Representation of follow-up

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IARC, Lyon,

June 2018

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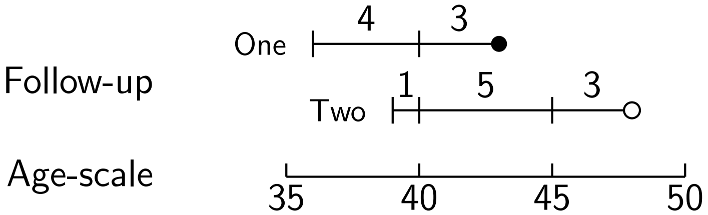
  - …
- Multiple timescales.
- Multiple states (little boxes — later)

Examples: stratification by age

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

If follow-up is long, use stratification by categories of **current age**, both for:

No. of events, D, and Risk time, Y.



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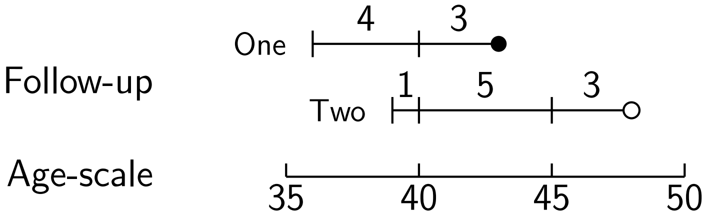


— assuming a constant rate λ throughout.

Representation of follow-up data

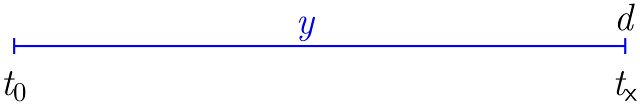
A cohort or follow-up study records:
Events and **Risk time**.

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

Follow-up **data** for each individual must therefore have (at least) three variables:

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

Specific for each **type** of outcome.

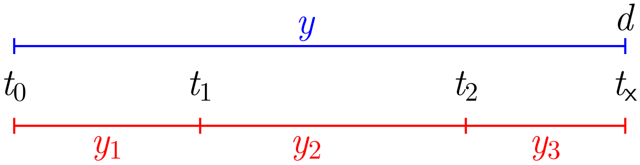


Probability

$\mathrm{P}(d \text{ at } t_x | \text{entry } t_0)$

log-Likelihood

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



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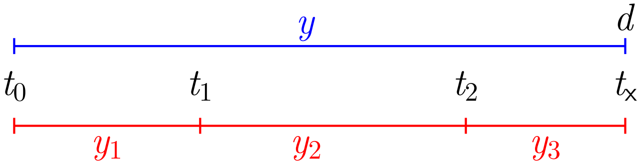


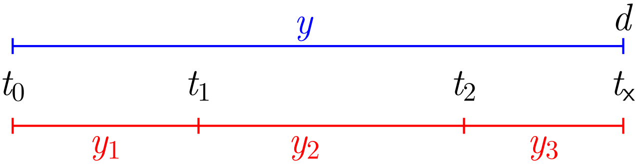
Probability

$\mathrm{P}(d \text{ at } t_x|\text{entry } t_0)$

$= \mathrm{P}(\text{surv } t_0 \rightarrow t_1|\text{entry } t_0)$

log-Likelihood

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



Probability

$\mathrm{P}(d \text{ at } t_x | \text{entry } t_0)$

$= \mathrm{P}(\text{surv } t_0 \rightarrow t_1 | \text{entry } t_0)$

$\times \mathrm{P}(\text{surv } t_1 \rightarrow t_2 | \text{entry } t_1)$

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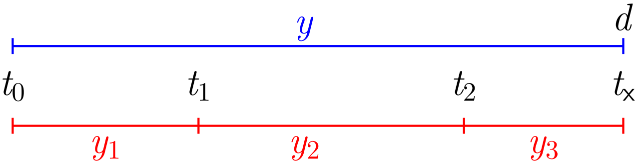

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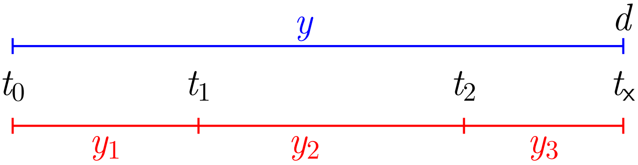

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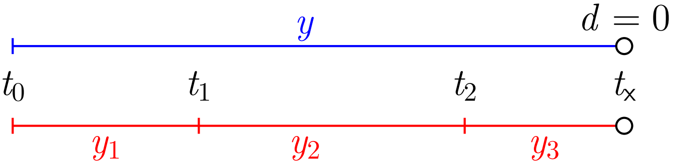
$$= \mathrm{P}(\text{surv } t_0 \rightarrow t_1 | \text{entry } t_0)$$
$$\times \mathrm{P}(\text{surv } t_1 \rightarrow t_2 | \text{entry } t_1)$$
$$\times \mathrm{P}(d \text{ at } t_x | \text{entry } t_2)$$

log-Likelihood

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

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



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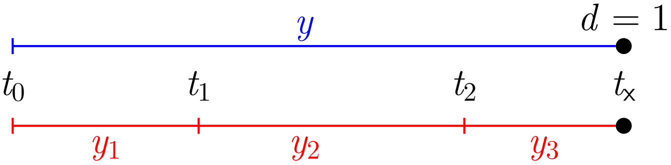
log-Likelihood

$$0 \log(\lambda) - \lambda y$$

$$\begin{aligned} &= 0 \log(\lambda) - \lambda y_1 \\ &+ 0 \log(\lambda) - \lambda y_2 \\ &+ 0 \log(\lambda) - \lambda y_3 \end{aligned}$$



Probability

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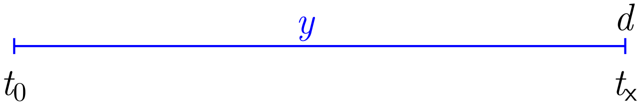
log-Likelihood

$1 \log(\lambda) - \lambda y$

$= 0 \log(\lambda) - \lambda y_1$

$+ 0 \log(\lambda) - \lambda y_2$

$+ 1 \log(\lambda) - \lambda y_3$



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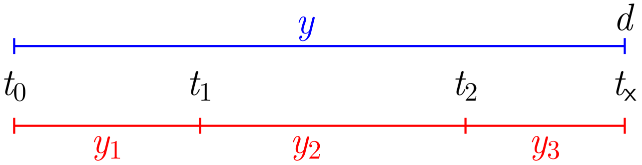

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$\mathrm{P}(d \text{ at } t_x \mid \text{entry } t_0)$	$d \log(\lambda) - \lambda y$
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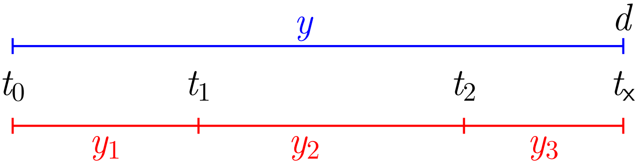

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log-Likelihood

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

$$= 0 \log(\lambda_1) - \lambda_1 y_1$$
$$+ 0 \log(\lambda_2) - \lambda_2 y_2$$
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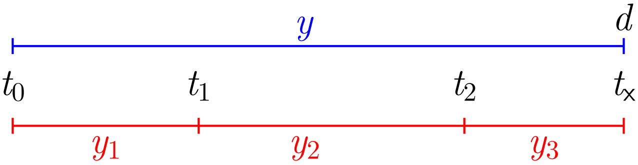

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— allows different rates (λ_i) in each interval

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Aim: Separate rate in each interval

Example: cohort with 3 persons:

Id	Bdate	Entry	Exit	St
1	14/07/1952	04/08/1965	27/06/1997	1
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- Split Y for every subject accordingly
- Treat each segment as a separate unit of observation.
- Keep track of exit status 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?

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Timescales

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  - Age
  - Calendar time
  - Time since treatment
  - Time since relapse
- All timescales advance at the same pace (1 year per year ...)
- Note: Cumulative exposure is **not** a timescale.

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

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  - other (fixed) measurements
- ...do not confuse **duration** and **timescale** !

Follow-up data in Epi — Lexis objects

```
> 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
```

Follow-up data in `Epi` — `Lexis` objects

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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
```

Timescales of interest:

- Age
- Calendar time
- Time since injection

Definition of `Lexis` object

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

:

Definition of `Lexis` object

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

`entry` is defined on **three** timescales,

:

Definition of `Lexis` object

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

`entry` is defined on **three** timescales,
but `exit` is only needed on **one** timescale:

Definition of `Lexis` object

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

`entry` is defined on **three** timescales,
but `exit` is only needed on **one** timescale:
Follow-up time is the same on all timescales:

Definition of `Lexis` object

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

`entry` is defined on **three** timescales,
but `exit` is only needed on **one** timescale:
Follow-up time is the same on all timescales:

`exitdat - injecdat`

Definition of `Lexis` object

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

`entry` is defined on **three** timescales,
but `exit` is only needed on **one** timescale:
Follow-up time is the same on all timescales:

`exitdat - injecdat`

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

The looks of a `Lexis` object

```
> thL[1:4,1:9]
    age     per 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
...
```

The looks of a `Lexis` object

```
> thL[1:4,1:9]
    age     per 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
```

The looks of a `Lexis` object

```
> thL[1:4,1:9]
    age     per 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
```

The looks of a `Lexis` object

```
> thL[1:4,1:9]
    age     per 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
```

The looks of a `Lexis` object

```
> thL[1:4,1:9]
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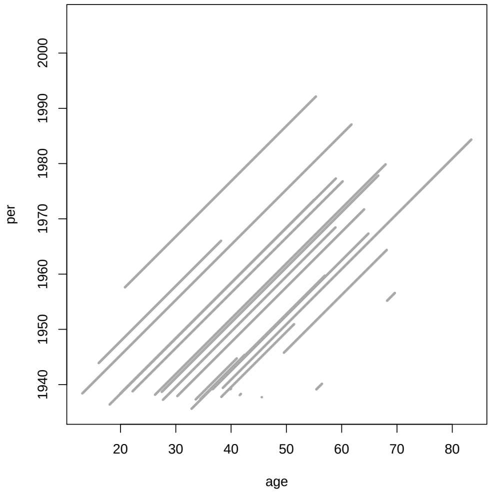
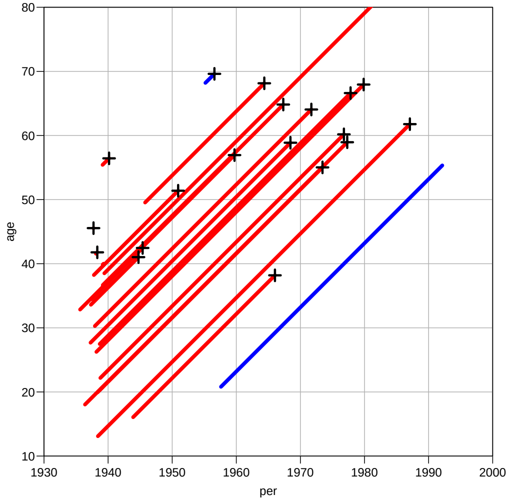
1 22.18 1938.79   0   37.99       0       1      1
2 49.54 1945.77   0   18.59       0       1      2
3 68.20 1955.18   0    1.40       0       1      3
4 20.80 1957.61   0   34.52       0       0      4
...

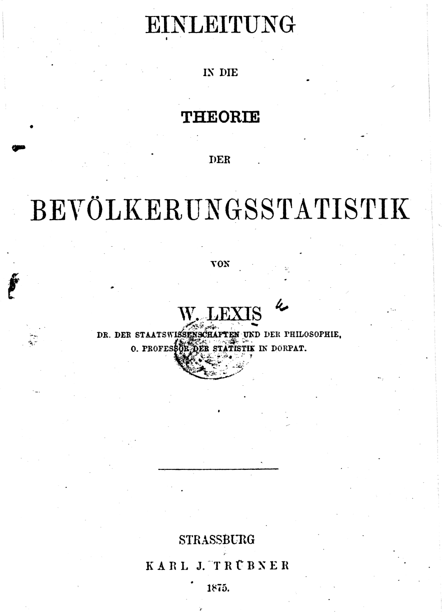
> summary( thL )
Transitions:
     To
From   0    1 Records:  Events: Risk time:  Persons:
   0 504 1964     2468     1964   51934.08      2468
```




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




```
> 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

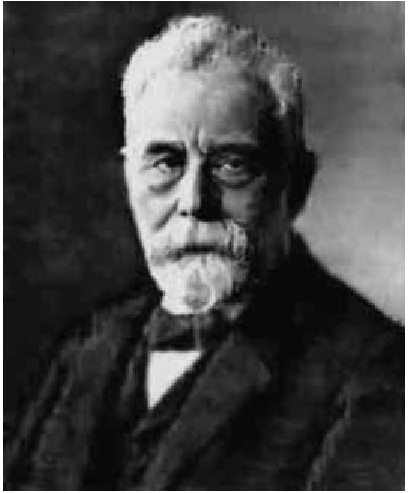
DR. DER STAATSWISSENSCHAFTEN UND DER PHILOSOPHIE,

O. PROFESSOR DER STATISTIK IN DORPAT.

STRASSBURG

KARL J. TRÜBNER

1875.



Splitting follow-up time

```
> spl1 <- splitLexis( thL, breaks=seq(0,100,20),
>                          time.scale="age" )
> round(spl1,1)
   age    per  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
...
```

Splitting follow-up time

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> spl1 <- splitLexis( thL, breaks=seq(0,100,20),
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   age    per  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
...
```

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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
...
```

Splitting follow-up time

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>                              time.scale="age" )
> round(spl1,1)
   age    per  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
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...
```

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   age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast injecdat vol
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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    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                      breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                      breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
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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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                      breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                      breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
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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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                      breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per  tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
```

Split on another timescale

```
> spl2 <- splitLexis( spl1, time.scale="tfi",
                          breaks=c(0,1,5,20,100) )
> round( spl2, 1 )
   lex.id  age    per   tfi lex.dur lex.Cst lex.Xst   id sex birthdat contrast inje
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
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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
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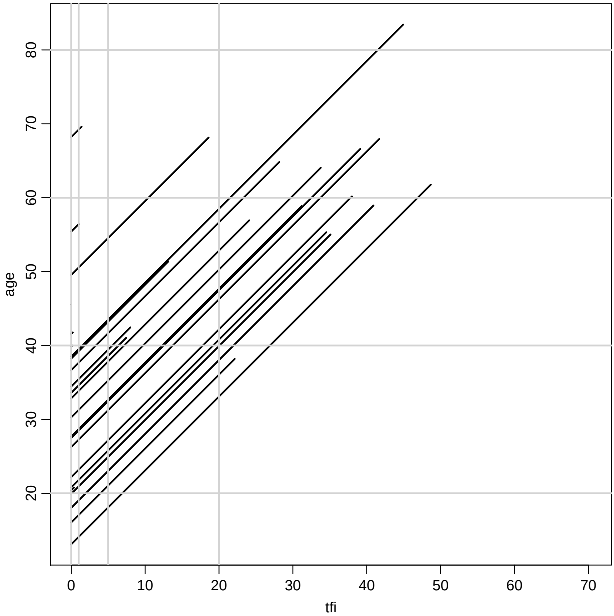
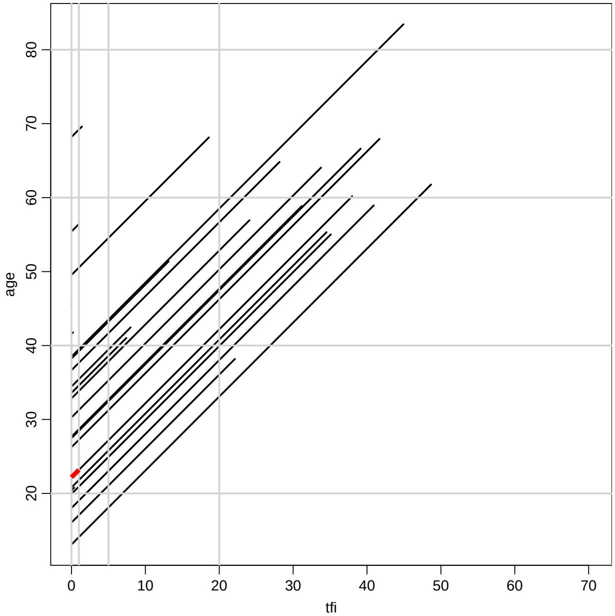
```



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 )
```



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
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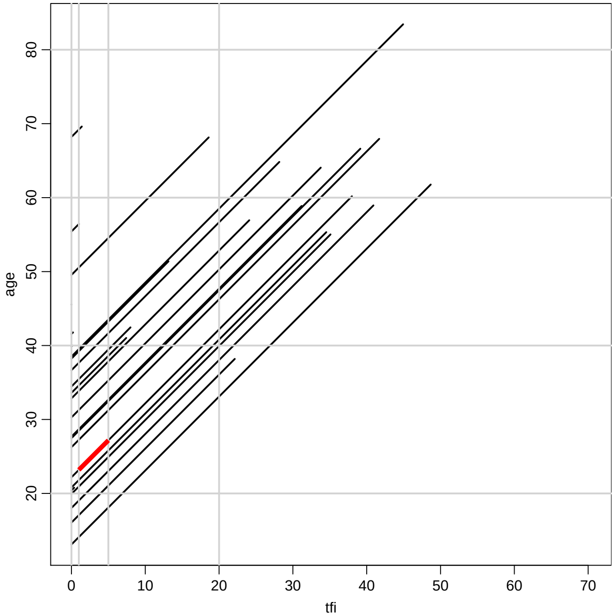

age	tfi	lex.dur	lex.Cst	lex.Xst
22.2	0.0	1.0	0	0
23.2	1.0	4.0	0	0
27.2	5.0	12.8	0	0
40.0	17.8	2.2	0	0
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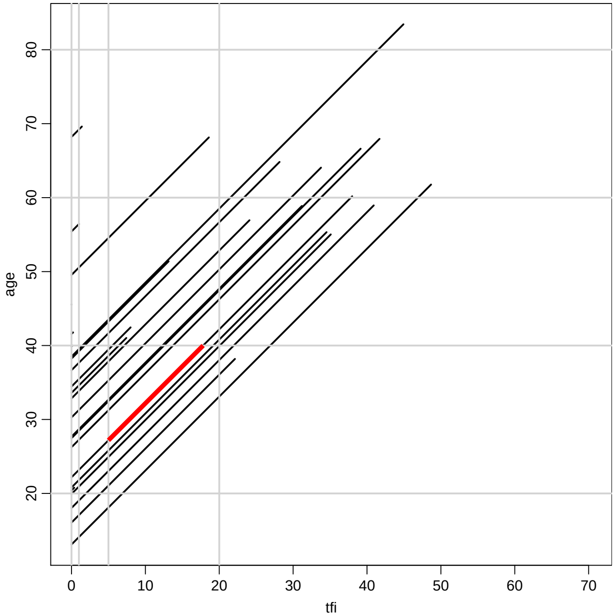

age	tfi	lex.dur	lex.Cst	lex.Xst
22.2	0.0	1.0	0	0
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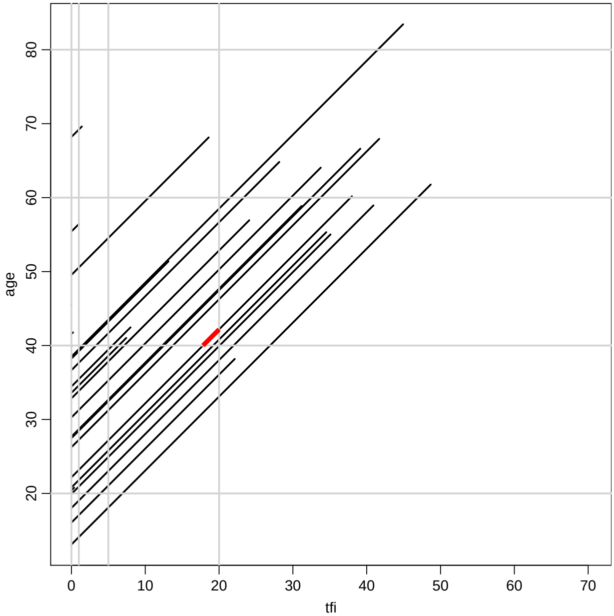

age	tfi	lex.dur	lex.Cst	lex.Xst
22.2	0.0	1.0	0	0
23.2	1.0	4.0	0	0
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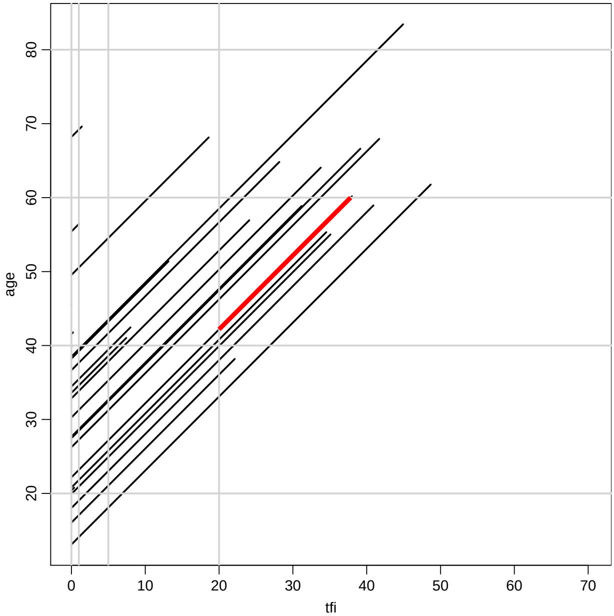

age	tfi	lex.dur	lex.Cst	lex.Xst
22.2	0.0	1.0	0	0
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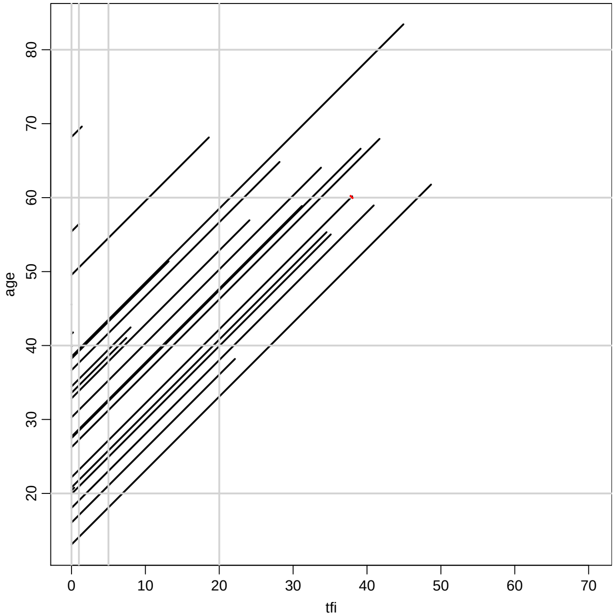

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- The latter is where we will need splines.

The Poisson likelihood for split data

- Split records (one per **p**erson-**i**nterval (p, i)):

$$\sum_{p,i}\big(d_{pi}\log(\lambda) - \lambda y_{pi}\big) = D\log(\lambda) - \lambda Y$$

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- If we assume that rates are constant we get the simple expression with (D, Y)
- ...but the split data allows models that assume different rates for different (d_{pi}, y_{pi}), so rates can vary **within** a person's follow-up.

Where is (d_{pi}, y_{pi}) in the split data?

```
> spl1 <- splitLexis( thL , breaks=seq(0,100,20)  , time.scale="age" )
> spl2 <- splitLexis( spl1, breaks=c(0,1,5,20,100), time.scale="tfi" )
> options( digits=5 )
> spl2[1:10,1:11]

   lex.id    age    per    tfi  lex.dur lex.Cst lex.Xst id sex birthdat contrast
1       1 22.182 1938.8  0.000  1.00000       0       0  1   2   1916.6        1
2       1 23.182 1939.8  1.000  4.00000       0       0  1   2   1916.6        1
3       1 27.182 1943.8  5.000 12.81793       0       0  1   2   1916.6        1
4       1 40.000 1956.6 17.818  2.18207       0       0  1   2   1916.6        1
5       1 42.182 1958.8 20.000 17.81793       0       0  1   2   1916.6        1
6       1 60.000 1976.6 37.818  0.17796       0       1  1   2   1916.6        1
7       2 16.063 1943.9  0.000  1.00000       0       0  2   2   1927.8        1
8       2 17.063 1944.9  1.000  2.93703       0       0  2   2   1927.8        1
9       2 20.000 1947.8  3.937  1.06297       0       0  2   2   1927.8        1
10      2 21.063 1948.9  5.000 15.00000       0       0  2   2   1927.8        1
```

— and what are covariates for the rates?

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- d_{pi} — events in the variable: `lex.Xst`:
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- Covariates are:
  - timescales (age, period, time in study)
  - other variables for this person (constant or *assumed* constant in each interval).
- Model rates using the covariates in `glm`:
  — no difference between time-scales and other covariates.

Fitting a simple model

```
> 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
```

SMR

Bendix Carstensen

Representation of follow-up

IARC, Lyon,

June 2018

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

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- Hospital registers (disease rates)

Cohort rates vs. population rates: RSR

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- Note that the survival (since $a = a_0$, say) is:

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

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

- Additive model for rates $\Leftrightarrow$ Relative survival model.

Cohort rates vs. population rates: SMR

- **Multiplicative:** $\lambda(a) = \theta\lambda_P(a)$

Cohort rates vs. population rates: SMR

- **Multiplicative:** $\lambda(a) = \theta\lambda_P(a)$
- Cohort rates proportional to reference rates:
  $\lambda(a) = \theta \times \lambda_P(a)$ — θ the same in all age-bands.

Cohort rates vs. population rates: SMR

- **Multiplicative:** $\lambda(a) = \theta\lambda_P(a)$
- Cohort rates proportional to reference rates:
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- D_a deaths during Y_a person-years an age-band a gives the likelihood:

$$
\begin{aligned}
D_a \log(\lambda(a)) - \lambda(a)\,Y_a &= D_a \log(\theta\lambda_P(a)) - \theta\lambda_P(a)\,Y_a \\
&= D_a \log(\theta) + D_a \log(\lambda_P(a)) - \theta(\lambda_P(a)\,Y_a
\end{aligned}
$$

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- The constant $D_a \log(\lambda_P(a))$ does not involve θ, and so can be dropped.

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

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- SMR is the maximum likelihood estimator of the relative mortality in the cohort.

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- As for the rates, the SMR can be modelled using individual data.

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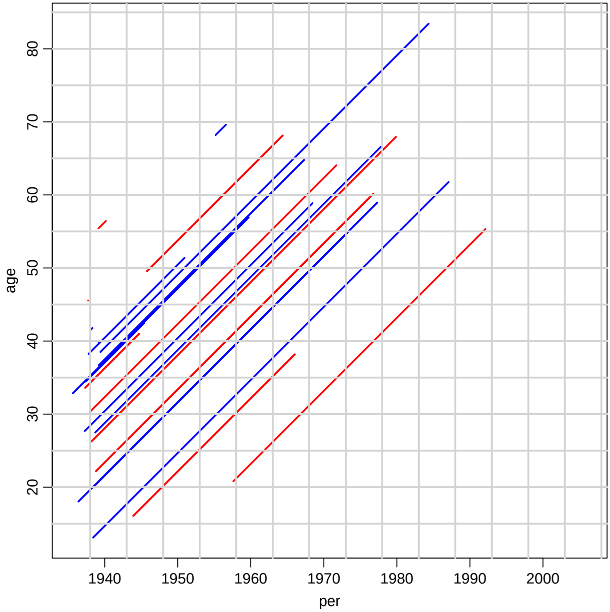
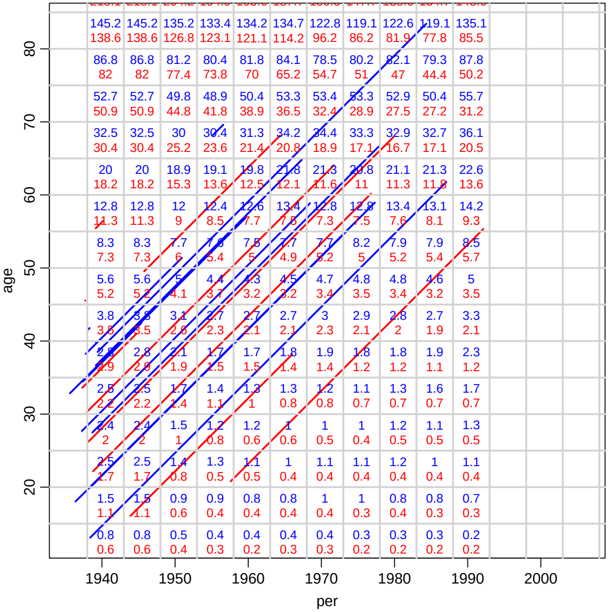
Modelling the SMR in practise

- 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, $e_i = y_i \times \lambda_P$ (`lex.dur * rate`)
- λ_P is the population rate corresponding to the age, period and sex of the follow-up period y_i.



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


145.2 145.2 135.2 133.4 134.2 134.7 122.8 119.1 122.6 119.1 135.1
138.6 138.6 126.8 123.1 121.1 114.2 96.2 86.2 81.9 77.8 85.5
86.8 86.8 81.2 80.4 81.8 84.1 78.5 80.2 82.1 79.3 87.8
82 82 77.4 73.8 70 65.2 54.7 51 47 44.4 50.2
52.7 52.7 49.8 48.9 50.4 53.3 53.4 53.3 52.9 50.4 55.7
50.9 50.9 44.8 41.8 38.9 36.5 32.4 28.9 27.5 27.2 31.2
32.5 32.5 30 30.4 31.3 34.2 34.4 33.3 32.9 32.7 36.1
30.4 30.4 25.2 23.6 21.4 20.8 18.9 17.1 16.7 17.1 20.5
20 20 18.9 19.1 19.8 21.8 21.3 20.8 21.1 21.3 22.6
18.2 18.2 15.3 13.6 12.5 12.1 11.6 11 11.3 11.8 13.6
12.8 12.8 12 12.4 12.6 13.4 12.8 12.8 13.4 13.1 14.2
11.3 11.3 9 8.5 7.7 7.5 7.3 7.5 7.6 8.1 9.3
8.3 8.3 7.7 7.6 7.5 7.7 7.7 8.2 7.9 7.9 8.5
7.3 7.3 6 5.4 5 4.9 5.2 5 5.2 5.4 5.7
5.6 5.6 5 4.4 4.3 4.5 4.7 4.8 4.8 4.6 5
5.2 5.2 4.1 3.7 3.2 3.2 3.4 3.5 3.4 3.2 3.5
3.8 3.8 3.1 2.7 2.7 2.7 3 2.9 2.8 2.7 3.3
3.5 3.5 2.6 2.3 2.1 2.1 2.3 2.1 2 1.9 2.1
2.8 2.8 2.1 1.7 1.7 1.8 1.9 1.8 1.8 1.9 2.3
2.9 2.9 1.9 1.5 1.5 1.4 1.4 1.2 1.2 1.1 1.2
2.5 2.5 1.7 1.4 1.3 1.3 1.2 1.1 1.3 1.6 1.7
2.2 2.2 1.4 1.1 1 0.8 0.8 0.7 0.7 0.7 0.7
2.4 2.4 1.5 1.2 1.2 1 1 1 1.2 1.1 1.3
2 2 1 0.8 0.6 0.6 0.5 0.4 0.5 0.5 0.5
2.5 2.5 1.4 1.3 1.1 1 1.1 1.1 1.2 1 1.1
1.7 1.7 0.8 0.5 0.5 0.4 0.4 0.4 0.4 0.4 0.4
1.5 1.5 0.9 0.9 0.8 0.8 1 1 0.8 0.8 0.7
1.1 1.1 0.6 0.4 0.4 0.4 0.4 0.3 0.4 0.3 0.3
0.8 0.8 0.5 0.4 0.4 0.4 0.4 0.3 0.3 0.3 0.2
0.6 0.6 0.4 0.3 0.2 0.3 0.3 0.2 0.2 0.2 0.2
age
80
70
60
50
40
30
20
1940
1950
1960
1970
1980
1990
2000
per

Split the data to fit with population data

```
> tha  <- splitLexis(thL, time.scale="age", breaks=seq(0,90,5) )
> thap <- splitLexis(tha, time.scale="per", breaks=seq(1938,2038,5) )
> dim( thap )

[1] 23094    21
```

Split the data to fit with population data

```
> tha  <- splitLexis(thL, time.scale="age", breaks=seq(0,90,5) )
> thap <- splitLexis(tha, time.scale="per", breaks=seq(1938,2038,5) )
> dim( thap )

[1] 23094    21
```

Create variables to fit with the population data

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

  lex.id   age agr     per  cal lex.dur lex.Xst sex
1      1 22.18  20 1938.79 1938    2.82       0   2
2      1 25.00  25 1941.61 1938    1.39       0   2
3      1 26.39  25 1943.00 1943    3.61       0   2
4      1 30.00  30 1946.61 1943    1.39       0   2
5      1 31.39  30 1948.00 1948    3.61       0   2
```

```
> data( gmortDK )
> 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$cal <- gmortDK$per+1900
> #
> thapx <- merge( thap, gmortDK[,c("agr","cal","sex","rt")] )
> #
> thapx$E <- thapx$lex.dur * thapx$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 = thapx )
```

```
 --------------------------------------------
 contrast          D          Y        E     SMR
 --------------------------------------------
 1            923.00 20072.53   222.01    4.16
 2           1036.00 31839.35   473.88    2.19

 Total       1959.00 51911.87   695.89    2.82
 --------------------------------------------
```

```
-----------------------------------------------
contrast           D         Y        E     SMR
-----------------------------------------------
1             923.00  20072.53   222.01    4.16
2            1036.00  31839.35   473.88    2.19

Total        1959.00  51911.87   695.89    2.82
-----------------------------------------------
```

```
> m.SMR <- glm( lex.Xst ~ factor(contrast) - 1,
+               offset = log(E),
+               family = poisson,
+                 data = thapx )
> round( ci.exp( m.SMR ), 2 )

                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.16 3.90  4.43
factor(contrast)2      2.19 2.06  2.32
```

```
 ----------------------------------------------
 contrast          D          Y        E      SMR
 ----------------------------------------------
 1               923.00  20072.53   222.01     4.16
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 Total          1959.00  51911.87   695.89     2.82
 ----------------------------------------------
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> round( ci.exp( m.SMR ), 2 )

                  exp(Est.) 2.5% 97.5%
factor(contrast)1      4.16 3.90  4.43
factor(contrast)2      2.19 2.06  2.32
```

- Analysis of SMR is like analysis of rates:
- Replace Y with E — that's all!