2021 SISCER APC Course, R Notes Set 2

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Overview of R notes

In these notes we will continue to analyze data on male lung cancer mortality in Denmark, for the period 1943–1996 in ages 40–89. Data are in the `Epi` package. Age, period and cohort effects will all be modeled in 5-year intervals.

We will illustrate:

- Factor and spline models in the `Epi` package (Carstensen)
- The convenient parameterization in the `apc` package (Nielsen)

Danish male lung cancer incidence data

Recall, from the data description:

A data frame with 220 observations on the following 9 variables.

- A5: Left end point of the age interval, a numeric vector.
- P5: Left end point of the period interval, a numeric vector.
- C5: Left end point of the birth cohort interval, a numeric vector.
- up: Indicator of upper triangles of each age by period rectangle in the Lexis diagram. (up=(P5-A5-C5)/5).
- Ax: The mean age of diagnosis (at risk) in the triangle.
- Px: The mean date of diagnosis (at risk) in the triangle.
- Cx: The mean date of birth in the triangle, a numeric vector.
- D: Number of diagnosed cases of male lung cancer.
- Y: Risk time in the male population, person-years.

Massaging the data into a convenient form

```
library(Epi)
data(lungDK)
attach(lungDK)
dftempEpi = data.frame(D = lungDK$D, Y = lungDK$Y,
    A = 37.5 + 5 * ((lungDK$A5 - min(lungDK$A5))/5 +
        1), P = 1945.5 + 5 * (lungDK$P5 - min(lungDK$P5))/5 +
        1)
```

Massaging the data into a convenient form

Sum over the upper and lower triangles in the Lexis diagram to get data in age-period squares, see Carstensen (2007).

```
names(dftempEpi)
## [1] "D" "Y" "A" "P"
head(dftempEpi, 2)
##    D         Y    A      P
## 1 52 336233.8 42.5 1946.5
## 2 28 357812.7 42.5 1946.5
# Sum over upper and lower triangles
dfEpi = aggregate(dftempEpi[, c("D", "Y")], by = list(A = dftemp
    P = dftempEpi$P), sum)
head(dfEpi, 2)
##      A      P   D         Y
## 1 42.5 1946.5  80 694046.5
## 2 47.5 1946.5 135 622256.7
```

Fitting a sequence of factor models in the Epi package

Recall there are $P = 11$ periods and $A = 10$ age groups and so $A + P - 1 = 20$ cohorts.

```
fit1 <- apc.fit(dfEpi, model = "factor", parm = "ACP",
    scale = 10^5)
## [1] "ML of APC-model Poisson with log(Y) offset : ( ACP ):\n"
##                Model Mod. df.  Mod. dev. Test df. Test dev.      Pr(>Chi)
## 1                Age      100 15103.0013       NA        NA             NA
## 2          Age-drift       99  6417.3811        1 8685.6202  0.000000e+00
## 3        Age-Cohort       81   829.6293       18 5587.7518  0.000000e+00
## 4 Age-Period-Cohort       72   208.5476        9  621.0817 6.244637e-128
## 5        Age-Period       90  2723.4660       18 2514.9184  0.000000e+00
## 6          Age-drift       99  6417.3811        9 3693.9151  0.000000e+00
##   Test dev/df    H0
## 1          NA
## 2  8685.62024 zero drift
## 3   310.43065 Coh eff|dr.
## 4    69.00907 Per eff|Coh
## 5   139.71769 Coh eff|Per
## 6   410.43501 Per eff|dr.
## No reference cohort given;  reference cohort for age-effects is chosen as
##  the median date of birth for persons  with event:  1914 .
```

Factor models

The function `apc.fit` fits a sequence of models.

Notice the `model="factor"` to give a different level for each of age, period and cohort, later we will present alternative smoother (spline) models.

For comparison we fit models using the `glm` function.

For example, for the `Age+Period` model we have factors for age and period, $E[Y_{ap}] = N_{ap} \exp(\delta + \alpha_a + \beta_p)$.

The fits are the same (e.g., compare deviances and degrees of freedom), but the parameterizations are different.

The default corner-point parameterization in the GLM version takes the first groups as reference, i.e., $\alpha_1 = \beta_1 = 0$.

Factor models $A = 10, P = 11, C = A + P - 1 = 20$

Degrees of freedom and parameters:

- There are $11 \times 10 = 110$ total degrees of freedom (DF)
- Age only model has 10 parameters and so 100 Residual DF
- Age-drift model has $10 + 1 = 11$ parameters and so 99 Residual DF
- Age-Cohort model has $10 + 19 = 29$ parameters and so 81 Residual DF
- Age-Period-Cohort model has $10 + 19 + 11 - 2 = 38$ parameters and so 72 Residual DF
- Age-Period model has $10 + 11 - 1 = 20$ parameters and so 90 Residual DF

Factor models

The cohort drift model provides an identical fit to the period drift model because of the linear dependence relationship between period and cohort: $c = A - a + p$.

In terms of significance, the counts are very large and so very small deviations from the null are detectable.

Everything is significant!

Factor APC models in Epi

```
names(fit1)
## [1] "Type"  "Model" "Age"   "Per"   "Coh"   "Drift" "Ref"   "Anova"
dim(fit1$Coh)
## [1] 20  4
dim(fit1$Per)
## [1] 11  4
dim(fit1$Age)
## [1] 10  4
fit1$Ref
##  Per  Coh
##   NA 1914
```

Factor APC models in Epi

```
head(fit1$Coh, n = 3)
##      Coh        C-RR        2.5%      97.5%
## 10 1859 0.07960723 0.03785991 0.1673884
## 9  1864 0.07939452 0.05546108 0.1136561
## 8  1869 0.13101490 0.11055245 0.1552648
head(fit1$Per, n = 3)
##       Per       P-RR       2.5%      97.5%
## 1  1946.5 0.8527416 0.8144673 0.8928145
## 11 1951.5 0.9344356 0.8994733 0.9707568
## 21 1956.5 0.9395033 0.9085332 0.9715291
head(fit1$Age, n = 3)
##    Age       Rate      2.5%      97.5%
## 1 42.5  9.013028  8.44474  9.619559
## 2 47.5 24.453671 23.47509 25.473051
## 3 52.5 59.161763 57.52394 60.846220
```

Age factor model, using the glm function

```
glmMA <- glm(D ~ as.factor(A) + offset(log(Y)), data = dfEpi,
    family = "poisson")
glmMA
##
## Call:  glm(formula = D ~ as.factor(A) + offset(log(Y)), family = "poisson",
##     data = dfEpi)
##
## Coefficients:
##      (Intercept)  as.factor(A)47.5  as.factor(A)52.5  as.factor(A)57.5
##          -9.0172            0.9504            1.7841            2.4288
## as.factor(A)62.5  as.factor(A)67.5  as.factor(A)72.5  as.factor(A)77.5
##           2.8938            3.1962            3.3750            3.3788
## as.factor(A)82.5  as.factor(A)87.5
##           3.2636            3.0228
##
## Degrees of Freedom: 109 Total (i.e. Null);  100 Residual
## Null Deviance:       71780
## Residual Deviance: 15100     AIC: 15980
```

Age factor model, using the `glm` function

Notice that the residual DF and deviance are identical to the previous fit.

```
glmMA$deviance
## [1] 15103
glmMA$df.residual
## [1] 100
fit1$Anova[1, ]
##   Model Mod. df. Mod. dev. Test df. Test dev. Pr(>Chi) 
## 1   Age      100     15103        NA         NA       NA
```

Age-Period factor model, using the glm function

Similarly for the age-period model

```
glmMAP <- glm(D ~ as.factor(A) + as.factor(P) + offset(log(Y)),
    data = dfEpi, family = "poisson")
glmMAP$df.residual
## [1] 90
glmMAP$deviance
## [1] 2723.466
fit1$Anova[5, ]
##          Model Mod. df. Mod. dev. Test df. Test dev. Pr(>Chi) T
## 5 Age-Period       90  2723.466       18  2514.918         0
##       H0
## 5 Coh eff|Per
```

Period drift model, using the glm function

```
glmMdrift <- glm(D ~ as.factor(A) + P + offset(log(Y)),
    data = dfEpi, family = "poisson")
glmMdrift
##
## Call:  glm(formula = D ~ as.factor(A) + P + offset(log(Y)), family = "poisson
##     data = dfEpi)
##
## Coefficients:
##      (Intercept)  as.factor(A)47.5  as.factor(A)52.5  as.factor(A)57.5
##         -55.05841           0.94972           1.79355           2.44053
## as.factor(A)62.5  as.factor(A)67.5  as.factor(A)72.5  as.factor(A)77.5
##          2.89467           3.18094           3.34283           3.33145
## as.factor(A)82.5  as.factor(A)87.5                 P
##          3.19513           2.93045           0.02331
##
## Degrees of Freedom: 109 Total (i.e. Null);  99 Residual
## Null Deviance:       71780
## Residual Deviance: 6417  AIC: 7296
```

Period drift model, using the glm function

```
glmMdrift$df.residual
## [1] 99
glmMdrift$deviance
## [1] 6417.381
exp(coefficients(glmMdrift)["P"])
##       P
## 1.02358
fit1[["Drift"]]
##                  exp(Est.)     2.5%    97.5%
## APC (Y-weights)  1.021348 1.020444 1.022253
## A-d              1.023580 1.023065 1.024096
```

Under the age-drift model there is an estimated 1.0235804% increase in mortality per cohort.

Age-Cohort model

We create the cohort factors and then fit a GLM to show the equivalence in terms of fit.

```
Cterm <- dfEpi$P - dfEpi$A
sort(unique(Cterm))
##  [1] 1859 1864 1869 1874 1879 1884 1889 1894 1899 1904 1909 1
## [16] 1934 1939 1944 1949 1954
length(unique(Cterm))
## [1] 20
```

Recall $A = 10$, $P = 11$ and so $C = A + P - 1 = 20$.

Age-Cohort factor model

```
glmMAC <- glm(D ~ as.factor(A) + as.factor(Cterm) +
    offset(log(Y)), data = dfEpi, family = "poisson")
glmMAC$df.residual
## [1] 81
glmMAC$deviance
## [1] 829.6293
```

Age-Period factor model

Now fit two Age+Period factor models using default parameterization, and fixing a particular level for the period effects.

```
APv1 <- glm(D ~ factor(A) + factor(P) + offset(log(Y)),
    family = poisson, data = dfEpi)
APv1$df.residual
## [1] 90
APv1$deviance
## [1] 2723.466
APv2 <- glm(D ~ factor(A) + relevel(factor(P), "1971.5") +
    offset(log(Y)), family = poisson, data = dfEpi)
APv2$df.residual
## [1] 90
APv2$deviance
## [1] 2723.466
```

Age Period factor model

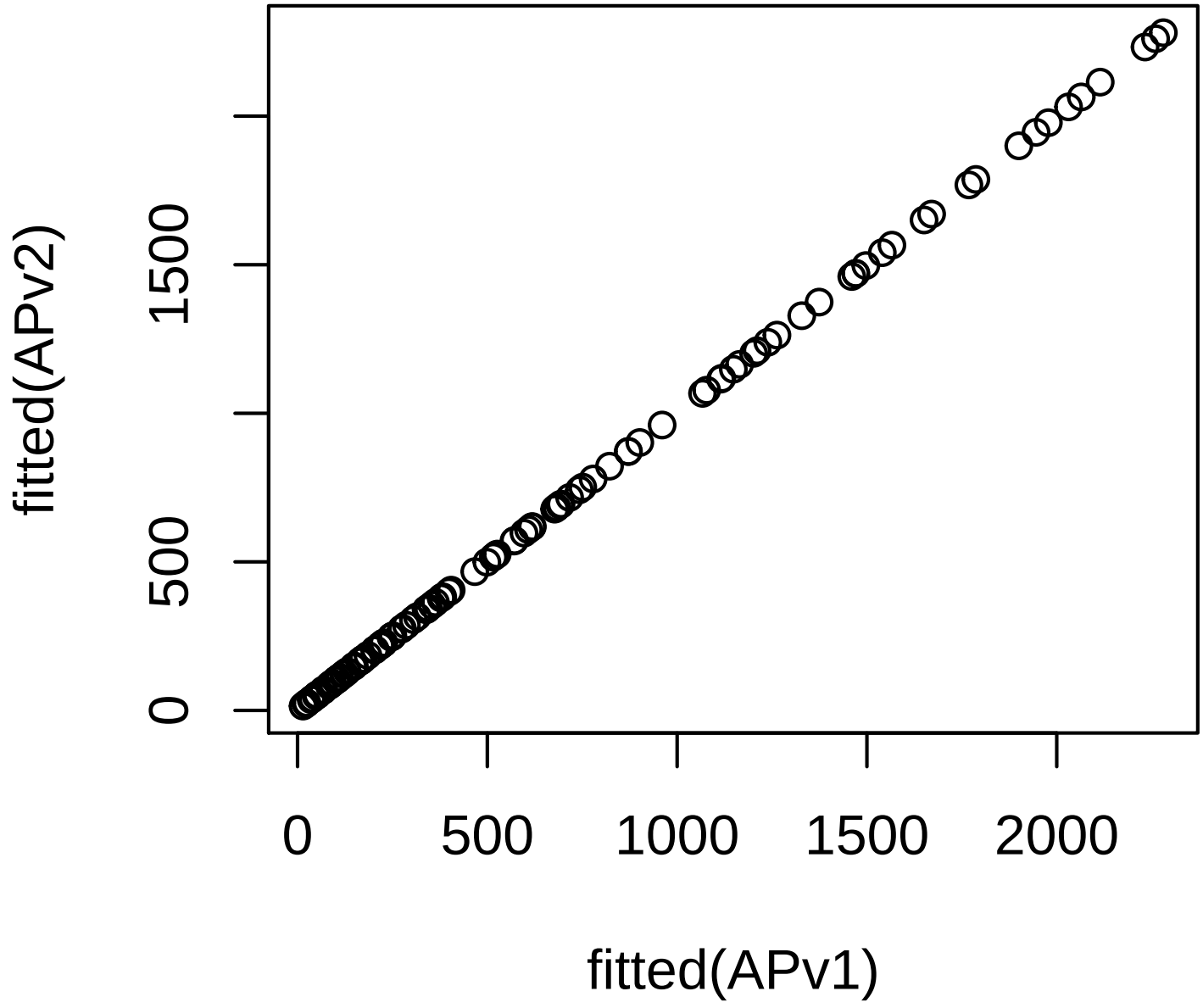
```
summary(APv1)
##
## Call:
## glm(formula = D ~ factor(A) + factor(P) + offset(log(Y)), family = poisson,
##     data = dfEpi)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -10.400   -3.728   -0.984    3.685   11.203
##
## Coefficients:
##                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)     -10.34235    0.04192 -246.71   <2e-16 ***
## factor(A)47.5     0.95258    0.03673   25.93   <2e-16 ***
## factor(A)52.5     1.78237    0.03383   52.69   <2e-16 ***
## factor(A)57.5     2.41412    0.03265   73.94   <2e-16 ***
## factor(A)62.5     2.86259    0.03216   89.01   <2e-16 ***
## factor(A)67.5     3.15159    0.03201   98.47   <2e-16 ***
## factor(A)72.5     3.31784    0.03209  103.40   <2e-16 ***
## factor(A)77.5     3.30980    0.03261  101.50   <2e-16 ***
## factor(A)82.5     3.17640    0.03423   92.81   <2e-16 ***
## factor(A)87.5     2.90983    0.04024   72.32   <2e-16 ***
## factor(P)1951.5   0.39206    0.03629   10.80   <2e-16 ***
## factor(P)1956.5   0.67592    0.03404   19.86   <2e-16 ***
## factor(P)1961.5   1.01434    0.03226   31.44   <2e-16 ***
## factor(P)1966.5   1.26666    0.03130   40.47   <2e-16 ***
## factor(P)1971.5   1.48717    0.03067   48.49   <2e-16 ***
## factor(P)1976.5   1.59239    0.03039   52.40   <2e-16 ***
## factor(P)1981.5   1.67994    0.03020   55.62   <2e-16 ***
## factor(P)1986.5   1.69902    0.03015   56.35   <2e-16 ***
## factor(P)1991.5   1.59958    0.03028   52.83   <2e-16 ***
## factor(P)1996.5   1.52558    0.03078   49.57   <2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for poisson family taken to be 1)
```

Age Period factor model

```
summary(APv2)
##
## Call:
## glm(formula = D ~ factor(A) + relevel(factor(P), "1971.5") +
##     offset(log(Y)), family = poisson, data = dfEpi)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -10.400   -3.728   -0.984    3.685   11.203
##
## Coefficients:
##                                      Estimate Std. Error  z value Pr(>|z|)
## (Intercept)                          -8.85517    0.03267 -271.034  < 2e-16 ***
## factor(A)47.5                         0.95258    0.03673   25.932  < 2e-16 ***
## factor(A)52.5                         1.78237    0.03383   52.692  < 2e-16 ***
## factor(A)57.5                         2.41412    0.03265   73.938  < 2e-16 ***
## factor(A)62.5                         2.86259    0.03216   89.007  < 2e-16 ***
## factor(A)67.5                         3.15159    0.03201   98.468  < 2e-16 ***
## factor(A)72.5                         3.31784    0.03209  103.401  < 2e-16 ***
## factor(A)77.5                         3.30980    0.03261  101.497  < 2e-16 ***
## factor(A)82.5                         3.17640    0.03423   92.805  < 2e-16 ***
## factor(A)87.5                         2.90983    0.04024   72.316  < 2e-16 ***
## relevel(factor(P), "1971.5")1946.5 -1.48717    0.03067  -48.493  < 2e-16 ***
## relevel(factor(P), "1971.5")1951.5 -1.09512    0.02481  -44.134  < 2e-16 ***
## relevel(factor(P), "1971.5")1956.5 -0.81125    0.02137  -37.958  < 2e-16 ***
## relevel(factor(P), "1971.5")1961.5 -0.47284    0.01842  -25.674  < 2e-16 ***
## relevel(factor(P), "1971.5")1966.5 -0.22051    0.01667  -13.227  < 2e-16 ***
## relevel(factor(P), "1971.5")1976.5  0.10522    0.01488    7.071 1.54e-12 ***
## relevel(factor(P), "1971.5")1981.5  0.19276    0.01449   13.300  < 2e-16 ***
## relevel(factor(P), "1971.5")1986.5  0.21184    0.01439   14.724  < 2e-16 ***
## relevel(factor(P), "1971.5")1991.5  0.11241    0.01465    7.670 1.71e-14 ***
## relevel(factor(P), "1971.5")1996.5  0.03840    0.01566    2.453   0.0142 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for poisson family taken to be 1)
```

Age-Period Model: Fits are the same

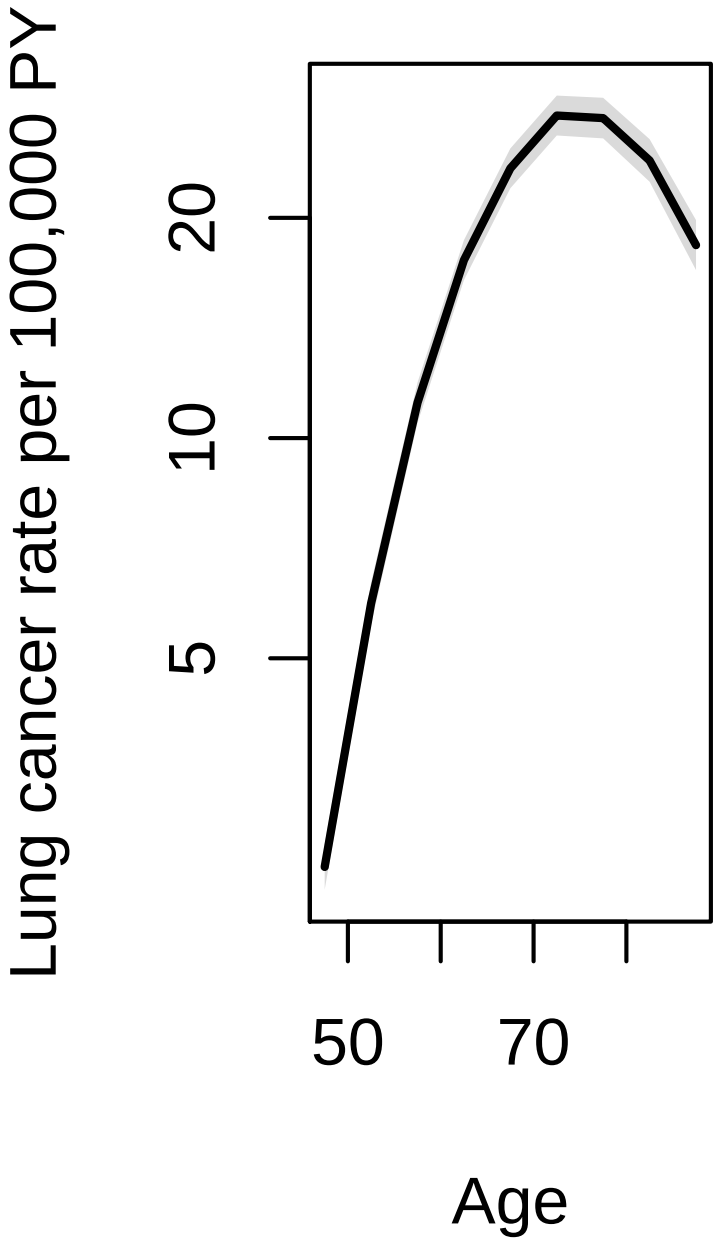
```
plot(fitted(APv2) ~ fitted(APv1))
```

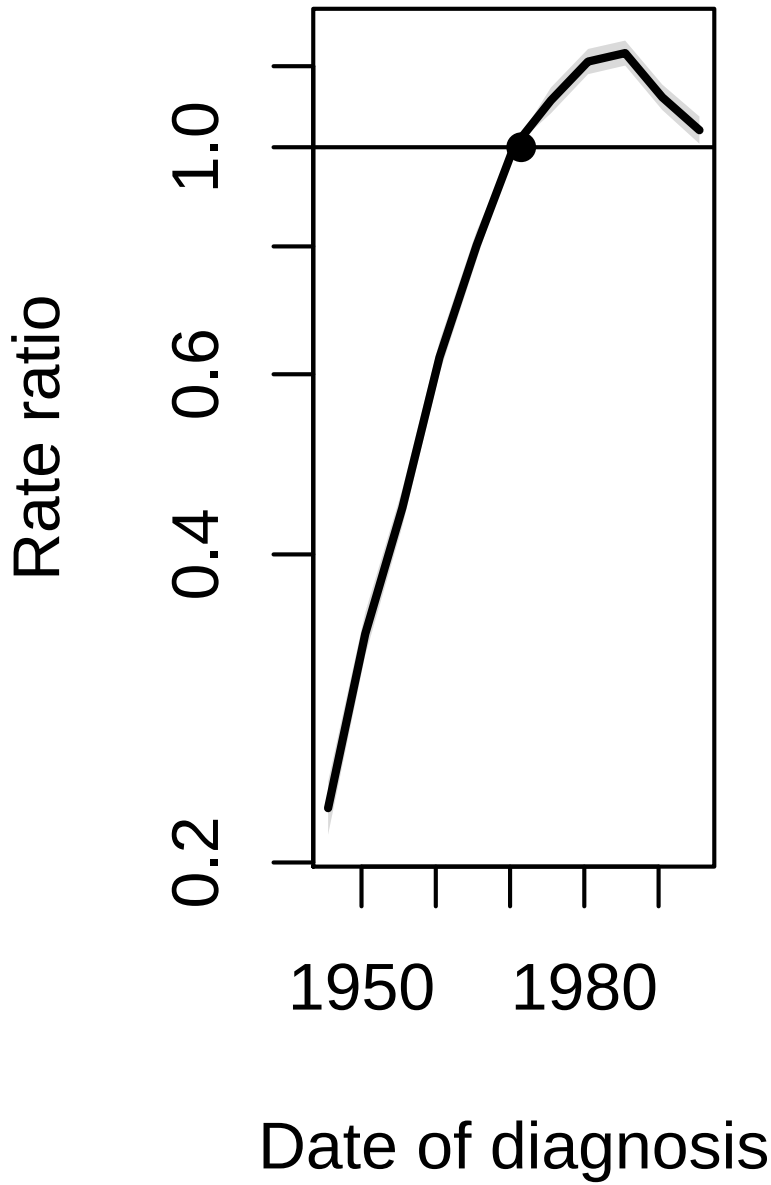


Age-Period factor model: Chosen Parameterization

```
par(mfrow = c(1, 2))
matshade(seq(47.5, 87.5, 5), ci.exp(APv2, subset = "A"),
    plot = TRUE, log = "y", lwd = 2, xlab = "Age",
    ylab = "Lung cancer rate per 100,000 PY")
matshade(seq(1945.5, 1996.5, 5), rbind(ci.exp(APv2,
    subset = "P")[1:5, ], 1, ci.exp(APv2, subset = "P")[6:10,
    ]), plot = TRUE, log = "y", lwd = 2, xlab = "Date of diagnos
    ylab = "Rate ratio")
abline(h = 1)
points(1971.5, 1, pch = 16)
```

Age-Period factor model: Chosen Parameterization

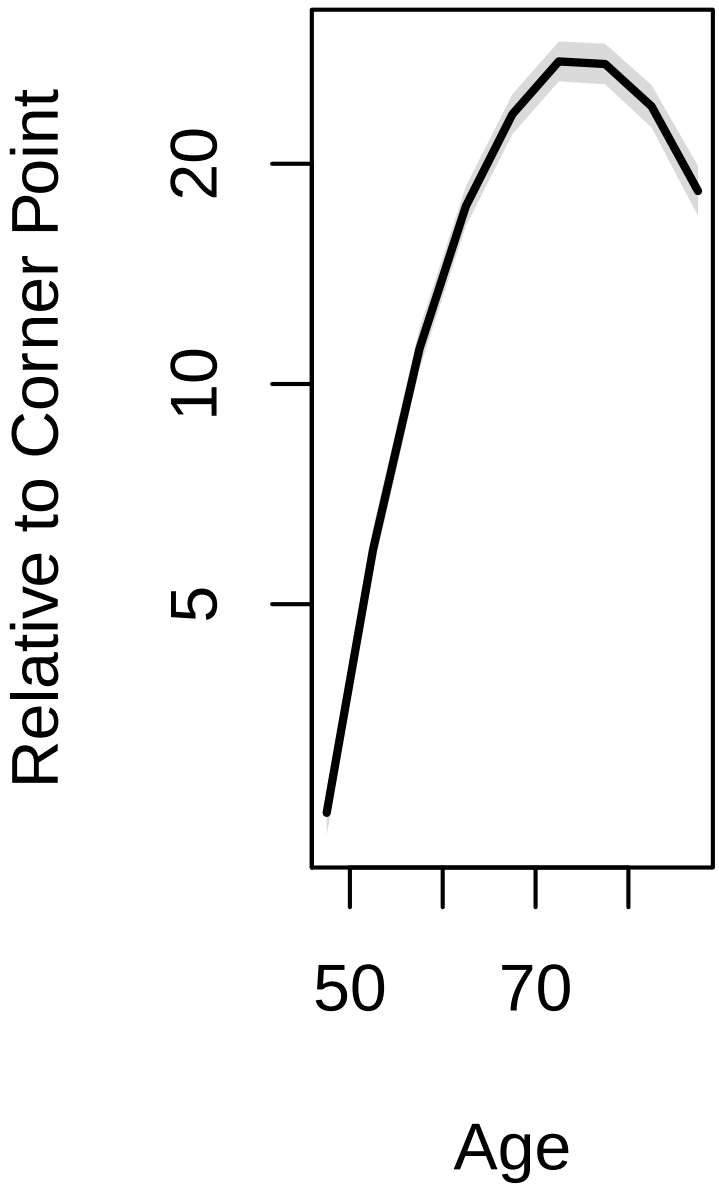


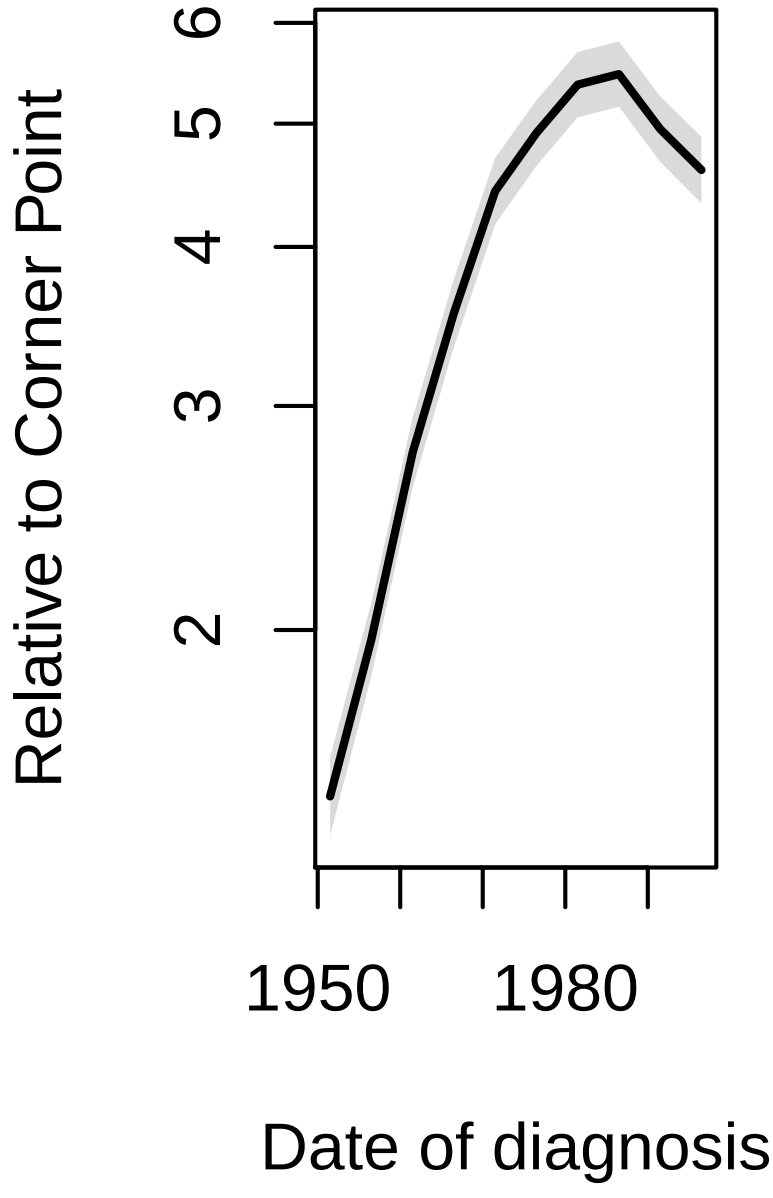


Age-Period factor model: Default Parameterization

```
par(mfrow = c(1, 2))
matshade(seq(47.5, 87.5, 5), ci.exp(APv1, subset = "A"),
    plot = TRUE, log = "y", lwd = 2, xlab = "Age",
    ylab = "Relative to Corner Point")
matshade(seq(1951.5, 1996.5, 5), ci.exp(APv1, subset = "P"),
    plot = TRUE, log = "y", lwd = 2, xlab = "Date of diagnosis",
    ylab = "Relative to Corner Point")
abline(h = 1)
points(1971.5, 1, pch = 16)
```

Age-Period factor model: Default Parameterization





Age cohort drift model

```
glmMdrift2 <- glm(D ~ as.factor(A) + Cterm + offset(log(Y)),
    data = dfEpi, family = "poisson")
glmMdrift2$df.residual
## [1] 99
glmMdrift2$deviance
## [1] 6417.381
coef(glmMdrift2)
##      (Intercept) as.factor(A)47.5 as.factor(A)52.5 as.factor(A)57.5
##      -54.0678788        1.0662500        2.0266201        2.7901274
## as.factor(A)62.5 as.factor(A)67.5 as.factor(A)72.5 as.factor(A)77.5
##        3.3608044        3.7636050        4.0420347        4.1471891
## as.factor(A)82.5 as.factor(A)87.5            Cterm
##        4.1274006        3.9792565        0.0233067
```

Fitted curves under a particular parameterization

```
apc.plot(fit1)
```

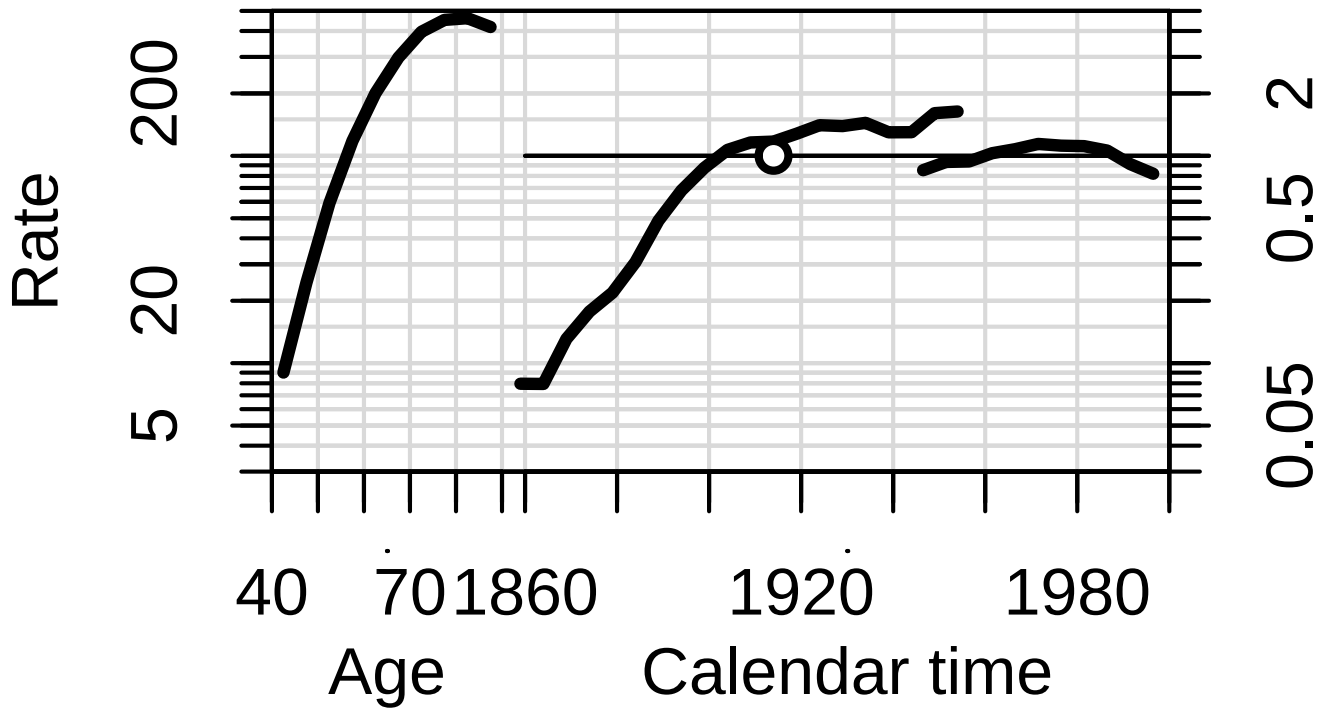


Figure 1: Age-period-cohort estimates under ACP factor model, “fit1“.

```
## cp.offset    RR.fac
##      1765       100
```

Full APC Model with Poisson Likelihood

```
glmMACP <- glm(D ~ as.factor(A) + as.factor(Cterm) +
    as.factor(P) + offset(log(Y)), data = dfEpi, family = "poisson")
glmMACP$df.residual
## [1] 72
glmMACP$deviance
## [1] 208.5476
tail(coef(glmMACP))
## as.factor(P)1971.5 as.factor(P)1976.5 as.factor(P)1981.5 as.factor(P)1986.5
##          0.3110585          0.2959105          0.2944408          0.2490253
## as.factor(P)1991.5 as.factor(P)1996.5
##          0.1031232                 NA
```

Note that 1 parameter estimate is `NA` because the model is over parameterized.

Full APC Model with quasi-Poisson Likelihood

Variance is $\kappa \times \mu$.

```
glmMACPexcess <- glm(D ~ as.factor(A) + as.factor(Cterm) +
    as.factor(P) + offset(log(Y)), data = dfEpi, family = "quasipoisson")
SSpears <- sum(residuals(glmMACPexcess, type = "pearson")^2)
excess <- SSpears/glmMACPexcess$df.residual
excess
## [1] 2.943842
```

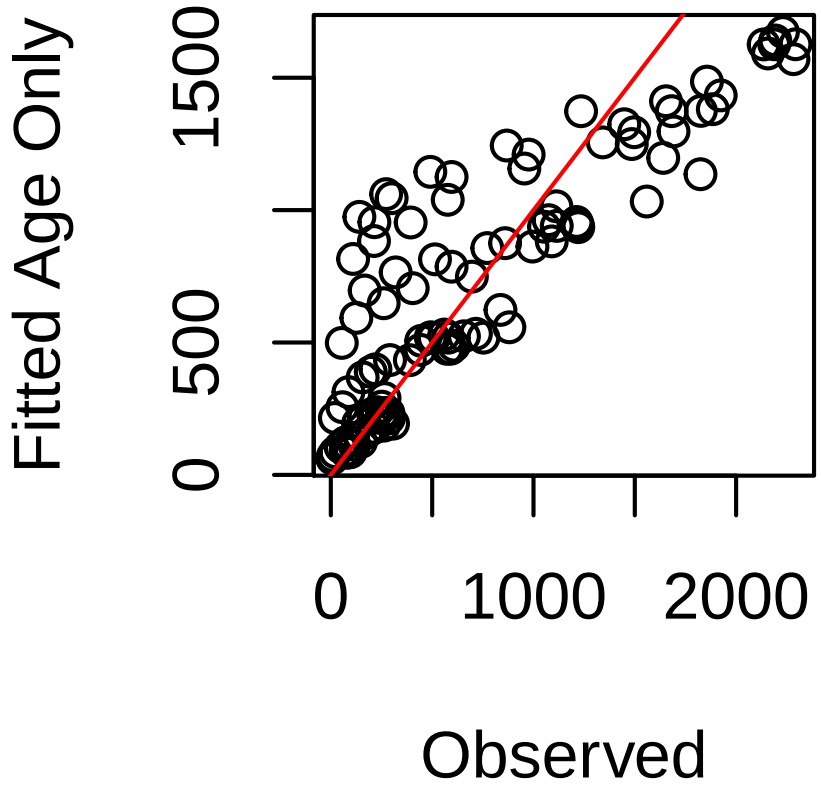
Quite a lot of overdispersion here, $\hat{\kappa} = 2.9438419$.

Full APC model with quasi-Poisson likelihood

```
summary(glmMACPexcess)
##
## Call:
## glm(formula = D ~ as.factor(A) + as.factor(Cterm) + as.factor(P) +
##     offset(log(Y)), family = "quasipoisson", data = dfEpi)
##
## Deviance Residuals:
##     Min       1Q   Median       3Q      Max
## -4.0478  -0.8303   0.0357   0.8045   3.1655
##
## Coefficients: (1 not defined because of singularities)
##                          Estimate Std. Error t value Pr(>|t|)
## (Intercept)           -11.968761   0.654109 -18.298  < 2e-16 ***
## as.factor(A)47.5        0.994171   0.065405  15.200  < 2e-16 ***
## as.factor(A)52.5        1.873728   0.062463  29.997  < 2e-16 ***
## as.factor(A)57.5        2.559631   0.062015  41.275  < 2e-16 ***
## as.factor(A)62.5        3.087159   0.062756  49.193  < 2e-16 ***
## as.factor(A)67.5        3.479003   0.064363  54.053  < 2e-16 ***
## as.factor(A)72.5        3.760496   0.066622  56.446  < 2e-16 ***
## as.factor(A)77.5        3.888688   0.069775  55.732  < 2e-16 ***
## as.factor(A)82.5        3.903883   0.074581  52.344  < 2e-16 ***
## as.factor(A)87.5        3.801889   0.085495  44.469  < 2e-16 ***
## as.factor(Cterm)1864   -0.006614   0.721242  -0.009 0.992709
## as.factor(Cterm)1869    0.490330   0.666741   0.735 0.464477
## as.factor(Cterm)1874    0.789467   0.656304   1.203 0.232956
## as.factor(Cterm)1879    0.994787   0.653326   1.523 0.132226
## as.factor(Cterm)1884    1.330029   0.651900   2.040 0.044996 *
## as.factor(Cterm)1889    1.786722   0.651097   2.744 0.007653 **
## as.factor(Cterm)1894    2.119172   0.650737   3.257 0.001721 **
## as.factor(Cterm)1899    2.367836   0.650552   3.640 0.000510 ***
## as.factor(Cterm)1904    2.560970   0.650471   3.937 0.000188 ***
## as.factor(Cterm)1909    2.640060   0.650475   4.059 0.000124 ***
## as.factor(Cterm)1914    2.645518   0.650605   4.066 0.000121 ***
## as.factor(Cterm)1919    2.728574   0.650700   4.193 7.72e-05 ***
## as.factor(Cterm)1924    2.819711   0.650847   4.332 4.70e-05 ***
## as.factor(Cterm)1929    2.806058   0.651161   4.309 5.10e-05 ***
```

Some diagnostics: more work needed

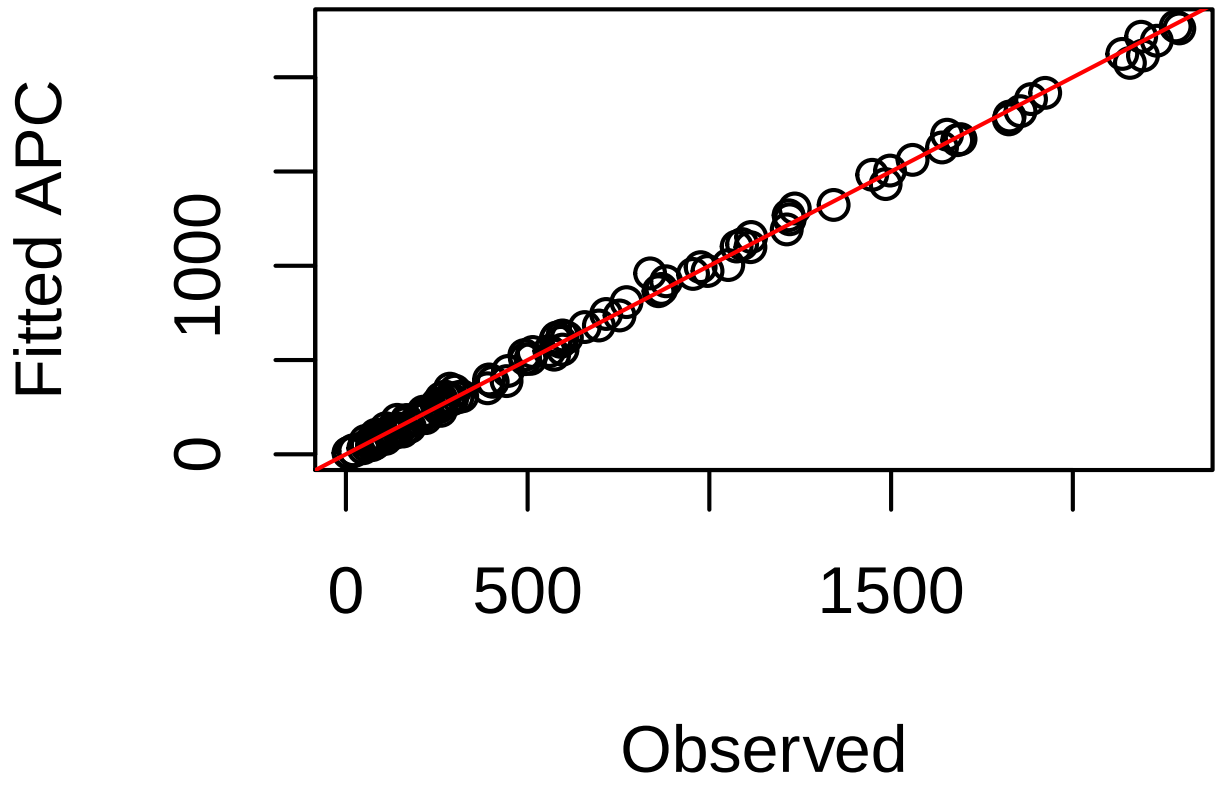
```
par(mfrow = c(1, 2))
plot(fitted(glmMA) ~ dfEpi$D, ylab = "Fitted Age Only",
    xlab = "Observed")
abline(a = 0, b = 1, col = "red")
```



Fit is clearly inadequate

Some diagnostics: more work needed

```
plot(fitted(glmMACPexcess) ~ dfEpi$D, ylab = "Fitted APC",
    xlab = "Observed")
abline(a = 0, b = 1, col = "red")
```



Nothing jumps out. . .

Nielsen apc package

First get the data into the right format

```
library(apc)
resp <- matrix(dfEpi$D, nrow = 10, ncol = 11, byrow = F)
risk <- matrix(dfEpi$Y, nrow = 10, ncol = 11, byrow = F)
apc.data <- apc.data.list(resp, data.format = "AP",
    risk, age1 = 42.5, per1 = 1946.5, unit = 5)
```

Initial plot to summarize data

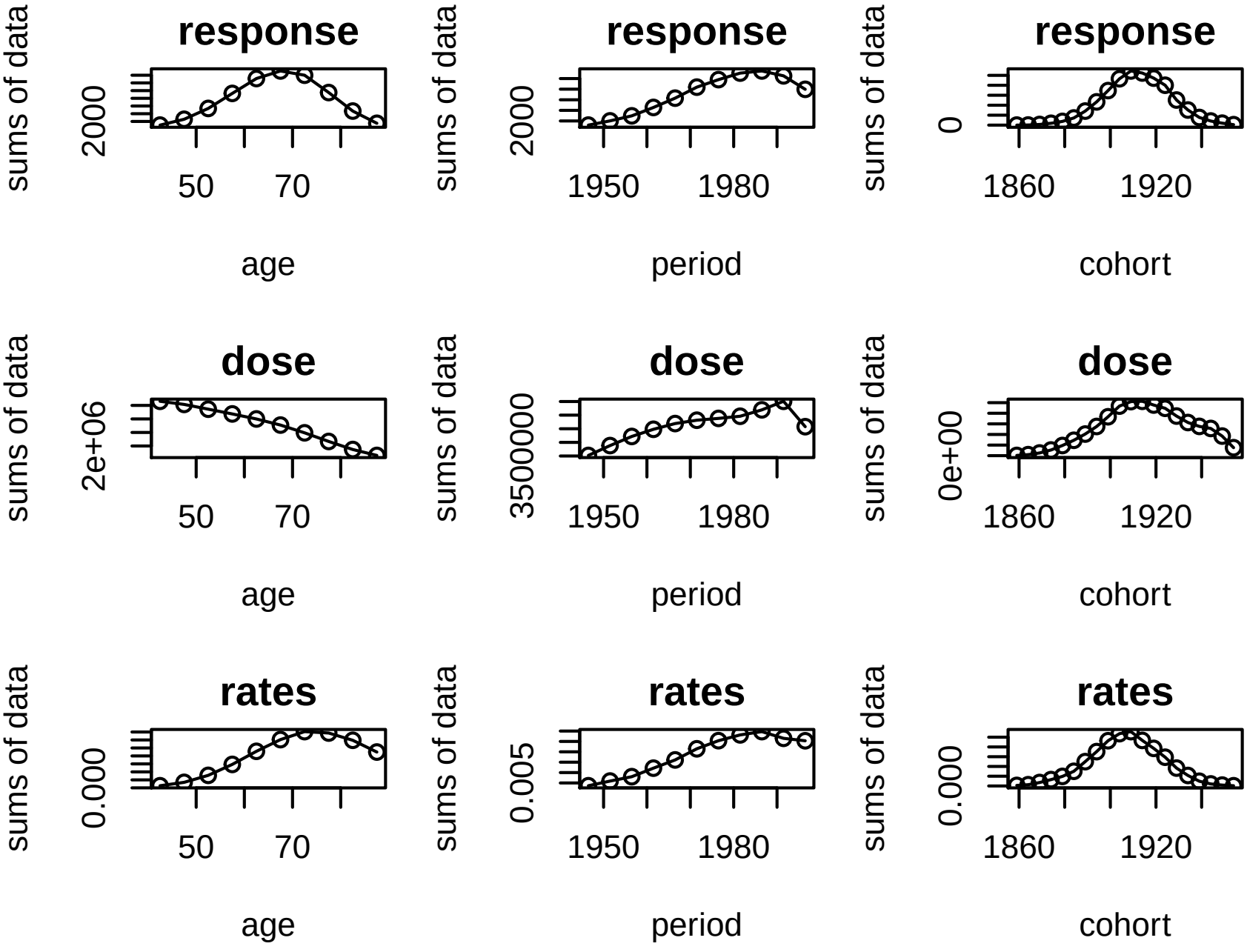
Note doses are the population at risk numbers.

```
apc.plot.data.sums(apc.data)
```

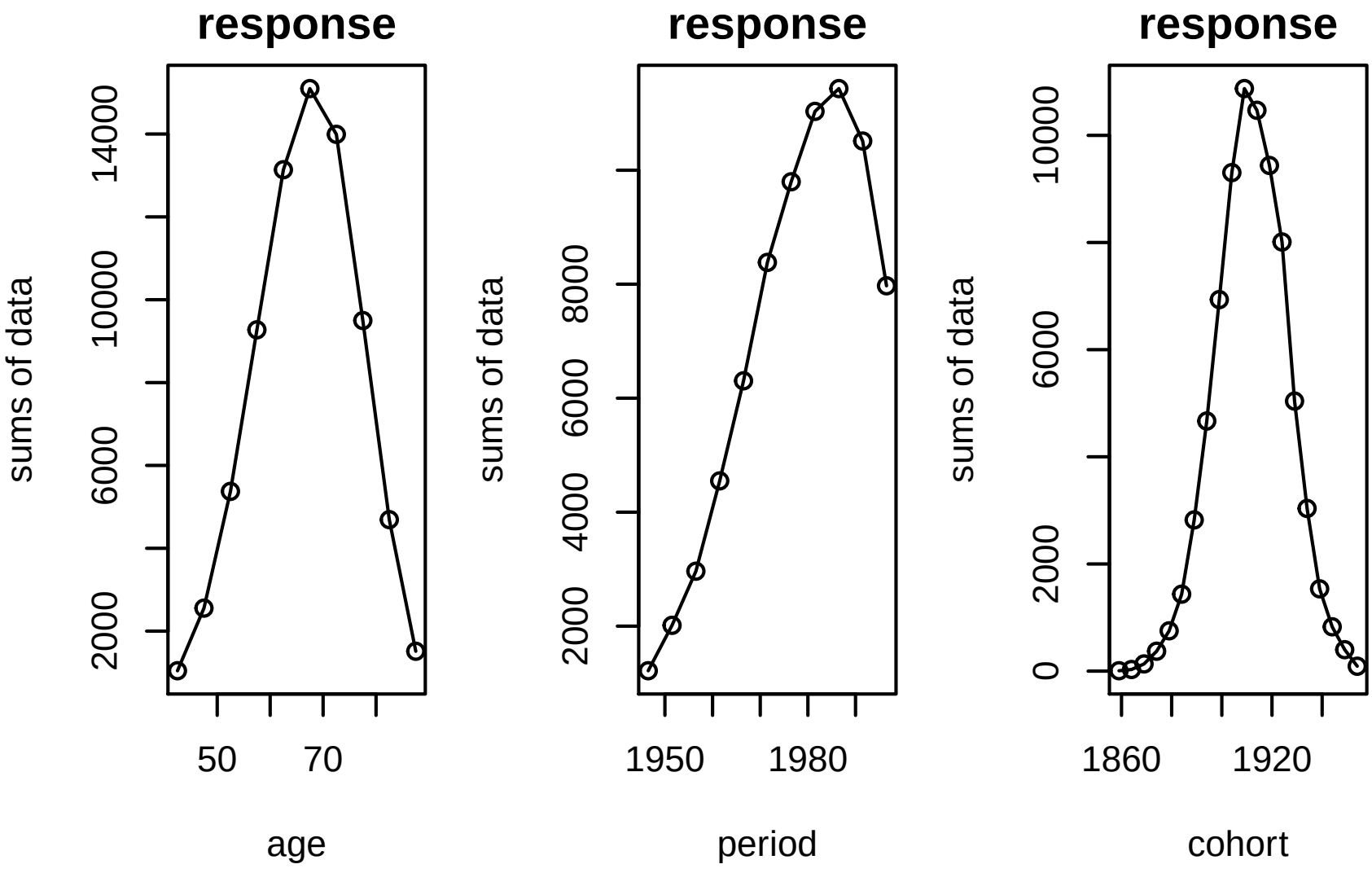
This isn't as pretty as the `Epi` version.

It produces marginal plots, i.e., numbers of cases (first row), population at risk (second row) and risk (third row), by age (first column), period (second column), cohort (third column).

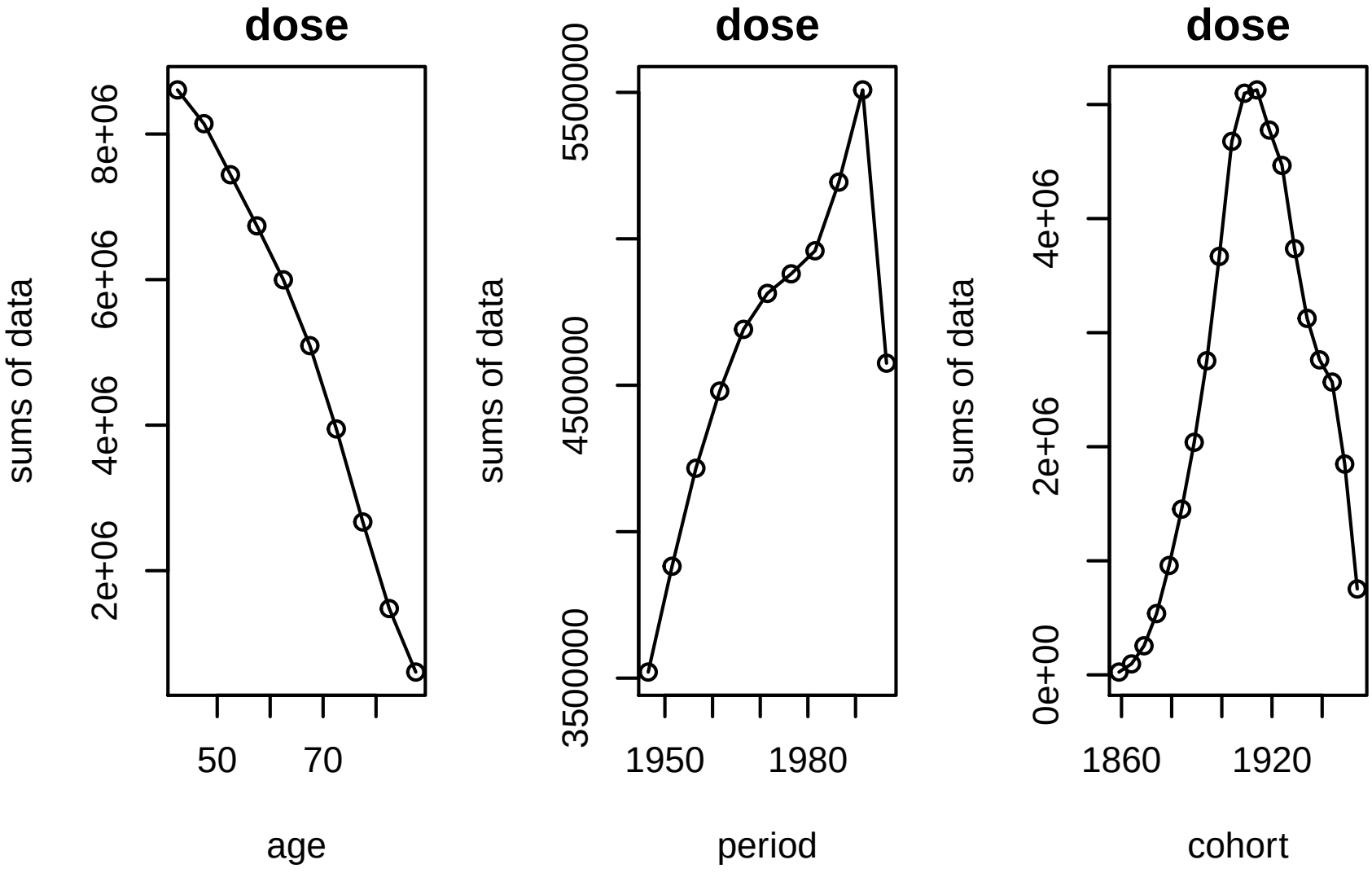
Sums of data is a little confusing...


response
sums of data
2000
50
70
age
response
sums of data
2000
1950
1980
period
response
sums of data
0
1860
1920
cohort
dose
sums of data
2e+06
50
70
age
dose
sums of data
3500000
1950
1980
period
dose
sums of data
0e+00
1860
1920
cohort
rates
sums of data
0.000
50
70
age
rates
sums of data
0.005
1950
1980
period
rates
sums of data
0.000
1860
1920
cohort

The counts only



The populations at risk only



The risks only

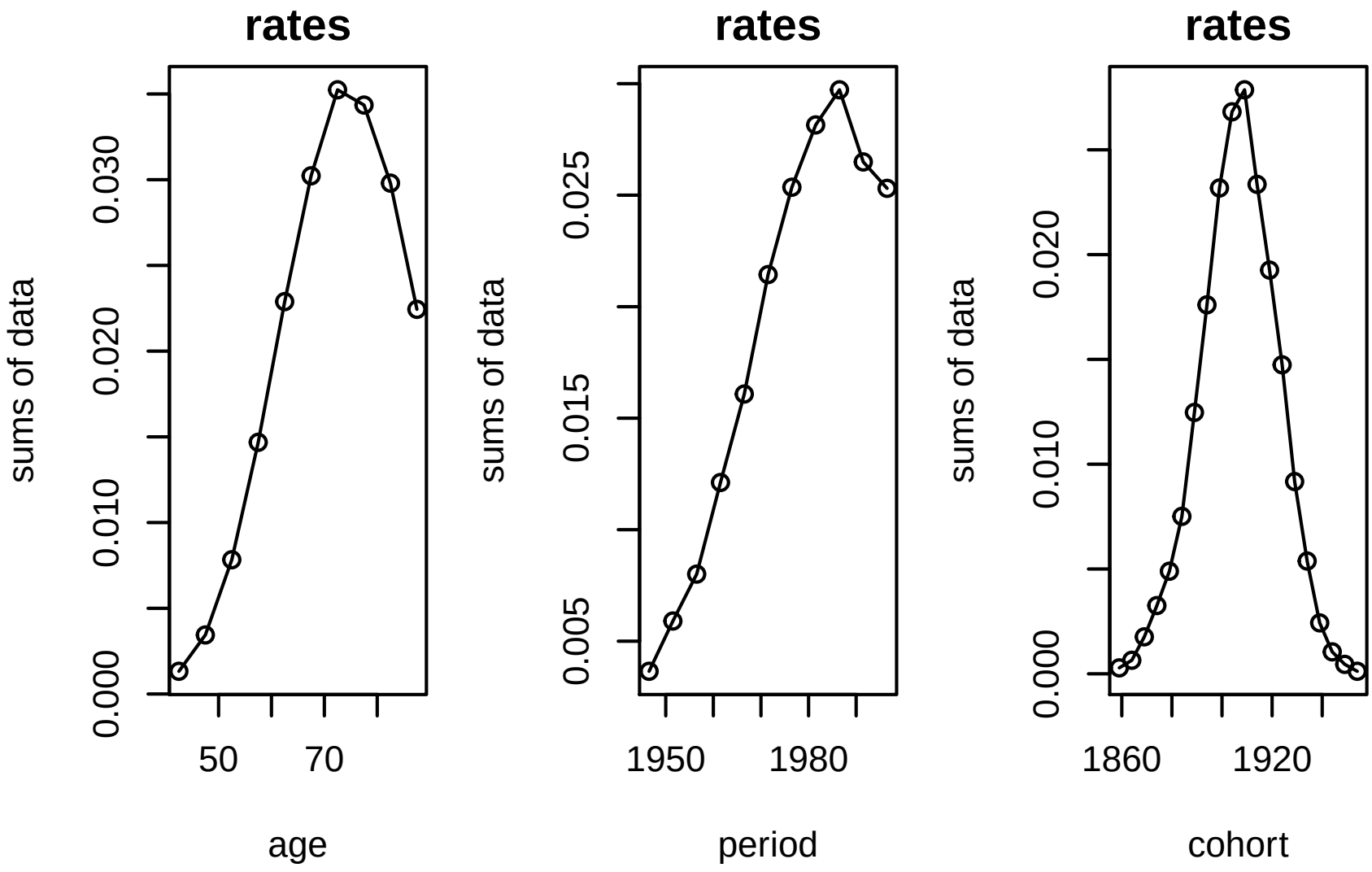


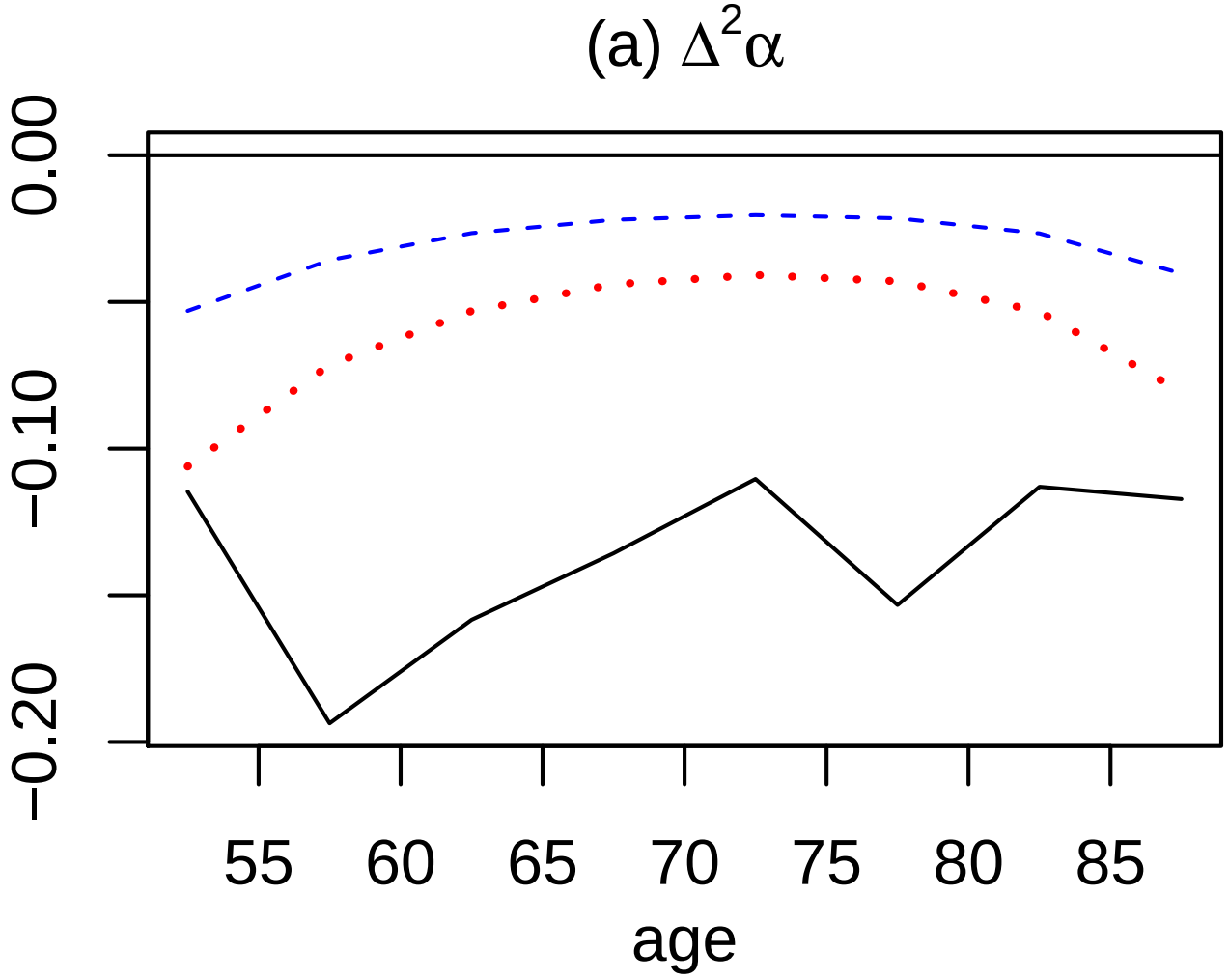
Table of deviances - agrees with Epi package!

Canonical parameterization of Kuang et al (2008)

```
apc.dev <- apc.fit.table(apc.data, "poisson.dose.response")
apc.dev[1:15, c(1, 2, 3, 4, 5, 6)]
##        -2logL df.residual prob(>chi_sq) LR.vs.APC df.vs.APC prob(>chi_sq)
## APC   208.548          72             0        NA        NA            NA
## AP   2723.466          90             0  2514.918        18             0
## AC    829.629          81             0   621.082         9             0
## PC   8609.929          80             0  8401.381         8             0
## Ad   6417.381          99             0  6208.833        27             0
## Pd  15470.469          98             0 15261.922        26             0
## Cd   9434.668          89             0  9226.121        17             0
## A   15103.001         100             0 14894.454        28             0
## P   56122.067          99             0 55913.520        27             0
## C   55099.747          90             0 54891.199        18             0
## t   19656.557         107             0 19448.010        35             0
## tA  27614.467         108             0 27405.919        36             0
## tP  61251.648         108             0 61043.100        36             0
## tC  68874.518         108             0 68665.970        36             0
## 1   71776.177         109             0 71567.629        37             0
```

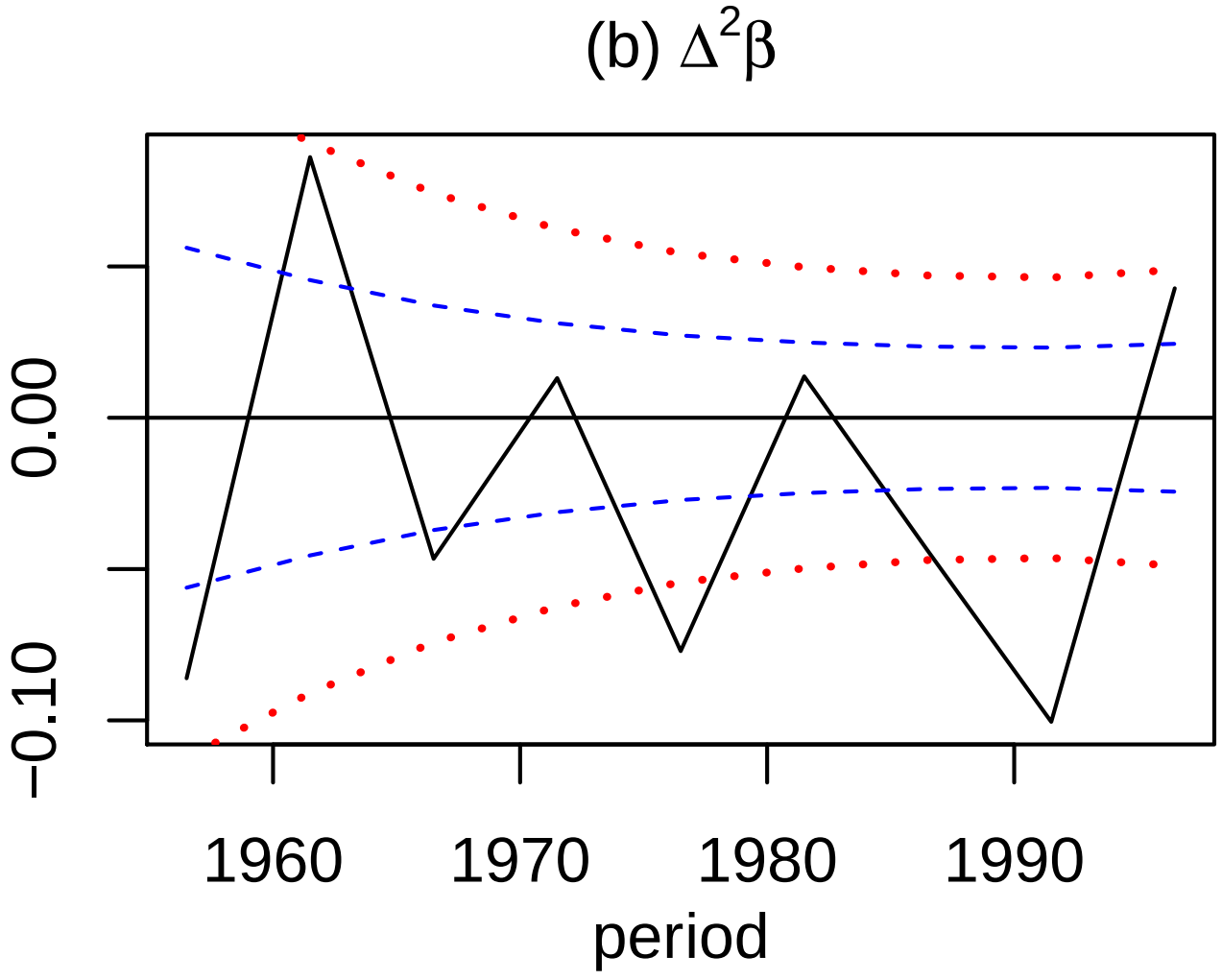
Second differences for age: 1/2 SE bands in blue/red

```
fit.apc <- apc.fit.model(apc.data, "poisson.dose.response",
    "APC")
apc.plot.fit(fit.apc, sub.plot = "a")
```



Second differences for period

```
apc.plot.fit(fit.apc, sub.plot = "b")
```



Second differences for cohort

```
apc.plot.fit(fit.apc, sub.plot = "c")
```