Random Effects (within cases) with R*

Rats

```
> rm(list=ls()); options(scipen=999)
> # install.packages("coxme",dependencies=TRUE) # Only need to do this once
> library(coxme)
Loading required package: survival
Loading required package: bdsmatrix

Attaching package: 'bdsmatrix'

The following object is masked from 'package:base':

    backsolve

>
> help(rats)
```

Three rats were chosen from each of 100 litters, one of which was treated with a drug, and then all followed for tumor incidence.

litter: litter number from 1 to 100
rx: treatment,(1=drug, 0=control)
time: time to tumor or last follow-up
status: event status, 1=tumor and 0=censored
sex: male or female

```
> head(rats)
  litter rx time status sex
1      1  1  101      0   f
2      1  0   49      1   f
3      1  0  104      0   f
4      2  1   91      0   m
5      2  0  104      0   m
6      2  0  102      0   m
> dim(rats)
[1] 300   5
```

* Copyright information is on the last page.

```
>
> trap1 = coxme(Surv(time,status) ~ rx + sex + (1|litter) , data=rats); trap1
Cox mixed-effects model fit by maximum likelihood
  Data: rats
  events, n = 42, 300
  Iterations= 9 67
                    NULL Integrated    Fitted
Log-likelihood -225.2822  -199.5321 -186.4517

                  Chisq    df                 p   AIC   BIC
Integrated loglik 51.50  3.00 0.000000000038276 45.50 40.29
 Penalized loglik 77.66 14.21 0.000000000093062 49.23 24.53

Model:  Surv(time, status) ~ rx + sex + (1 | litter)
Fixed coefficients
           coef exp(coef)  se(coef)     z        p
rx    0.7938387 2.2118710 0.3134784  2.53 0.011000
sexm -3.0952279 0.0452647 0.7354204 -4.21 0.000026

Random effects
 Group  Variable  Std Dev   Variance
 litter Intercept 0.6257281 0.3915356
> vcov(trap1)
             [,1]         [,2]
[1,]  0.098268701 -0.005159691
[2,] -0.005159691  0.540843195
> sqrt(vcov(trap1)[1,1])
[1] 0.3134784
```

Kidney

```
> rm(list=ls()); options(scipen=999)
> # install.packages("coxme",dependencies=TRUE) # Only need to do this once
> library(coxme)
Loading required package: survival
Loading required package: bdsmatrix

Attaching package: 'bdsmatrix'

The following object is masked from 'package:base':

    backsolve

> help(kidney)
```

Data on the recurrence times to infection, at the point of insertion of the catheter, for kidney patients using portable dialysis equipment. Catheters may be removed for reasons other than infection, in which case the observation is censored. Each patient has exactly 2 observations.

patient:	id
time:	time
status:	event status
age:	in years
sex:	1=male, 2=female
disease:	disease type (0=GN, 1=AN, 2=PKD, 3=Other)
frail:	frailty estimate from original paper

```
> head(kidney)
  id time status age sex disease frail
1  1    8      1  28   1   Other   2.3
2  1   16      1  28   1   Other   2.3
3  2   23      1  48   2      GN   1.9
4  2   13      0  48   2      GN   1.9
5  3   22      1  32   1   Other   1.2
6  3   28      1  32   1   Other   1.2

> dim(kidney)
[1] 76  7

> table(kidney$disease)

Other    GN    AN   PKD
   26    18    24     8
```

```
> kidney = within(kidney,{sex=sex-1}) # Makes 1=F, 0=M
>
> kmod = coxme(  Surv(time,status) ~ age + sex + disease + (1|id) , data=kidney )
> kmod
Cox mixed-effects model fit by maximum likelihood
  Data: kidney
  events, n = 58, 76
  Iterations= 5 28
                    NULL Integrated    Fitted
Log-likelihood -187.9028  -179.0217 -173.7424

                   Chisq   df          p   AIC   BIC
Integrated loglik 17.76 6.00 0.00685470  5.76 -6.60
 Penalized loglik 28.32 9.11 0.00090634 10.10 -8.66

Model:  Surv(time, status) ~ age + sex + disease + (1 | id)
Fixed coefficients
                    coef exp(coef)   se(coef)     z       p
age          0.003755551 1.0037626 0.01206409  0.31 0.76000
sex         -1.552913501 0.2116305 0.39038849 -3.98 0.00007
diseaseGN    0.119156978 1.1265467 0.44126751  0.27 0.79000
diseaseAN    0.358074826 1.4305727 0.43752739  0.82 0.41000
diseasePKD -1.329715978 0.2645524 0.69630860 -1.91 0.05600

Random effects
 Group Variable  Std Dev   Variance
 id    Intercept 0.3428171 0.1175235
>
>
> # Allowing for age, sex and type of disease, the risk of infection for a
> # patient one standard deviation above the mean is ______ times as great,
> # compared to a patient with average frailty.
>
> exp(0.3428171)
[1] 1.408911
>
> nodisease = update(kmod, . ~ . - disease)
> anova(nodisease,kmod)
Analysis of Deviance Table
 Cox model: response is  Surv(time, status)
 Model 1: ~age + sex + (1 | id)
 Model 2: ~age + sex + disease + (1 | id)
   loglik  Chisq Df P(>|Chi|)
1 -181.91
2 -179.02 5.7657  3    0.1236
```

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