Suppose your test for proportional hazards gives you a clear suggestion that the assumption isn't met. What should you do?

To answer this, you need to think about what having non-proportional hazards means. If the relation between males and females regarding their risk of death changes over time, it could mean, for instance, that males have a higher risk of death early on during the follow-up period but at some point the relation changes so that females have a higher risk of death. One way of putting this is that there is a statistical **interaction** between gender and time. The model is short of a coefficient. If you add a coefficient for this interaction, which allows for the difference in risk by gender to change over time, then the problem would be solved.

Trying this interaction term in the model and testing whether it is statistically significant is in fact another way of testing the proportionality assumption. If this interaction term is not statistically significant, then it follows that the assumption is valid. As is usual with any kind of regression, Cox included, you should do the statistical tests – i.e. get the p-values – but also do the plots. Some kinds of non-proportional relationships and other assumption violations can’t be detected just from a p value.

Let’s go through how to include this interaction term and test whether it’s statistically significant. For mathematical reasons, you can’t just include the follow-up time itself as part of the interaction but instead need to transform it. The easiest way to do this in R is via the “tt” function (short for “time transform”):

```
fit <- coxph(Surv(fu_time, death) ~ gender + tt(gender)) # "tt" is the time
  -transform function
summary(fit)


> fit <- coxph(Surv(fu_time, death) ~ gender + tt(gender))
> summary(fit)

Call:

coxph(formula = Surv(fu_time, death) ~ gender + tt(gender))


  n= 1000, number of events= 492

              coef exp(coef) se(coef)      z Pr(>|z|)

gender2     0.6405    1.8974   0.9800  0.654    0.513

tt(gender) -0.2003    0.8185   0.3182 -0.629    0.529


           exp(coef) exp(-coef) lower .95 upper .95

gender2       1.8974      0.527    0.2779    12.953

tt(gender)    0.8185      1.222    0.4387     1.527


Concordance= 0.497  (se = 0.197 )

Rsquare= 0   (max possible= 0.997 )

Likelihood ratio test= 0.49  on 2 df,   p=0.8

Wald test            = 0.48  on 2 df,   p=0.8

Score (logrank) test = 0.48  on 2 df,   p=0.8
```

This output agrees with the earlier approach and says that the interaction between gender and (transformed) time is not statistically significant, i.e. there's no apparent violation of the proportionality assumption. Again, good news. The p-value from this approach (about 0.5) isn't the same as that from the earlier one because the methods are different, though it's always nice when they give the same message!

So if the assumption is violated, then one option is to include this interaction. If the p-value is low but the hazards are proportional for most of the follow-up period, then that suggests another solution: divide the survival analysis into **two time periods**. You can fit one model when things are fine, i.e.

when the assumption is valid, and another model to cover the later follow-up period when the assumption is not valid. This second model may need an interaction term, but the first one won't.

There's also a third simple way of dealing with the problem: stratify the analysis by the variable that's causing the problems. If it's gender, for instance, then just fit separate models for males and females. The drawback of this approach is that it's no longer possible to compare the effect of each gender on mortality.

Source survival analysis r public health