Representation of follow-up

Bendix Carstensen Steno Diabetes Center Copenhagen
Herlev, Denmark
http://BendixCarstensen.com

SPE, Tartu, Estonia,

June 2023

http://BendixCarstensen.com/SPE

From C:\Bendix\teach\SPE\git\lectures\time-rep/time-rep.tex Tuesday 30 May, 2023, 08:43

Representation of follow-up

Bendix Carstensen

Representation of follow-up

SPE, Tartu, Estonia,

June 2023

- In follow-up studies we estimate rates from:
  - D — events, deaths
  - Y — person-years
  - $\hat{\lambda} = D/Y$ rates
  - …empirical counterpart of intensity — an **estimate**
- Rates differ between persons.
- Rates differ within persons:
  - by age
  - by calendar time
  - by disease duration
  - …
- Multiple timescales.
- Multiple states (little boxes — later)

Representation of follow-up data

A cohort or follow-up study records **events** and **risk time**

The outcome is thus **bivariate**: (d, y)

Follow-up **data** for each individual must therefore have (at least) three pieces of information recorded:

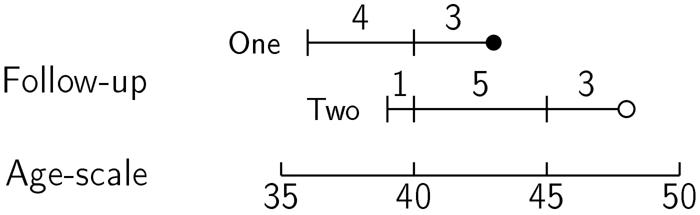
Date of entry	`entry`	date variable
Date of exit	`exit`	date variable
Status at exit	`fail`	indicator (mostly $0/1$)

These are specific for each **type** of outcome.

Stratification by age

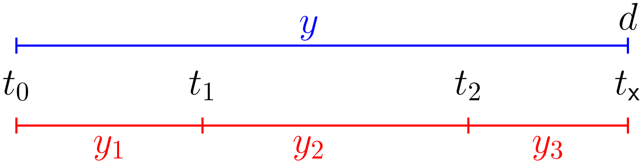
If follow-up is rather short, age at entry is OK for age-stratification.

If follow-up is long, stratification by categories of **current age** is preferable.



— allowing rates to vary across age-bands

— how do we do the split and why is it OK?



Probability

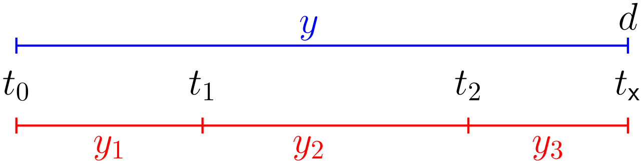
$$P(d \text{ at } t_\mathsf{x} | \text{entry } t_0)$$

$$= P(\text{surv } t_0 \rightarrow t_1 | \text{entry } t_0)$$
$$\times P(\text{surv } t_1 \rightarrow t_2 | \text{entry } t_1)$$
$$\times P(d \text{ at } t_\mathsf{x} | \text{entry } t_2)$$

log-Likelihood

$$d \log(\lambda) - \lambda y$$

$$= 0 \log(\lambda) - \lambda y_1$$
$$+ 0 \log(\lambda) - \lambda y_2$$
$$+ d \log(\lambda) - \lambda y_3$$



Probability	log-Likelihood
$\text{P}(d \text{ at } t_x \mid \text{entry } t_0)$	$d\log(\lambda) - \lambda y$
$= \text{P}(\text{surv } t_0 \rightarrow t_1 \mid \text{entry } t_0)$	$= 0\log(\lambda_1) - \lambda_1 y_1$
$\times\, \text{P}(\text{surv } t_1 \rightarrow t_2 \mid \text{entry } t_1)$	$+\, 0\log(\lambda_2) - \lambda_2 y_2$
$\times\, \text{P}(d \text{ at } t_x \mid \text{entry } t_2)$	$+\, d\log(\lambda_3) - \lambda_3 y_3$

— allows different rates (λ_i) in each interval

Dividing time into bands requires:

Origin: The date where the time scale is 0:

- Age — 0 at date of birth
- Disease duration — 0 at date of diagnosis
- Occupation exposure — 0 at date of hire

Intervals: How should it be subdivided:

- 1-year classes? 5-year classes?
- Equal length?

Aim: Separate rate in each interval, mimicking continuous time by using small intervals:
—time at the beginning of interval as quantitative variable.

Example: cohort with 3 persons:

```
Id      Bdate      Entry       Exit St
 1 14/07/1952 04/08/1965 27/06/1997  1
 2 01/04/1954 08/09/1972 23/05/1995  0
 3 10/06/1987 23/12/1991 24/07/1998  1
```

- Age bands: 10-years intervals of current age.
- Split Y for every subject accordingly
- Treat each segment as a separate unit of observation.
- Keep track of exit status (D) in each interval.

Splitting the follow-up

	subj. 1	subj. 2	subj. 3
Age at **E**ntry:	13.06	18.44	4.54
Age at e**X**it:	44.95	41.14	11.12
Status at exit:	Dead	Alive	Dead
Y	31.89	22.70	6.58
D	1	0	1

	subj. 1		subj. 2		subj. 3		$\sum$	
Age	Y	D	Y	D	Y	D	Y	D
0–	0.00	0	0.00	0	5.46	0	5.46	0
10–	6.94	0	1.56	0	1.12	1	8.62	1
20–	10.00	0	10.00	0	0.00	0	20.00	0
30–	10.00	0	10.00	0	0.00	0	20.00	0
40–	4.95	1	1.14	0	0.00	0	6.09	1
$\sum$	31.89	1	22.70	0	6.58	1	60.17	2

Splitting the follow-up

```
id       Bdate       Entry        Exit  St     risk  int

 1  14/07/1952  03/08/1965  14/07/1972   0   6.9432   10
 1  14/07/1952  14/07/1972  14/07/1982   0  10.0000   20
 1  14/07/1952  14/07/1982  14/07/1992   0  10.0000   30
 1  14/07/1952  14/07/1992  27/06/1997   1   4.9528   40
 2  01/04/1954  08/09/1972  01/04/1974   0   1.5606   10
 2  01/04/1954  01/04/1974  31/03/1984   0  10.0000   20
 2  01/04/1954  31/03/1984  01/04/1994   0  10.0000   30
 2  01/04/1954  01/04/1994  23/05/1995   0   1.1417   40
 3  10/06/1987  23/12/1991  09/06/1997   0   5.4634    0
 3  10/06/1987  09/06/1997  24/07/1998   1   1.1211   10
```

Keeping track of calendar time too?

Follow-up intervals on several timescales

- The risk-time is the same on all timescales
- Only need the entry point on each time scale:
  - Age at entry.
  - Date of entry.
  - Time since treatment at entry.

    — if time of treatment is the entry, this is 0 for all.
- Response variable in analysis of rates:

$$(d, y) \qquad (\text{event}, \text{duration})$$

- Covariates in analysis of rates:
  - timescales
  - other (fixed) measurements
- . . . do not confuse **duration** and **timescale** !

Follow-up data in Epi — Lexis objects I

```
> thoro[1:6,1:8]

  id sex birthdat contrast injecdat volume  exitdat exitstat
1  1   2 1916.609        1 1938.791     22 1976.787        1
2  2   2 1927.843        1 1943.906     80 1966.030        1
3  3   1 1902.778        1 1935.629     10 1959.719        1
4  4   1 1918.359        1 1936.396     10 1977.307        1
5  5   1 1902.931        1 1937.387     10 1945.387        1
6  6   2 1903.714        1 1937.316     20 1944.738        1
```

```
> thL <- Lexis(entry = list(age = injecdat-birthdat,
+                            dte = injecdat,
+                            tfi = 0 ),
+               exit = list(dte = exitdat),
+        exit.status = as.numeric(exitstat == 1),
+               data = thoro)
```

Follow-up data in Epi — Lexis objects II

```
NOTE: entry.status has been set to 0 for all.
NOTE: Dropping  2  rows with duration of follow up < tol

> summary(thL, timeScales = TRUE)

Transitions:
     To
From   0    1  Records:  Events: Risk time:  Persons:
   0 504 1964      2468     1964   51934.08      2468

Timescales:
age dte tfi
 ""  ""  ""
```

Definition of Lexis object

```
thL <- Lexis(entry = list(age = injecdat-birthdat,
                          dte = injecdat,
                          tfi = 0),
              exit = list(dte = exitdat),
       exit.status = as.numeric(exitstat==1),
              data = thoro)
```

entry is defined on **three** timescales,
but exit is only needed on **one** timescale (or vice versa):

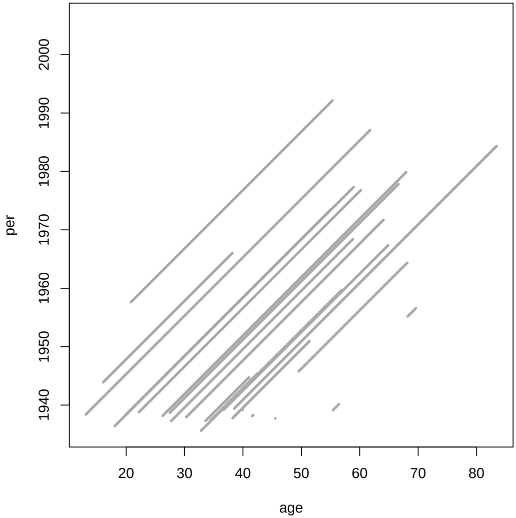
Follow-up time is the same on all timescales: `exitdat - injecdat`

One element of entry and exit must have same name (dte).

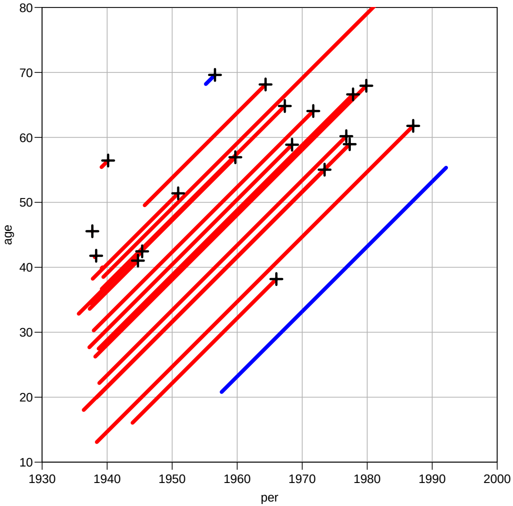
The looks of a Lexis object

```
> thL[1:4,1:9]
    age     dte tfi lex.dur lex.Cst lex.Xst lex.id
1 22.18 1938.79   0   37.99       0       1      1
2 49.54 1945.77   0   18.59       0       1      2
3 68.20 1955.18   0    1.40       0       1      3
4 20.80 1957.61   0   34.52       0       0      4
...

> summary(thL)
Transitions:
     To
From   0    1 Records:  Events: Risk time:  Persons:
   0 504 1964     2468     1964   51934.08      2468
```

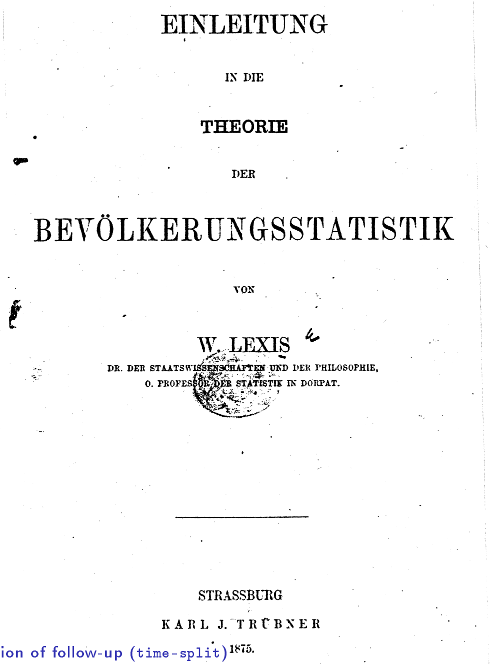


```
> plot( thL, lwd=3 )
```



Lexis diagram

```
> plot( thL, 2:1, lwd=5, col=c("red","blue")[thL$contrast],
+        grid=TRUE, lty.grid=1, col.grid=gray(0.7),
+        xlim=1930+c(0,70), xaxs="i", ylim=  10+c(0,70), yaxs="i", las=1 )
> points( thL, 2:1, pch=c(NA,3)[thL$lex.Xst+1],lwd=3, cex=1.5 )
```



EINLEITUNG

IN DIE

THEORIE

DER

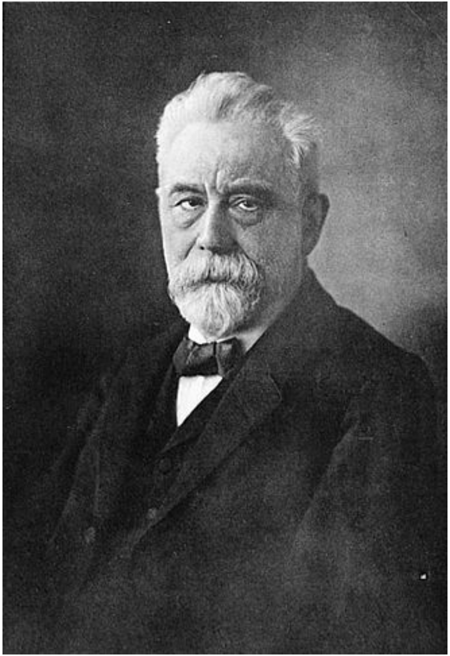
BEVÖLKERUNGSSTATISTIK

VON

W. LEXIS

DR. DER STAATSWISSENSCHAFTEN UND DER PHILOSOPHIE,
O. PROFESSOR DER STATISTIK IN DORPAT.

STRASSBURG
KARL J. TRÜBNER
1875.

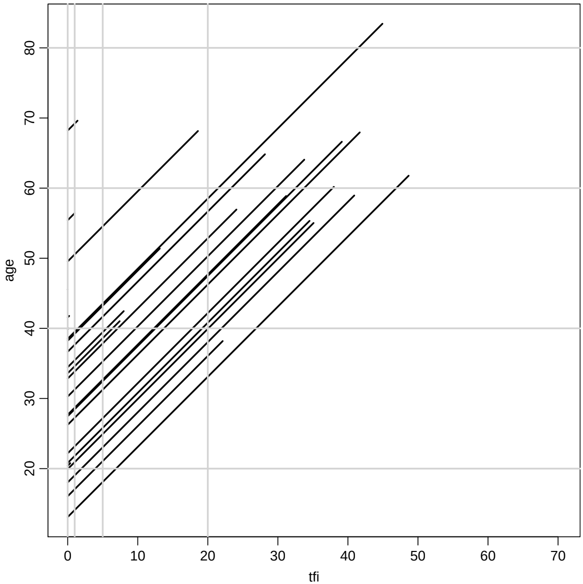


Splitting follow-up time

```
> spl1 <- splitLexis( thL, time.scale="age", breaks=seq(0,100,20) )
> round(spl1,1)
   age    dte  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast injecdat vol
1 22.2 1938.8  0.0    17.8       0       0    1   2   1916.6        1   1938.8
2 40.0 1956.6 17.8    20.0       0       0    1   2   1916.6        1   1938.8
3 60.0 1976.6 37.8     0.2       0       1    1   2   1916.6        1   1938.8
4 49.5 1945.8  0.0    10.5       0       0  640   2   1896.2        1   1945.8
5 60.0 1956.2 10.5     8.1       0       1  640   2   1896.2        1   1945.8
6 68.2 1955.2  0.0     1.4       0       1 3425   1   1887.0        2   1955.2
7 20.8 1957.6  0.0    19.2       0       0 4017   2   1936.8        2   1957.6
8 40.0 1976.8 19.2    15.3       0       0 4017   2   1936.8        2   1957.6
...
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi", breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    dte  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inj
1       1 22.2 1938.8  0.0     1.0       0       0    1   2   1916.6        1   19
2       1 23.2 1939.8  1.0     4.0       0       0    1   2   1916.6        1   19
3       1 27.2 1943.8  5.0    12.8       0       0    1   2   1916.6        1   19
4       1 40.0 1956.6 17.8     2.2       0       0    1   2   1916.6        1   19
5       1 42.2 1958.8 20.0    17.8       0       0    1   2   1916.6        1   19
6       1 60.0 1976.6 37.8     0.2       0       1    1   2   1916.6        1   19
7       2 49.5 1945.8  0.0     1.0       0       0  640   2   1896.2        1   19
8       2 50.5 1946.8  1.0     4.0       0       0  640   2   1896.2        1   19
9       2 54.5 1950.8  5.0     5.5       0       0  640   2   1896.2        1   19
10      2 60.0 1956.2 10.5     8.1       0       1  640   2   1896.2        1   19
11      3 68.2 1955.2  0.0     1.0       0       0 3425   1   1887.0        2   19
12      3 69.2 1956.2  1.0     0.4       0       1 3425   1   1887.0        2   19
13      4 20.8 1957.6  0.0     1.0       0       0 4017   2   1936.8        2   19
14      4 21.8 1958.6  1.0     4.0       0       0 4017   2   1936.8        2   19
15      4 25.8 1962.6  5.0    14.2       0       0 4017   2   1936.8        2   19
16      4 40.0 1976.8 19.2     0.8       0       0 4017   2   1936.8        2   19
17      4 40.8 1977.6 20.0    14.5       0       0 4017   2   1936.8        2   19
```



```
 age  tfi lex.dur lex.Cst lex.Xst
22.2  0.0     1.0       0       0
23.2  1.0     4.0       0       0
27.2  5.0    12.8       0       0
40.0 17.8     2.2       0       0
42.2 20.0    17.8       0       0
60.0 37.8     0.2       0       1
```

```
plot(spl2, c(1, 3), col = "black", lwd = 2)
```

Splitting on several timescales

```
> spl1 <- splitLexis(thL , time.scale = "age", breaks = seq(0, 100, 20))
> spl2 <- splitLexis(spl1, time.scale = "tfi", breaks = c(0, 1, 5, 20, 100))
> summary(spl2)

Transitions:
     To
From    0    1  Records:  Events: Risk time:  Persons:
   0 8250 1964     10214     1964   51934.08      2468

> library(popEpi)
> splx <- splitMulti(thL, age = seq(0, 100, 20), tfi = c(0, 1, 5, 20, 100))
> summary(splx)

Transitions:
     To
From    0    1  Records:  Events: Risk time:  Persons:
   0 8248 1964     10212     1964   51916.98      2468

> # NOTE: splitMulti excludes follow-up outside range of breaks
```

Likelihood for time-split data

- We assume that rates are constant in each (small) intervals
- Each observation in the dataset represents an interval, contributing a term to the (log-)likelihood for the rate
- Each **term** looks like a contribution from a Poisson variate (albeit with values only 0 or 1)
- So the likelihood from a single **person** looks like the likelihood from several independent Poisson variates
- . . . but the data are neither independent nor Poisson

Analysis of time-split data

Observations (records) classified by p—person and i—interval

- d_{pi} — events in the variable: `lex.Xst & lex.Xst!=lex.Cst`
- y_{pi} — risk time: `lex.dur` (duration)
- Covariates are:
  - timescales (age, period, time in study)
  - other variables for this person (constant in each interval).
- Likelihood for rates for one person is identical to a Poisson likelihood for many independent Poisson variates
- Modeling rates using `glm` or `gam`:
  time-scales and other covariates are treated alike

Fitting a simple model—data:

```
> stat.table(contrast,
+            list(D = sum(lex.Xst),
+                 Y = sum(lex.dur),
+              Rate = ratio(lex.Xst, lex.dur, 100)),
+            margin = TRUE,
+              data = spl2)
 ------------------------------------
 contrast         D        Y     Rate
 ------------------------------------
 1           928.00 20094.74     4.62
 2          1036.00 31839.35     3.25

 Total      1964.00 51934.08     3.78
 ------------------------------------
```

Fitting a simple model

```
 -------------------------------------
 contrast          D         Y    Rate
 -------------------------------------
 1            928.00  20094.74    4.62
 2           1036.00  31839.35    3.25
 -------------------------------------
```

```
> m0 <- glm((lex.Xst==1) ~ factor(contrast) - 1,
+            offset = log(lex.dur / 100),
+            family = poisson,
+              data = spl2)
> round(ci.exp(m0), 2)
                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.62 4.33  4.93
factor(contrast)2      3.25 3.06  3.46
```

. . . a Poisson model for mortality using log-person-years as offset

Fitting a simple model

```
-------------------------------------
contrast           D        Y    Rate
-------------------------------------
1             928.00 20094.74    4.62
2            1036.00 31839.35    3.25
-------------------------------------
```

```
> m0 <- glm(cbind(lex.Xst, lex.dur / 100) ~ factor(contrast) - 1,
+           family = poisreg,
+             data = spl2)
> round(ci.exp(m0), 2)
                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.62 4.33  4.93
factor(contrast)2      3.25 3.06  3.46
```

. . . a Poisson model for mortality rates based on deaths and person-years

Fitting a simple model

The wrapper glm.Lexis requires that lex.Cst and lex.Xst are factors —use factorize to make them:

```
> splf <- factorize(spl2)
> m0 <- glm.Lexis(splf, ~ factor(contrast) - 1, scale = 100)
```

```
stats::glm Poisson analysis of Lexis object splf with log link:
Rates for the transition:
0->1
, lex.dur (person-time) scaled by 100
```

```
> round(ci.exp(m0), 2)
```

```
                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.62 4.33  4.93
factor(contrast)2      3.25 3.06  3.46
```

. . . a Poisson model for mortality rates based on deaths and person-years in a Lexis object

Fitting a simple model — aggregate data

```
------------------------------------
contrast           D        Y    Rate
------------------------------------
1             928.00 20094.74    4.62
2            1036.00 31839.35    3.25
------------------------------------
```

As long as we only use covariates that take only a few values, we can model the aggregate data directly:

```
> mx <- glm(cbind(c(928, 1036), c(20094.74, 31839.35) / 100) ~ factor(1:2) - 1,
+           family = poisreg )
> round(ci.exp(mx), 2)
```

```
             exp(Est.) 2.5% 97.5%
factor(1:2)1      4.62 4.33  4.93
factor(1:2)2      3.25 3.06  3.46
```

SMR

Bendix Carstensen

Representation of follow-up

SPE, Tartu, Estonia,

June 2023

Cohorts where all are exposed

When there is no comparison group we may ask:
Do mortality rates in cohort differ from those of an **external** population, for example:

Rates from:

- Occupational cohorts
- Patient cohorts

compared with reference rates obtained from:

- Population statistics (mortality rates)
- Hospital registers (disease rates)

Cohort rates vs. population rates: RSR

- **Additive:** $\lambda(a) = \delta(a) + \lambda_{\mathsf{p}}(a)$
- Note that the survival (since $a = a_0$, say) is:

$$
\begin{aligned}
S(a) &= \exp\left(-\int_{a_0}^{a} \delta(a) + \lambda_{\mathsf{p}}(a)\,\mathrm{d}a\right) \\
&= \exp\left(-\int_{a_0}^{a} \delta(a)\,\mathrm{d}a\right) \times S_{\mathsf{p}}(a) \\
\Rightarrow \quad r(a) = S(a)/S_{\mathsf{p}}(a) &= \exp\left(-\int_{a_0}^{a} \delta(a)\,\mathrm{d}a\right)
\end{aligned}
$$

- **Additive** model for **rates** ⇔ **Relative survival** model.

Cohort rates vs. population rates: SMR

- **Multiplicative:** $\lambda(a) = \theta \times \lambda_\mathsf{p}(a)$
- Cohort rates proportional to reference rates, λ_p:
  $\lambda(a) = \theta \times \lambda_\mathsf{p}(a)$ — θ the same in all age-bands.
- D_a deaths during Y_a person-years an age-band a gives the likelihood:

$$\begin{aligned} D_a \log(\lambda(a)) - \lambda(a)Y_a &= D_a \log(\theta\lambda_\mathsf{p}(a)) - \theta\lambda_\mathsf{p}(a)Y_a \\ &= D_a \log(\theta) + \color{red}{D_a \log(\lambda_\mathsf{p}(a))} - \theta(\lambda_\mathsf{p}(a)Y_a) \end{aligned}$$

- The constant $\color{red}{D_a \log(\lambda_\mathsf{p}(a))}$ does not involve θ, and so can be dropped.

- $\lambda_{\mathsf{p}}(a)Y_a = E_a$ is the "expected" number of cases in age a, so the log-likelihood contribution from age a is:

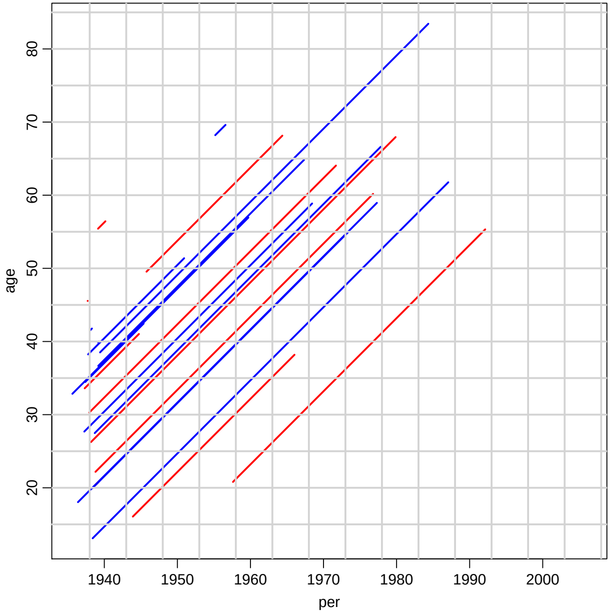
$$D_a\text{log}(\theta) - \theta\big(\lambda_{\mathsf{p}}(a)Y_a\big) = D_a\text{log}(\theta) - \theta(E_a)$$

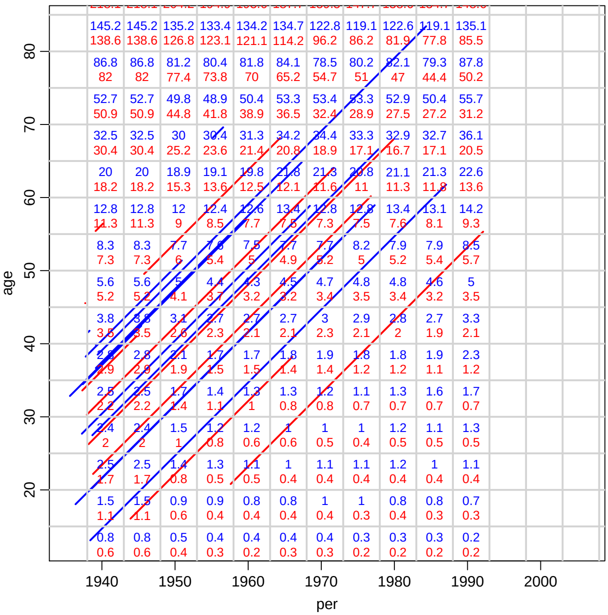
- The log-likelihood is similar to the log-likelihood for a rate, so:

$$\hat{\theta} = \sum_a D_a \Big/ \sum_a E_a = \text{Observed}/\text{Expected} = \text{SMR}$$

Modeling the SMR in practice

- As for the rates, the SMR can be modelled using individual data.
- Response is d_i, the event indicator (`lex.Xst`).
- $\log$-offset is the expected value for each piece of follow-up, $e_i = y_i \times \lambda_\mathsf{p}$ (`lex.dur * rate`)
- λ_p is the population rate corresponding to the age, period and sex of the follow-up period y_i.


age
20
30
40
50
60
70
80
1940
1950
1960
1970
1980
1990
2000
per



145.2 138.6	145.2 138.6	135.2 126.8	133.4 123.1	134.2 121.1	134.7 114.2	122.8 96.2	119.1 86.2	122.6 81.9	119.1 77.8	135.1 85.5
86.8 82	86.8 82	81.2 77.4	80.4 73.8	81.8 70	84.1 65.2	78.5 54.7	80.2 51	82.1 47	79.3 44.4	87.8 50.2
52.7 50.9	52.7 50.9	49.8 44.8	48.9 41.8	50.4 38.9	53.3 36.5	53.4 32.4	53.3 28.9	52.9 27.5	50.4 27.2	55.7 31.2
32.5 30.4	32.5 30.4	30 25.2	30.4 23.6	31.3 21.4	34.2 20.8	34.4 18.9	33.3 17.1	32.9 16.7	32.7 17.1	36.1 20.5
20 18.2	20 18.2	18.9 15.3	19.1 13.6	19.8 12.5	21.8 12.1	21.3 11.6	20.8 11	21.1 11.3	21.3 11.8	22.6 13.6
12.8 11.3	12.8 11.3	12 9	12.4 8.5	12.6 7.7	13.4 7.5	12.8 7.3	12.8 7.5	13.4 7.6	13.1 8.1	14.2 9.3
8.3 7.3	8.3 7.3	7.7 6	7.6 5.4	7.5 5	7.7 4.9	7.7 5.2	8.2 5	7.9 5.2	7.9 5.4	8.5 5.7
5.6 5.2	5.6 5.2	5 4.1	4.4 3.7	4.3 3.2	4.5 3.2	4.7 3.4	4.8 3.5	4.8 3.4	4.6 3.2	5 3.5
3.8 3.5	3.8 3.5	3.1 2.6	2.7 2.3	2.7 2.1	2.7 2.1	3 2.3	2.9 2.1	2.8 2	2.7 1.9	3.3 2.1
2.8 2.9	2.8 2.9	2.1 1.9	1.7 1.5	1.7 1.5	1.8 1.4	1.9 1.4	1.8 1.2	1.8 1.2	1.9 1.1	2.3 1.2
2.5 2.2	2.5 2.2	1.7 1.4	1.4 1.1	1.3 1	1.3 0.8	1.2 0.8	1.1 0.7	1.3 0.7	1.6 0.7	1.7 0.7
2.4 2	2.4 2	1.5 1	1.2 0.8	1.2 0.6	1 0.6	1 0.5	1 0.4	1.2 0.5	1.1 0.5	1.3 0.5
2.5 1.7	2.5 1.7	1.4 0.8	1.3 0.5	1.1 0.5	1 0.4	1.1 0.4	1.1 0.4	1.2 0.4	1 0.4	1.1 0.4
1.5 1.1	1.5 1.1	0.9 0.6	0.9 0.4	0.8 0.4	0.8 0.4	1 0.4	1 0.3	0.8 0.4	0.8 0.3	0.7 0.3
0.8 0.6	0.8 0.6	0.5 0.4	0.4 0.3	0.4 0.2	0.4 0.3	0.4 0.3	0.3 0.2	0.3 0.2	0.3 0.2	0.2 0.2

Split the data to fit with population data

```
> thad <- splitMulti(thL, age=seq(0,90,5), dte=seq(1938,2038,5) )
> summary( thad )
```

```
Transitions:
     To
From     0    1  Records:  Events: Risk time:  Persons:
   0 21059 1939     22998     1939   51787.96      2463
```

Create variables to fit with the population data

```
> thad$agr <- timeBand( thad, "age", "left" )
> thad$per <- timeBand( thad, "dte", "left" )
> round( thad[1:5,c("lex.id","age","agr","dte","per","lex.dur","lex.Xst","sex")],
```

```
 lex.id   age     dte lex.dur lex.Xst agr  per sex
      1 22.18 1938.79    2.82       0  20 1938   2
      1 25.00 1941.61    1.39       0  25 1938   2
      1 26.39 1943.00    3.61       0  25 1943   2
      1 30.00 1946.61    1.39       0  30 1943   2
      1 31.39 1948.00    3.61       0  30 1948   2
```

```
> data( gmortDK )
> dim( gmortDK )

[1] 418  21

> gmortDK[1:6,1:6]

  agr per sex   risk    dt     rt
1   0  38   1 996019 14079 14.135
2   5  38   1 802334   726  0.905
3  10  38   1 753017   600  0.797
4  15  38   1 773393  1167  1.509
5  20  38   1 813882  2031  2.495
6  25  38   1 789990  1862  2.357

> gmortDK$per <- gmortDK$per+1900
> #
> thadx <- merge( thad, gmortDK[,c("agr","per","sex","rt")] )
> #
> thadx$E <- thadx$lex.dur * thadx$rt / 1000
> stat.table(contrast,
+            list( D = sum(lex.Xst),
+                  Y = sum(lex.dur),
+                  E = sum(E),
+                SMR = ratio(lex.Xst, E)),
+             margin = TRUE,
+               data = thadx)
 --------------------------------------------
 contrast         D        Y       E     SMR
 --------------------------------------------
 1           917.00 20045.46  214.66    4.27
 2          1022.00 31742.51  447.21    2.29

 Total      1939.00 51787.96  661.87    2.93
 --------------------------------------------
 --------------------------------------------
 contrast          D        Y        E     SMR
 --------------------------------------------
 1            917.00 20045.46   214.66    4.27
 2           1022.00 31742.51   447.21    2.29
 --------------------------------------------
```

```
> m.SMR <- glm(cbind(lex.Xst, E) ~ factor(contrast) - 1,
+                family = poisreg,
+                  data = thadx)
> round(ci.exp(m.SMR), 2)
```

```
                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.27 4.00  4.56
factor(contrast)2      2.29 2.15  2.43
```

- Analysis of SMR is like analysis of rates:
- Replace Y with E — that's all! (`glm.Lexis` not usable)
- ...it's the calculation of E that is difficult