Stanford heart transplants

This set of data is analysed by Kalbfleisch and Prentice (1980, §5.5.3). (The data given in Kalbfleisch & Prentice are rounded, but the full data are supplied as data frame `heart`.) It is on survival from early heart transplant operations at Stanford. The new feature is that patients may change treatment during the study, moving from the control group to the treatment group at transplantation, so some of the covariates such as waiting time for a transplant are time-dependent (in the simplest possible way). Patients who received a transplant are treated as two cases, before and after the operation, so cases in the transplant group are in general both right-censored and left-truncated. This is handled by `Surv` by supplying entry and exit times. For example, patient 4 has the rows

```
start   stop event      age        year   surgery transplant
  0.0   36.0   0  -7.73716632  0.49007529       0          0
 36.0   39.0   1  -7.73716632  0.49007529       0          1
```

which show that he waited 36 days for a transplant and then died after 3 days. The proportional hazards model is fitted from this set of cases, but some summaries need to take account of the splitting of patients.

The covariates are age (in years minus 48), year (after 1 October 1967) and an indicator for previous surgery. Rather than use the six models considered by Kalbfleisch & Prentice, we do our own model selection.

```
> coxph(Surv(start, stop, event) ~ transplant*
     (age + surgery + year), data = heart)
    ....
Likelihood ratio test=18.9  on 7 df, p=0.00852  n= 172
> coxph(Surv(start, stop, event) ~ transplant*(age + year) +
     surgery, data = heart)
    ....
Likelihood ratio test=18.4  on 6 df, p=0.0053  n= 172
> (stan <- coxph(Surv(start, stop, event) ~ transplant*year +
     age + surgery, data = heart))
    ....
                  coef exp(coef) se(coef)     z     p
     transplant -0.6213     0.537   0.5311 -1.17 0.240
           year -0.2526     0.777   0.1049 -2.41 0.016
            age  0.0299     1.030   0.0137  2.18 0.029
        surgery -0.6641     0.515   0.3681 -1.80 0.071
transplant:year  0.1974     1.218   0.1395  1.42 0.160

Likelihood ratio test=17.1  on 5 df, p=0.00424  n= 172

> stan1 <- coxph(Surv(start, stop, event) ~ strata(transplant) +
     year + year:transplant + age + surgery, heart)
> plot(survfit(stan1), conf.int = T, log = T, lty = c(1, 3),
       col = 2:3)
> legend(locator(1), c("before", "after"), lty = c(1, 3),
         col = 2:3)
```

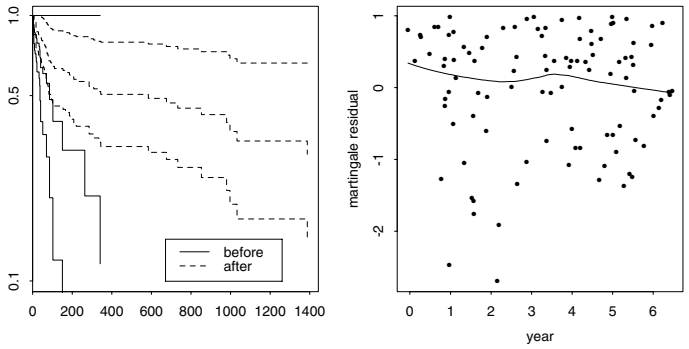

Figure 13.9: Plots for the Stanford heart transplant study. Left: log survivor curves and confidence limits for the two groups. Right: martingale residuals against calendar time.

```
> attach(heart)
> plot(year[transplant==0], residuals(stan1, collapse = id),
      xlab = "year", ylab = "martingale residual")
> lines(lowess(year[transplant == 0],
              residuals(stan1, collapse = id)))
> sresid <- resid(stan1, type = "dfbeta", collapse = id)
> detach()
> -100 * sresid %*% diag(1/stan1$coef)
```

This analysis suggests that survival rates over the study improved *prior* to transplantation, which Kalbfleisch & Prentice suggest could be due to changes in recruitment. The diagnostic plots of Figure 13.9 show nothing amiss. The `collapse` argument is needed as those patients who received transplants are treated as two cases, and we need the residual per patient.

Now consider predicting the survival of future patient aged 50 on 1 October 1971 with prior surgery, transplanted after six months.

```
# Survivor curve for the "average" subject
> summary(survfit(stan))
#  follow-up for two years
> stan2 <- data.frame(start = c(0, 183), stop= c(183, 2*365),
     event = c(0, 0), year = c(4, 4), age = c(50, 50) - 48,
     surgery = c(1, 1), transplant = c(0, 1))
> summary(survfit(stan, stan2, individual = T,
                  conf.type = "log-log"))
 time n.risk n.event survival std.err lower 95% CI upper 95% CI
    ....
  165     43       1    0.654 0.11509        0.384        0.828
  186     41       1    0.643 0.11602        0.374        0.820
  188     40       1    0.632 0.11697        0.364        0.812
  207     39       1    0.621 0.11790        0.353        0.804
  219     38       1    0.610 0.11885        0.343        0.796
  263     37       1    0.599 0.11978        0.332        0.788
```

```
285     35      2    0.575 0.11524       0.325       0.762
308     33      1    0.564 0.11618       0.314       0.753
334     32      1    0.552 0.11712       0.302       0.744
340     31      1    0.540 0.11799       0.291       0.735
343     29      1    0.527 0.11883       0.279       0.725
584     21      1    0.511 0.12018       0.263       0.713
675     17      1    0.492 0.12171       0.245       0.699
```

The argument `individual = T` is needed to avoid averaging the two cases (which are the same individual).

Australian AIDS survival

The data on the survival of AIDS patients within Australia are of unusually high quality within that field, and jointly with Dr Patty Solomon we have studied survival up to 1992.[6] There are a large number of difficulties in defining survival from AIDS (acquired immunodeficiency syndrome), in part because as a syndrome its diagnosis is not clear-cut and has almost certainly changed with time. (To avoid any possible confusion, we are studying survival from AIDS and not the HIV infection which is generally accepted as the cause of AIDS.)

The major covariates available were the reported transmission category, and the state or territory within Australia. The AIDS epidemic had started in New South Wales and then spread, so the states have different profiles of cases in calendar time. A factor that was expected to be important in survival is the widespread availability of zidovudine (AZT) to AIDS patients from mid-1987 which has enhanced survival, and the use of zidovudine for HIV-infected patients from mid-1990, which it was thought might delay the onset of AIDS without necessarily postponing death further.

The transmission categories were:

hs	male homosexual or bisexual contact
hsid	as **hs** and also intravenous drug user
id	female or heterosexual male intravenous drug user
het	heterosexual contact
haem	haemophilia or coagulation disorder
blood	receipt of blood, blood components or tissue
mother	mother with or at risk of HIV infection
other	other or unknown

The data file gave data on all patients whose AIDS status was diagnosed prior to January 1992, with their status then. Since there is a delay in notification of death, some deaths in late 1991 would not have been reported and we adjusted the endpoint of the study to 1 July 1991. A total of 2 843 patients were included, of whom about 1 770 had died by the end date. The file contained an ID number, the dates of first diagnosis, birth and death (if applicable), as well as the state and the coded transmission category. We combined the states `ACT` and `NSW` (as

[6] We are grateful to the Australian National Centre in HIV Epidemiology and Clinical Research for making these data available to us.