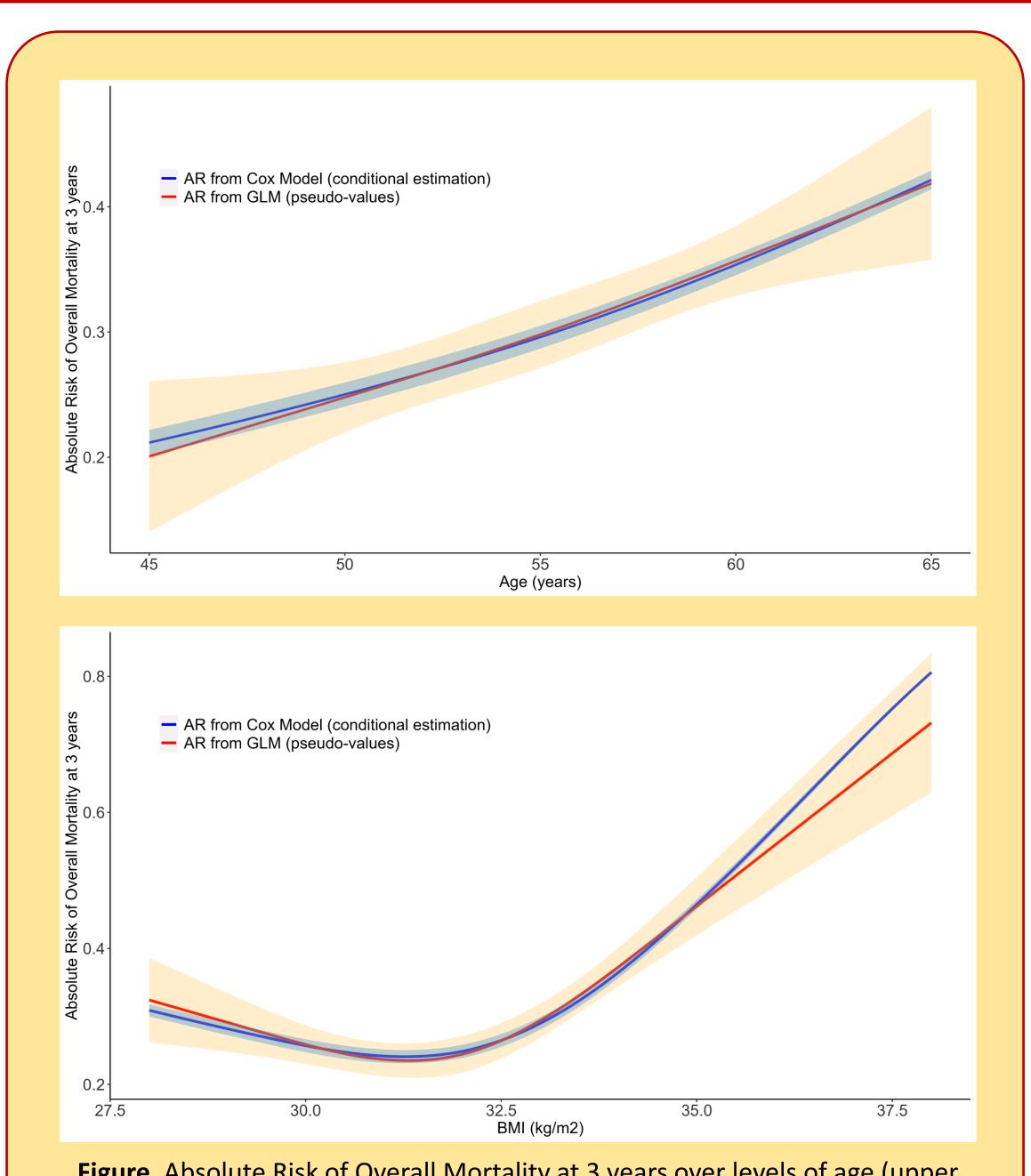


Figure. Absolute Risk of Overall Mortality at 3 years over levels of age (upper panel) and BMI (lower panel), modeled with restricted cubic splines in a Cox model (blue lines) and GLM model with pseudo-values (red line), in a simulated population.



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References:

1Sjölander A. Estimat 2 Gerds TA et al. Abs 3 Sachs MC, Gabriel 4 Klein JP, et al.. SAS in biomedicine. 2008

phy¹, Andrea Bellavia¹ I, Boston, MA (US);



Table: R and SAS function to estimate Absolute Risks from statistical models	
Risk prediction after regression modeling of the hazard	<pre>R: • predict functions from survival and rms packages • predictSurvProb from pec package • stdReg¹ SAS: • PROC PHREG (BASELINE) • %ANALY_PHREG_RCS*</pre>
Direct modeling of absolute risk	<pre>R: • eventglm (GLM with PV)² • riskRegression³ SAS: • Original macro for pseudo values⁴ • Extension: %ANALY_PSEUDO_RCS*</pre>

* SAS macros developed by the Authors and downloadable using the QR code link

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
- Tools are available to present results in terms of both hazard and risk after multivariable adjustment in survival analysis

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

4 Klein JP, et al.. SAS and R functions to compute pseudo-values for censored data regression. Computer methods and programs