HR for Cox PH model - Methods in Biostatistics

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Framingham Heart Study Long-term follow-up and cardiovascular risk factor data on almost 5000 residents of the town of Framingham, MA. Recruitment started in 1948 (went for 40+ years). These data are 4699 patients who were free of coronary heart disease at their baseline exam:

variable		code
sex	=	gender coded as 1=if subject is male 0= if subject is female
dbp	=	diastolic blood pressure (DBP) in mm Hg
chdfate	=	1= if the patient develops CHD at the end of follow-up 0= otherwise
followup	=	the subject's follow-up in days

```
# Table 7.2  (additive model)
coxph(Surv(followup,chdfate) ~ dbpf + sex, data = heart) %>% tidy()
```

```
## # A tibble: 7 x 7
##   term        estimate std.error statistic  p.value conf.low conf.high
##   <chr>          <dbl>     <dbl>     <dbl>    <dbl>    <dbl>     <dbl>
## 1 dbpf60-70      0.648    0.247       2.62 8.74e- 3    0.164     1.13
## 2 dbpf70-80      0.888    0.241       3.69 2.27e- 4    0.416     1.36
## 3 dbpf80-90      1.02     0.241       4.24 2.25e- 5    0.549     1.49
## 4 dbpf90-100     1.40     0.243       5.76 8.48e- 9    0.924     1.88
## 5 dbpf100-110    1.79     0.254       7.02 2.29e-12    1.29      2.28
## 6 dbpfover110    2.22     0.271       8.17 2.97e-16    1.69      2.75
## 7 sexmale        0.606    0.0528     11.5  1.54e-30    0.503     0.710
```

```
# Table 7.3  (interaction model)
coxph(Surv(followup,chdfate) ~ dbpf * sex, data = heart) %>% tidy()
```

```
## # A tibble: 13 x 7
##    term            estimate std.error statistic  p.value conf.low conf.high
##    <chr>              <dbl>     <dbl>     <dbl>    <dbl>    <dbl>     <dbl>
##  1 dbpf60-70         0.603      0.352    1.71   8.66e- 2  -0.0867     1.29
##  2 dbpf70-80         0.887      0.342    2.60   9.44e- 3   0.217      1.56
##  3 dbpf80-90         1.26       0.341    3.68   2.30e- 4   0.589      1.93
##  4 dbpf90-100        1.55       0.347    4.46   8.29e- 6   0.866      2.23
##  5 dbpf100-110       2.03       0.358    5.67   1.41e- 8   1.33       2.74
##  6 dbpfover110       2.61       0.372    7.02   2.18e-12   1.88       3.34
##  7 sexmale           0.864      0.471    1.83   6.68e- 2  -0.0599     1.79
##  8 dbpf60-70:sexm~   0.0570     0.495    0.115  9.08e- 1  -0.912      1.03
##  9 dbpf70-80:sexm~  -0.0379     0.482   -0.0787 9.37e- 1  -0.982      0.906
## 10 dbpf80-90:sexm~  -0.458      0.482   -0.951  3.42e- 1  -1.40       0.486
## 11 dbpf90-100:sex~  -0.296      0.487   -0.608  5.43e- 1  -1.25       0.658
## 12 dbpf100-110:se~  -0.508      0.509   -0.999  3.18e- 1  -1.51       0.489
## 13 dbpfover110:se~  -0.913      0.549   -1.66   9.66e- 2  -1.99       0.164
```

Consider the output given above for the additive and interaction models. For each model:

(a) Compute the hazard ratio for a woman dpb 90-100 vs woman dpb 70-80.

(b) Compute the hazard ratio for a man dpb 90-100 vs man dpb 70-80.

(c) Compute the hazard ratio for a man dpb 90-100 vs woman dpb 70-80.

(d) Is there evidence that dpb should be used as a linear function in predicting log(HR) [as opposed to breaking it up into the categorical groups used in the problem]?

Answer:

Additive model:

(a) HR = $e^{1.4}/e^{0.888} = 1.6686251$.
(b) HR = $e^{1.40+0.606}/e^{0.888+0.606} = 1.6686251$.
(c) HR = $e^{1.40+0.606}/e^{0.888} = 3.0587306$.
(d) It seems like a 10 unit increase in dbp gives a reasonably constant (i.e., linear) increase in the coefficient: 0.888 - 0.648 = 0.24, 1.02 - 0.888 = 0.132, 1.4 - 1.02 = 0.38, 1.79 - 1.40 = 0.39.

In terms of the **model**, there does not seem to be a strong indication that dbp should be categorized (as was done here) instead of used as a continuous variable. However, one reason to categorize dbp is so that communicating results to patients is easier.

Interaction model:

(a) HR = $e^{1.55}/e^{0.887} = 1.9406054$.
(b) HR = $e^{1.55+0.864-0.296}/e^{0.887+0.864-0.0379} = 1.4991526$.
(c) HR = $e^{1.55+0.864-0.296}/e^{0.887} = 3.4246525$.
(d) It seems like a 10 unit increase in dbp gives a reasonably constant (i.e., linear) increase in the coefficient:

Women: 0.887 - 0.603 = 0.284, 1.26 - 0.887 = 0.373, 1.55 - 1.26 = 0.29, 2.03 - 1.55 = 0.48.

Men: 0.887 - 0.0379 - 0.603 - 0.057= 0.1891, 1.26 - 0.458 - 0.887 + 0.0379 = -0.0471, 1.55 - 0.296 - 1.26 + 0.458= 0.452, 2.03 - 0.508 - 1.55 + 0.296 = 0.268.

Now we see that for men, the change in coefficient for 80-90 is much different from the other changes! Note that the handout shows how the RR is really different for that group, too. However, when we look more carefully at the SEs and p-values, we see quite a bit of variability in the coefficients, so we do not necessarily believe that interaction is necessary to model, and therefore, it is probably not important to categorize dbp.