Visualizing covariates in proportional hazards model using R

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Outline

- An illustrative example
- Elements of interpretation
- Rank-hazard plots
- Model comparison with rank-hazard plots
- Conclusion

Model

- Data from the MORGAM Project
- Inclusion criteria
  - Men from Finland, 30–65 years at baseline
  - No cardiovascular disease at baseline
  - No hypercholesterolemia ($\Rightarrow$ very high RCHOL)
  - No missing covariates
- Response variable: The age at the first event of coronary heart disease (CHD)
- Covariates
  - BPM, the mean of diastolic and systolic blood pressure (mmHg)
  - RCHOL, the ratio of total cholesterol to HDL cholesterol
  - BMI, body mass index (kg/m^2)
  - DSMOKER, daily smoker (1=yes, 0=no)
- Cox's proportional hazards model

Fitted model

```
Call:
coxph(formula = Surv(AGE1, CHDAGE1, status) ~ BPM + RCHOL + BMI +
    DSMOKER + strata(COHORT) + strata(region), data = f31[f31$basestat !=
    1 & f31$exclusion == 0, ], subset = (SEX == 1 & RCHOL <=
    rchollimit))

  n=12698 (7 observations deleted due to missing)
          coef exp(coef) se(coef)     z       p
BPM     0.0163      1.02  0.00213  7.67 1.7e-14
RCHOL   0.2125      1.24  0.01559 13.63 0.0e+00
BMI     0.0152      1.02  0.00813  1.87 6.2e-02
DSMOKER 0.5725      1.77  0.06119  9.36 0.0e+00

        exp(coef) exp(-coef) lower .95 upper .95
BPM          1.02      0.984      1.01      1.02
RCHOL        1.24      0.809      1.20      1.28
BMI          1.02      0.985      1.00      1.03
DSMOKER      1.77      0.564      1.57      2.00

Rsquare= 0.029   (max possible= 0.679 )
Likelihood ratio test= 373  on 4 df,   p=0
Wald test            = 415  on 4 df,   p=0
Score (logrank) test = 414  on 4 df,   p=0
```

Elements of interpretation

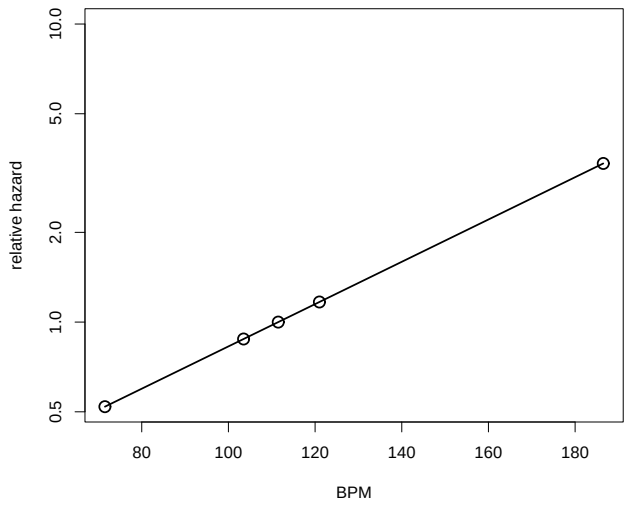
- Study design
- The type of model
- Definition of the covariate
- Estimated model parameter
- Unit of measurement
- Distribution of the covariate in the cohort (e.g. how common is smoking?)

Interpreting the results

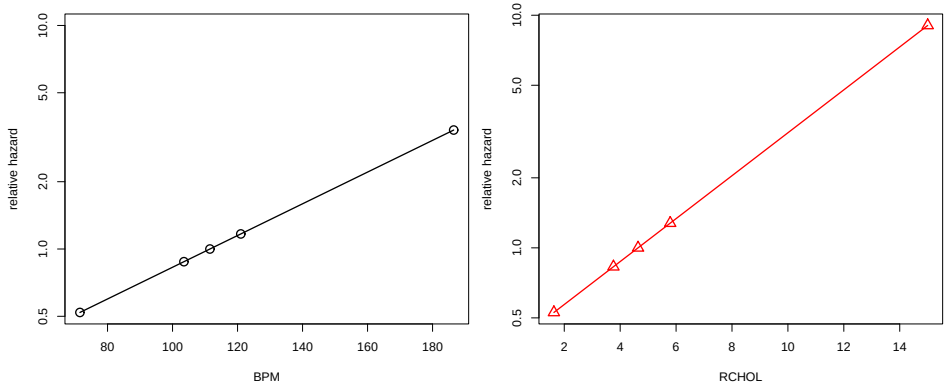
- p-value oriented interpretation
  - In the fitted model BPM, RCHOL and DSMOKER are statistically significant at 5 % risk level.
  - Covariates in ascending order by the p-values: RCHOL, DSMOKER, BPM, BMI.
  - The p-values will change if covariates are added or removed $\Leftarrow$ covariates in the model are correlated.
- Other interesting questions
  - What is the epidemiological relevance of these risk factors?
  - Is smoking a more serious risk factor of CHD than overweight in the population?
  - How the model will change if we add, remove or transform covariates?
  - How to visualize the fitted model?

First visualization attempt

Relative risk as a function of covariate values



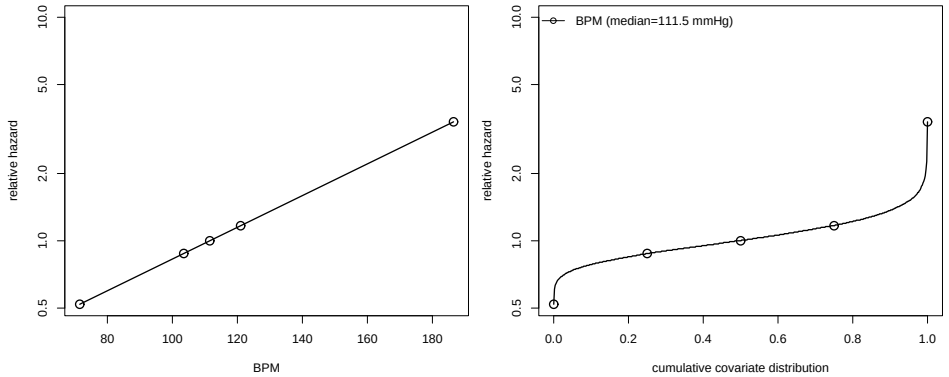
First attempt: BPM vs RCHOL



Information on the covariate distributions still not fully utilized.

Second attempt: ranks

Relative risk as a function of ranks of covariate values

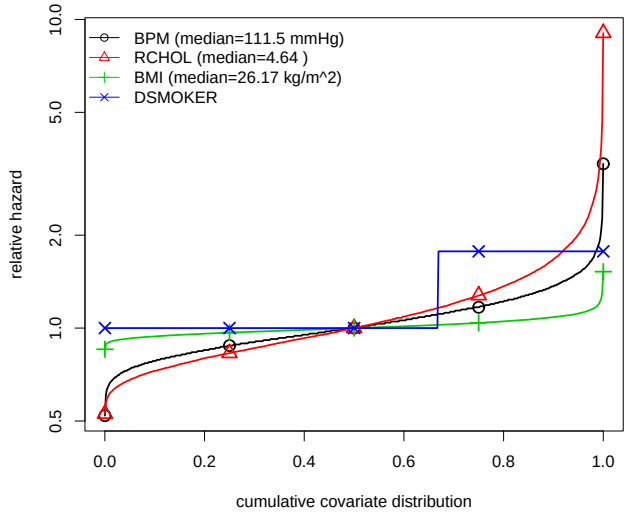


R implementation

```
n<-length(x)
x<-sort(x)
relativehazard<-exp(beta*(x-median(x)))
plot((1:n)/n,relativehazard,type="l",log="y")
```

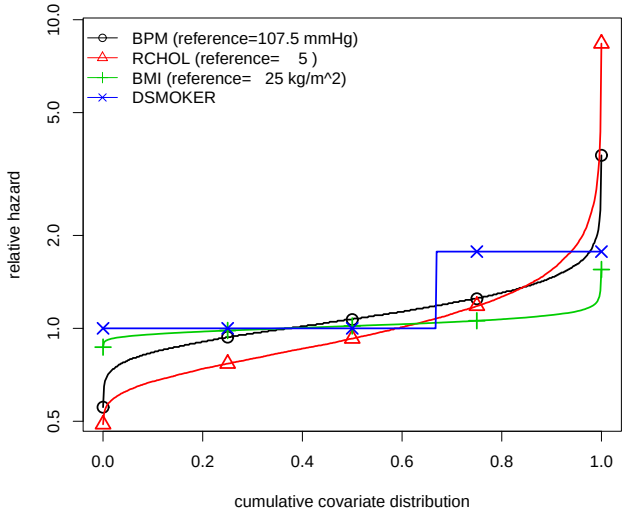
Rank-hazard plot

Reference: medians

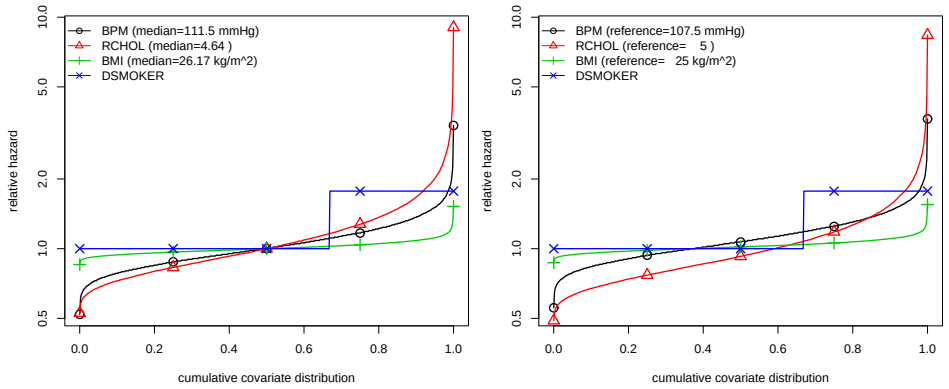


Rank-hazard plot

Reference: normal upper limits

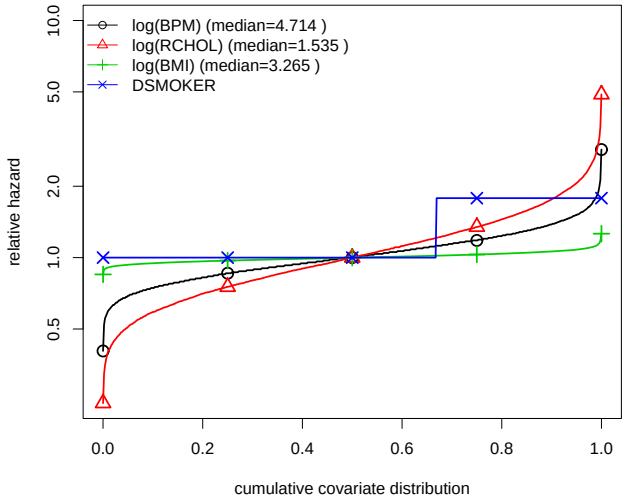


Rank-hazard plot

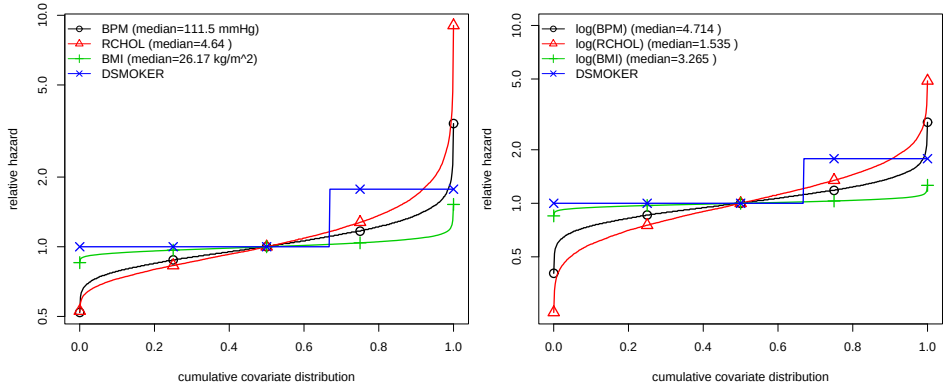


Model comparison

Model with logarithms of covariates

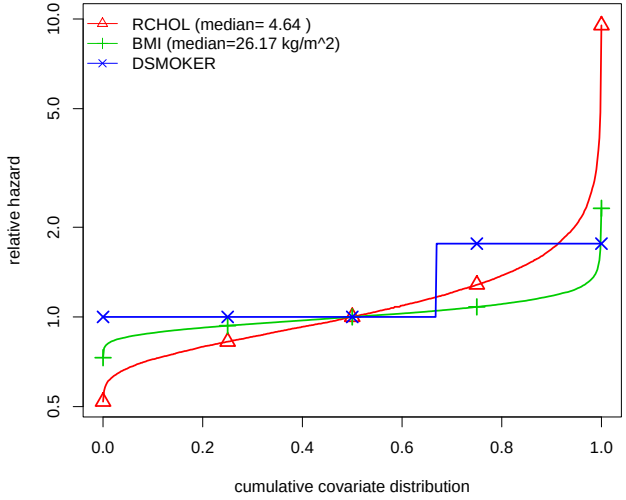


Model comparison

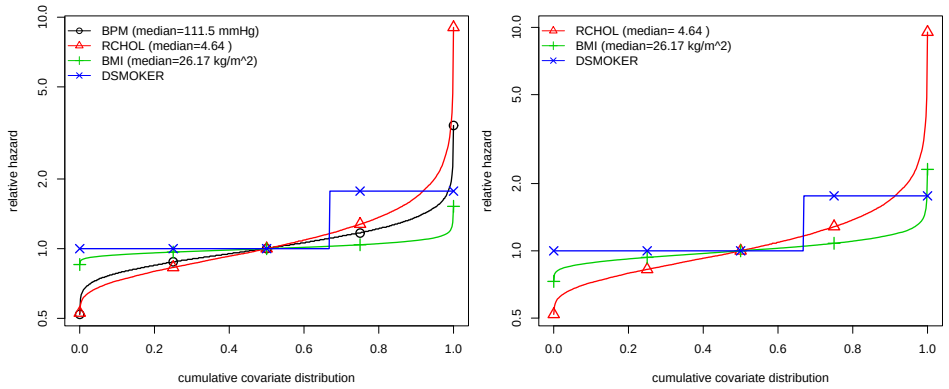


Model comparison

Model without blood pressure

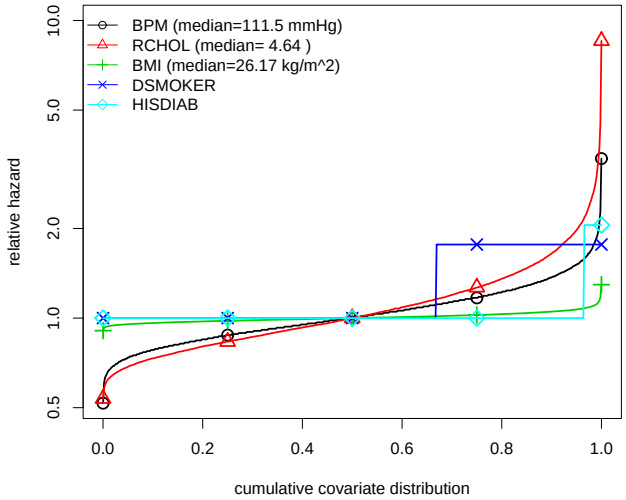


Model comparison

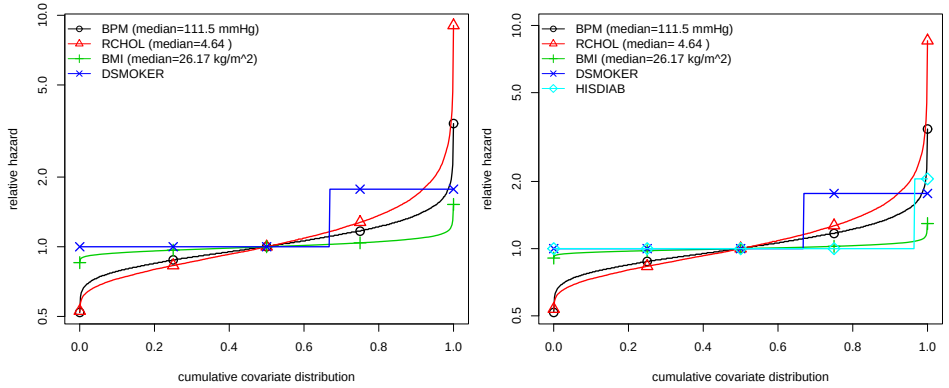


Model comparison

Adding history of diabetes



Model comparison



Conclusion

- Rank-hazard plots visualize several covariates in the same plot.
- Visualization may help interpreting the epidemiological relevance of the covariates.
- Visualization is easy to implement in R.
- Future directions: How to visualize correlation between the covariates in rank-hazard plots?