Representation and prediction in multistate models

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Representation of FU

- Many different ways of representing follow-up:
  - `msm`
  - `mstate`
  - `etm`
- some dedicated to a special model
- mostly on one timescale (the `st` machinery in Stata)
- generally derived from follow-up in a clinical trial with
  - entry at 0
  - exit at t
  - risk time t

MSM representation

Epochs (time-intervals)

- **Time** at start: The value of the timescale**s** of interest.
- **Length** of the epoch — risk time ("exposure")
- **State** in which the the time is spent
- **next** state: the state the person moves on to

This is a representation of the **risk time**

Representation of likelihood

- The likelihood terms in a multistate model comes naturally as one per **transition**:
- $$\exp\left(\int_{\text{in}}^{\text{out}} \lambda_j(u)\,\mathrm{d}u\right)$$
- . . . and for the events, additionally $\lambda_j(\text{out})$
- This is the **stacked** representation, allowing joint modeling of all transition rates in one go:
- Separate or joint parameters for each transition.

Lexis objects

data.frame with a few extra features:

timescales — chose any number, name as you please

lex.id — person identification

lex.dur — length of the epoch represented

lex.Cst — state of risk time (Current state)

lex.Xst — neXt state

`Lexis` objects - split objects

Splitting time with `splitLexis`:

- risk time in many small intervals
- assuming constant rates in each
- allows simple parametric modeling with `glm`
- using any number of time scales
- prediction of rates
- calculation of any derived measure

glm modeling form object Lx

```
> w2i <- glm( lex.Xst=="Ill" ~ v1 + v2 + v3,
+             family=poisson, offset=log(lex.dur),
+             data = subset( Lx, lex.Cst=="Well" ) )
> #
> w2d <- glm( lex.Xst=="Dead" ~ v1 + v2 + v3,
+             family=poisson, offset=log(lex.dur),
+             data = subset( Lx, lex.Cst=="Well" ) )
> #
> i2d <- glm( lex.Xst=="Dead" ~ v1 + v2 + v3,
+             family=poisson, offset=log(lex.dur),
+             data = subset( Lx, lex.Cst=="Ill" ) )
```

coxph modeling form object Lx

```
> w2i <- coxph( Surv( time, time+lex.dur, lex.Xst=="Ill" ) ~ v1 + v2 + v3,
+               data = subset( Lx, lex.Cst=="Well" ) )
> #
> w2d <- coxph( Surv( time, time+lex.dur, lex.Xst=="Dead" ) ~ v1 + v2 + v3,
+               data = subset( Lx, lex.Cst=="Well" ) )
> #
> i2d <- coxph( Surv( time, time+lex.dur, lex.Xst=="Dead" ) ~ v1 + v2 + v3,
+               data = subset( Lx, lex.Cst=="Ill" ) )
```

glm modeling form object Lx with update

```
> w2i <- glm( lex.Xst=="Ill" ~ v1 + v2 + v3,
+             family=poisson, offset=log(lex.dur),
+             data = subset( Lx, lex.Cst=="Well" ) )
> #
> w2d <- update( w2i, lex.Xst=="Dead" ~ . )
> #
> i2d <- update( w2d, data = subset( Lx, lex.Cst=="Ill" ) )
```

— but if you really **are** using the same covariates:

```
> mA <- glm( lex.Fail ~ lex.Tr + (v1 + v2 + v3):lex.Tr,
+            family=poisson, offset=log(lex.dur),
+            data = stack.Lexis( Lx ) )
```

lex.Tr has levels "Well->Ill", "Well->Dead" and "Ill->Dead"

Stacking – interface to `mstate`

- Stacking of the follow-up gives the terms that make up the likelihood
- `lex.Tr` has levels "`Well->Ill`", "`Well->Dead`" and "`Ill->Dead`"
- `lex.Fail` is logical.
- Used for the interface function `msdata.Lexis` — stacks the data and shaves away features.

Utilities — summaries

- `summary` — gives table of transitions and risk time
- `boxes` — shows it in a nice transition diagram (boxes)
- `plot` — plots follow-up in a Lexis diagram

Utilities — manipulation & restructuring

- `cutLexis` — cuts follow-up at a time point; transition to a new state.
- `splitLexis` — splits time in small intervals along a time scale at designated breaks.
- Both features need `stsplit` in Stata (+plus a bit of fidgeting)

Predicting using a single time scale

- With a parametric model for rates:
- closed form expressions for state probabilities etc.
- wrapping in a function with parameters as arguments
- parametric bootstrap does all for you
- `multistate` machinery from Michael C

Prediction using realistic models

- Simulation of an entire dataset through MS model
  - allowing multiple time scale
  - . . . also “time since state S”
- Enumeration of persons in states gives
- — state occupancy probabilities
- — expected sojourn times
- — expected life time probabilities

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ARTICLE

Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial

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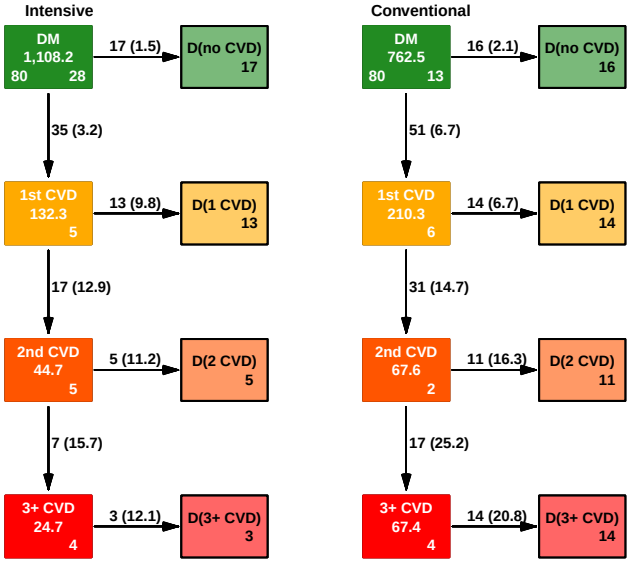
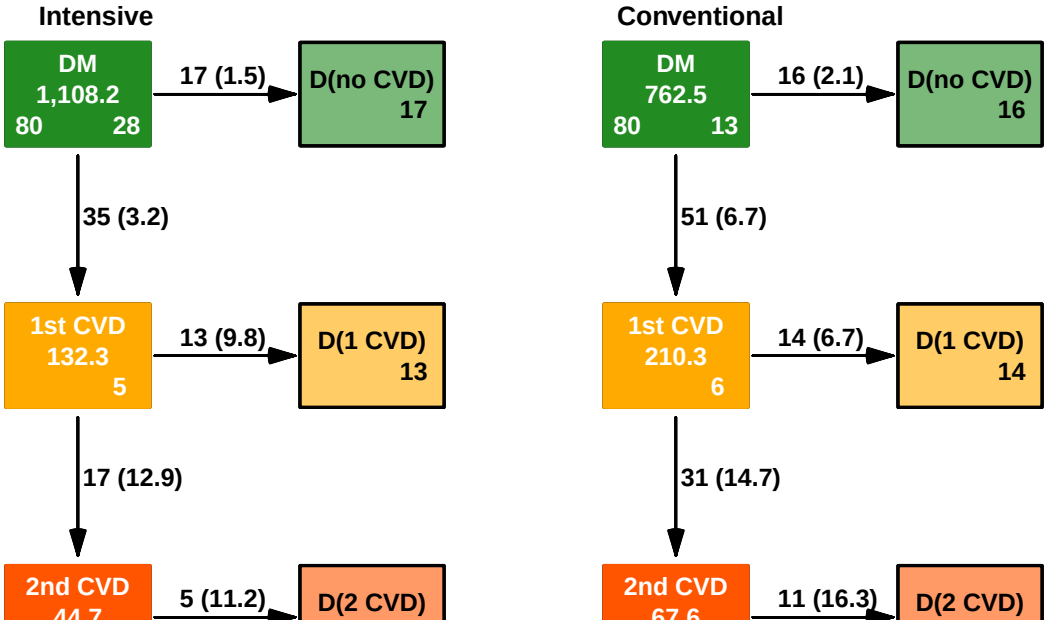
Abstract
Aims/hypothesis The aim of this work was to study the potential long-term impact of a 7.8 years intensified, multifactorial pharmacological approaches. After 7.8 years the study continued as an observational follow-up with all patients receiving treatment as for the original intensive-therapy group. The pri-


Intensive
DM
1,108.2
80 28
17 (1.5)
D(no CVD)
17
35 (3.2)
1st CVD
132.3
5
13 (9.8)
D(1 CVD)
13
17 (12.9)
2nd CVD
44.7
5
5 (11.2)
D(2 CVD)
5
7 (15.7)
3+ CVD
24.7
4
3 (12.1)
D(3+ CVD)
3
Conventional
DM
762.5
80 13
16 (2.1)
D(no CVD)
16
51 (6.7)
1st CVD
210.3
6
14 (6.7)
D(1 CVD)
14
31 (14.7)
2nd CVD
67.6
2
11 (16.3)
D(2 CVD)
11
17 (25.2)
3+ CVD
67.4
4
14 (20.8)
D(3+ CVD)
14


Intensive
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210.3
6
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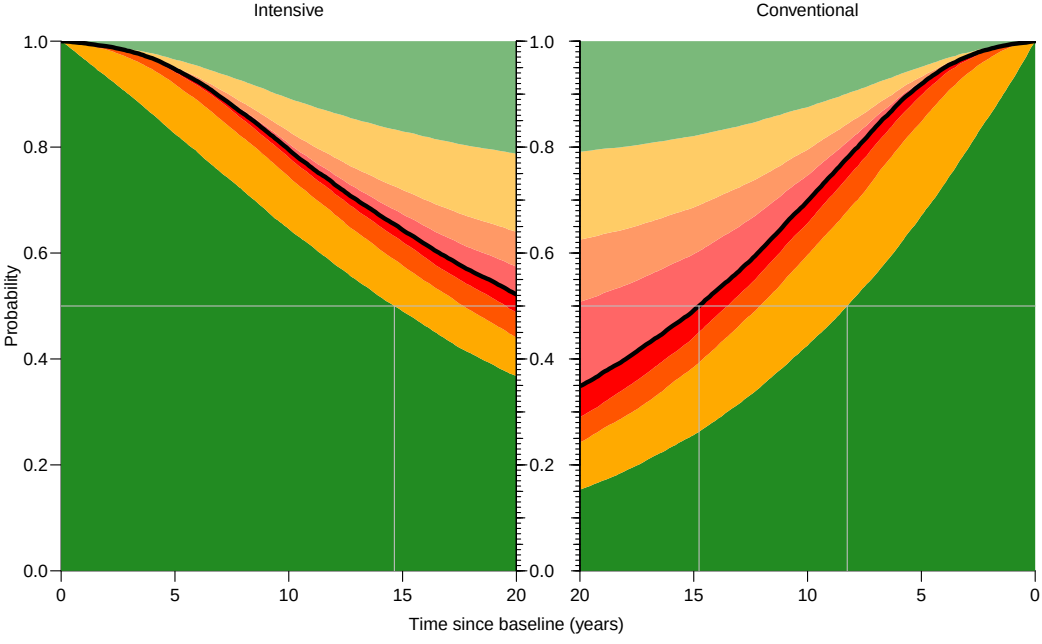
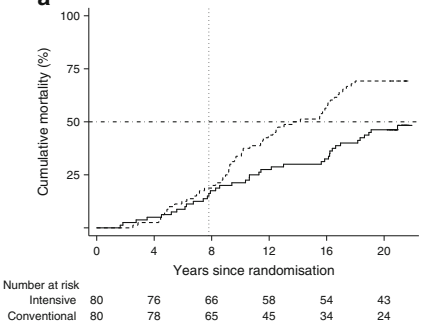
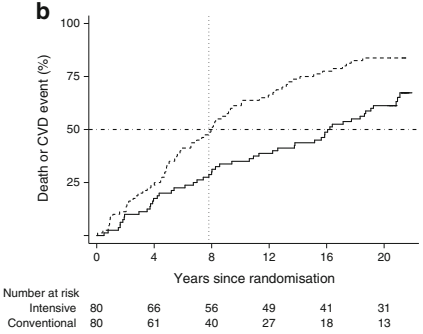
D(1 CVD)
14
31 (14.7)
2nd CVD
67.6
11 (16.3)
D(2 CVD)

Hazard ratios

	CVD event	Mortality
HR, Int. vs. Conv.	0.55 (0.39;0.77)	0.83 (0.54; 1.30)
H_0: PH btw. CVD groups	p=0.438	p=0.261
H_0: HR = 1	p=0.425	p=0.001
HR vs. 0 CVD events:		
0 (ref.)	1.00	1.00
1	2.43 (1.67;3.52)	3.08 (1.82; 5.19)
2	3.48 (2.15;5.64)	4.42 (2.36; 8.29)
3+		7.76 (4.11;14.65)


Intensive
Conventional
Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
Time since baseline (years)





between groups (HR 0.83 [95% CI 0.54, 1.30], $p = 0.43$). Thus, the reduced mortality was primarily due to reduced risk of CVD.

The patients in the intensive group experienced a total of 90 cardiovascular events vs 195 events in the conventional group. Nineteen intensive-group patients (24%) vs 34 conventional-group patients (43%) experienced more than one cardiovascular event. No significant between-group difference in the distribution of specific cardiovascular first-event types was observed (Table 2 and Fig. 4).

Microvascular complications Hazard rates of progression rates in microvascular complications compared with baseline status are shown Fig. 3. Sensitivity analyses showed a negligible effect of the random dates imputation.

Progression of retinopathy was decreased by 33% in the intensive-therapy group (Fig. 5). Blindness in at least one eye was reduced in the intensive-therapy group with an HR of 0.47 (95% CI 0.23, 0.98, $p = 0.044$). Autonomic neuropathy was decreased by 41% in the intensive-therapy group (Fig. 5). We observed no difference between groups in the progression of peripheral neuropathy (Fig. 5). Progression to diabetic nephropathy (macroalbuminuria) was reduced by 48% in the intensive-therapy group (Fig. 5). Ten patients in the conventional-therapy groups vs five patients in the intensive-therapy group progressed to end-stage renal disease ($p = 0.061$).

Discussion

Expected lifetime and YLL (well, gained)

Expected lifetime (years) in the Steno 2 cohort during the first 20 years after baseline by treatment group and CVD status.

State	Intensive	Conventional	Int.−Conv.
Alive	15.6	14.1	1.5
No CVD	12.7	10.0	2.6
Any CVD	3.0	4.1	−1.1

Expected lifetime (years) during the first 20 years after baseline by sex, age, treatment group and CVD status.

sex		Men			Women		
state	age	Int.	Conv.	Int.−Conv.	Int.	Conv.	Int.−Conv.
Alive	45	18.5	17.5	1.0	19.1	18.4	0.7
	50	17.2	16.1	1.1	18.0	17.2	0.8
	55	15.6	13.8	1.8	17.4	15.9	1.6
	60	13.9	11.6	2.2	15.5	13.7	1.8
	65	11.2	9.5	1.8	13.3	11.4	2.0
No CVD	45	14.9	12.5	2.4	15.8	14.3	1.5
	50	14.0	11.1	2.9	15.1	12.9	2.2
	55	12.2	9.7	2.5	14.3	11.6	2.7
	60	10.9	8.2	2.7	12.4	9.9	2.6
	65	9.0	6.7	2.2	10.7	8.3	2.4

Multistate models in practice:

- Representation:
  - States
  - Transitions
  - Sojourn times
  - Rates
- Analysis of rates:
  - Cox-model
  - Poisson model
- Reporting
  - Rates
  - HRs
  - Probabilities
  - Expected lifetime

Representation of multistate FU: Lexis

- Allowing multiple time scales
  - time-scale variables — the starting point on each time scale
  - sojourn time variable `lex.dur` — risktime, exposure
  - state variables:
- Allowing multiple states
  - `lex.Cst` — the state in which follow-up (`lex.dur`) occurs
  - `lex.Xst` — the state in which

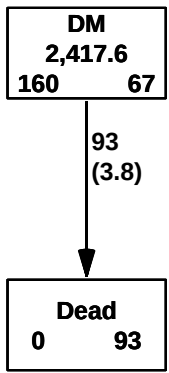
```
> head( st2[,-c(1,4:5,12,13)] )
```

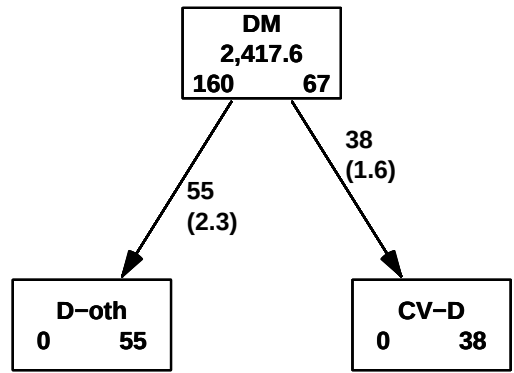
	allocation	sex	doBth	doDM	doBase	doCVD1	doCVD2	doCVD3	doDth
1	Intensive	M	1932.300	1991.093	1993.357	2014.457	NA	NA	NA
2	Intensive	M	1946.813	1982.130	1993.357	2009.231	2009.570	2010.162	NA
3	Conventional	M	1943.377	1982.560	1993.362	2001.639	NA	NA	2001.639
4	Conventional	M	1944.771	1976.791	1993.362	1995.415	1997.461	2003.443	2003.443
5	Conventional	M	1935.993	1986.346	1993.162	1993.959	1994.657	1998.047	1998.047
6	Conventional	M	1946.942	1986.404	1993.201	1998.769	NA	NA	NA

```
> L2 <- Lexis( entry = list( per = doBase,
+                            age = doBase-doBth,
+                            dur = doBase-doDM,
+                            tsb = 0 ),
+              exit = list( per = doEnd ),
+              exit.status = factor( ( !is.na(doDth) ) + deathCVD,
+                                    labels=c("DM","D-oth","CV-D") ),
+              data = st2 )

NOTE: entry.status has been set to "DM" for all.

> summary( L2 )

Transitions:
     To
From DM D-oth CV-D  Records:  Events: Risk time:  Persons:
  DM 67    55   38       160       93     2417.6       160
```

```
> L0 <- Lexis( entry = list( per = doBase,
+                            age = doBase-doBth,
+                            dur = doBase-doDM,
+                            tsb = 0 ),
+              exit = list( per = doEnd ),
+              exit.status = factor( ( !is.na(doDth) ),
+                                    labels=c("DM","Dead") ),
+              data = st2 )

NOTE: entry.status has been set to "DM" for all.

> summary( L0 )

Transitions:
     To
From DM Dead  Records:  Events: Risk time:  Persons:
  DM 67   93       160       93     2417.6       160
```

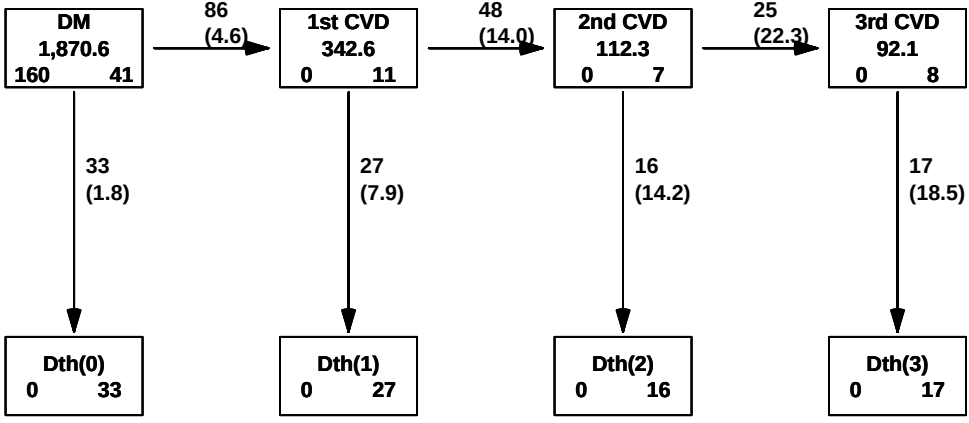
```
> par( mfrow=c(1,2) )
> boxes( L0, boxpos=list(x=c(50,50),y=c(85,15)),show.BE=T,scale.R=100)
> boxes( L2, boxpos=list(x=c(50,15,85),y=c(85,15,15)),show.BE=T,scale.R=100)
```

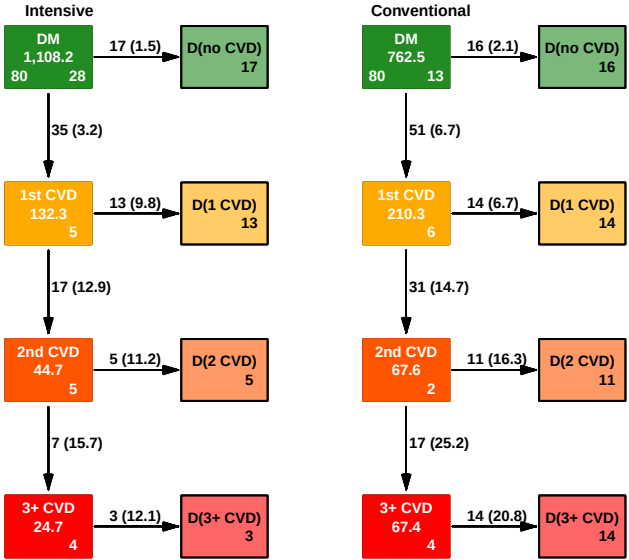




```
> L1 <- cutLexis( L0, cut = L0$doCVD1,
+                 new.state = "1st CVD",
+          precursor.states = c("DM"),
+              split.states = TRUE,
+                 new.scale = "tfCVD")
> #
> L1 <- cutLexis( L1, cut = L1$doCVD2,
+                 new.state = "2nd CVD",
+          precursor.states = c("DM","1st CVD"),
+              split.states = TRUE )
> #
> L1 <- cutLexis( L1, cut = L1$doCVD3,
+                 new.state = "3rd CVD",
+          precursor.states = c("DM","1st CVD","2nd CVD"),
+              split.states = TRUE )
> levels( L1 )

[1] "DM"                                "1st CVD"
[3] "2nd CVD"                           "3rd CVD"
[5] "Dead"                              "Dead(1st CVD)"
[7] "Dead(1st CVD)(2nd CVD)"            "Dead(1st CVD)(2nd CVD)(3rd CVD)"

> levels( L1$lex.Cst )[5:8] <-
+ levels( L1$lex.Xst )[5:8] <- paste("Dth(",0:3,")",sep="")
```

```
> boxes( L1, boxpos=list( x=c(rep(seq(15,85,,4),2) ),
+                         y=rep(c(85,20),each=4) ), show.BE=TRUE, scale.R=100 )
```




Intensive
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D(no CVD)
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35 (3.2)
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24.7
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D(3+ CVD)
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Conventional
DM
762.5
80 13
16 (2.1)
D(no CVD)
16
51 (6.7)
1st CVD
210.3
6
14 (6.7)
D(1 CVD)
14
31 (14.7)
2nd CVD
67.6
2
11 (16.3)
D(2 CVD)
11
17 (25.2)
3+ CVD
67.4
4
14 (20.8)
D(3+ CVD)
14

An added time scale

We added the timescale `tfCVD` using `new.scale="tfCVD"`

```
> subset( L1, lex.id==5 )[,1:9]
```

	per	age	dur	tsb	tfCVD	lex.dur	lex.Cst	lex.Xst	lex.id
10	1993.162	57.16906	6.815916	0.0000000	NA	0.7967146	DM	1st CVD	5
11	1993.959	57.96578	7.612631	0.7967146	0.000000	0.6981520	1st CVD	2nd CVD	5
12	1994.657	58.66393	8.310783	1.4948665	0.698152	3.3894593	2nd CVD	Dth(2)	5

An added time scale I

We added the timescale `tfCVD` using `new.scale="tfCVD"`

```
> S1 <- splitLexis( L1, breaks=seq(0,25,1/12), time.scale="tsb" )
> subset( S1, lex.id==5 )[,1:9]
```

	lex.id	per	age	dur	tsb	tfCVD	lex.dur	lex.Cst	le
741	5	1993.162	57.16906	6.815916	0.00000000	NA	0.08333333	DM	
742	5	1993.246	57.25240	6.899250	0.08333333	NA	0.08333333	DM	
743	5	1993.329	57.33573	6.982583	0.16666667	NA	0.08333333	DM	
744	5	1993.412	57.41906	7.065916	0.25000000	NA	0.08333333	DM	
745	5	1993.496	57.50240	7.149250	0.33333333	NA	0.08333333	DM	
746	5	1993.579	57.58573	7.232583	0.41666667	NA	0.08333333	DM	
747	5	1993.662	57.66906	7.315916	0.50000000	NA	0.08333333	DM	
748	5	1993.746	57.75240	7.399250	0.58333333	NA	0.08333333	DM	
749	5	1993.829	57.83573	7.482583	0.66666667	NA	0.08333333	DM	
750	5	1993.912	57.91906	7.565916	0.75000000	NA	0.04671458	DM	1s
751	5	1993.959	57.96578	7.612631	0.79671458	0.00000000	0.03661875	1st CVD	1s
752	5	1993.996	58.00240	7.649250	0.83333333	0.03661875	0.08333333	1st CVD	1s

An added time scale II

```
753      5 1994.079 58.08573  7.732583 0.91666667 0.11995209 0.08333333 1st CVD 1s
754      5 1994.162 58.16906  7.815916 1.00000000 0.20328542 0.08333333 1st CVD 1s
755      5 1994.246 58.25240  7.899250 1.08333333 0.28661875 0.08333333 1st CVD 1s
756      5 1994.329 58.33573  7.982583 1.16666667 0.36995209 0.08333333 1st CVD 1s
757      5 1994.412 58.41906  8.065916 1.25000000 0.45328542 0.08333333 1st CVD 1s
758      5 1994.496 58.50240  8.149250 1.33333333 0.53661875 0.08333333 1st CVD 1s
759      5 1994.579 58.58573  8.232583 1.41666667 0.61995209 0.07819986 1st CVD 2n
760      5 1994.657 58.66393  8.310783 1.49486653 0.69815195 0.00513347 2nd CVD 2n
761      5 1994.662 58.66906  8.315916 1.50000000 0.70328542 0.08333333 2nd CVD 2n
762      5 1994.746 58.75240  8.399250 1.58333333 0.78661875 0.08333333 2nd CVD 2n
763      5 1994.829 58.83573  8.482583 1.66666667 0.86995209 0.08333333 2nd CVD 2n
764      5 1994.912 58.91906  8.565916 1.75000000 0.95328542 0.08333333 2nd CVD 2n
765      5 1994.996 59.00240  8.649250 1.83333333 1.03661875 0.08333333 2nd CVD 2n
766      5 1995.079 59.08573  8.732583 1.91666667 1.11995209 0.08333333 2nd CVD 2n
767      5 1995.162 59.16906  8.815916 2.00000000 1.20328542 0.08333333 2nd CVD 2n
768      5 1995.246 59.25240  8.899250 2.08333333 1.28661875 0.08333333 2nd CVD 2n
769      5 1995.329 59.33573  8.982583 2.16666667 1.36995209 0.08333333 2nd CVD 2n
770      5 1995.412 59.41906  9.065916 2.25000000 1.45328542 0.08333333 2nd CVD 2n
771      5 1995.496 59.50240  9.149250 2.33333333 1.53661875 0.08333333 2nd CVD 2n
```

An added time scale III

```
772      5 1995.579 59.58573  9.232583 2.41666667 1.61995209 0.08333333 2nd CVD 2r
773      5 1995.662 59.66906  9.315916 2.50000000 1.70328542 0.08333333 2nd CVD 2r
774      5 1995.746 59.75240  9.399250 2.58333333 1.78661875 0.08333333 2nd CVD 2r
775      5 1995.829 59.83573  9.482583 2.66666667 1.86995209 0.08333333 2nd CVD 2r
776      5 1995.912 59.91906  9.565916 2.75000000 1.95328542 0.08333333 2nd CVD 2r
777      5 1995.996 60.00240  9.649250 2.83333333 2.03661875 0.08333333 2nd CVD 2r
778      5 1996.079 60.08573  9.732583 2.91666667 2.11995209 0.08333333 2nd CVD 2r
779      5 1996.162 60.16906  9.815916 3.00000000 2.20328542 0.08333333 2nd CVD 2r
780      5 1996.246 60.25240  9.899250 3.08333333 2.28661875 0.08333333 2nd CVD 2r
781      5 1996.329 60.33573  9.982583 3.16666667 2.36995209 0.08333333 2nd CVD 2r
782      5 1996.412 60.41906 10.065916 3.25000000 2.45328542 0.08333333 2nd CVD 2r
783      5 1996.496 60.50240 10.149250 3.33333333 2.53661875 0.08333333 2nd CVD 2r
784      5 1996.579 60.58573 10.232583 3.41666667 2.61995209 0.08333333 2nd CVD 2r
785      5 1996.662 60.66906 10.315916 3.50000000 2.70328542 0.08333333 2nd CVD 2r
786      5 1996.746 60.75240 10.399250 3.58333333 2.78661875 0.08333333 2nd CVD 2r
787      5 1996.829 60.83573 10.482583 3.66666667 2.86995209 0.08333333 2nd CVD 2r
788      5 1996.912 60.91906 10.565916 3.75000000 2.95328542 0.08333333 2nd CVD 2r
789      5 1996.996 61.00240 10.649250 3.83333333 3.03661875 0.08333333 2nd CVD 2r
790      5 1997.079 61.08573 10.732583 3.91666667 3.11995209 0.08333333 2nd CVD 2r
```

An added time scale IV

```
791      5 1997.162 61.16906 10.815916 4.00000000 3.20328542 0.08333333 2nd CVD 2r
792      5 1997.246 61.25240 10.899250 4.08333333 3.28661875 0.08333333 2nd CVD 2r
793      5 1997.329 61.33573 10.982583 4.16666667 3.36995209 0.08333333 2nd CVD 2r
794      5 1997.412 61.41906 11.065916 4.25000000 3.45328542 0.08333333 2nd CVD 2r
795      5 1997.496 61.50240 11.149250 4.33333333 3.53661875 0.08333333 2nd CVD 2r
796      5 1997.579 61.58573 11.232583 4.41666667 3.61995209 0.08333333 2nd CVD 2r
797      5 1997.662 61.66906 11.315916 4.50000000 3.70328542 0.08333333 2nd CVD 2r
798      5 1997.746 61.75240 11.399250 4.58333333 3.78661875 0.08333333 2nd CVD 2r
799      5 1997.829 61.83573 11.482583 4.66666667 3.86995209 0.08333333 2nd CVD 2r
800      5 1997.912 61.91906 11.565916 4.75000000 3.95328542 0.08333333 2nd CVD 2r
801      5 1997.996 62.00240 11.649250 4.83333333 4.03661875 0.05099247 2nd CVD  I
```

Representation of multistate FU: `Lexis` I

lex.id	per	age	dur	tsb	tfCVD	lex.dur	lex.Cst	lex.Xst
5	1993.162	57.16906	6.815916	0.000000	NA	0.0833333	DM	DM
5	1993.246	57.25240	6.899250	0.083333	NA	0.0833333	DM	DM
...								
5	1993.912	57.91906	7.565916	0.750000	NA	0.0467145	DM	1st CVD
5	1993.959	57.96578	7.612631	0.796714	0.000000	0.0366187	1st CVD	1st CVD
5	1993.996	58.00240	7.649250	0.833333	0.036618	0.0833333	1st CVD	1st CVD
...								
5	1994.579	58.58573	8.232583	1.416666	0.619952	0.0781998	1st CVD	2nd CVD
5	1994.657	58.66393	8.310783	1.494866	0.698151	0.0051334	2nd CVD	2nd CVD
...								
5	1997.912	61.91906	11.565916	4.750000	3.953285	0.0833333	2nd CVD	2nd CVD
5	1997.996	62.00240	11.649250	4.833333	4.036618	0.0509924	2nd CVD	Dth(2)

Modeling mortality rates in Lexis objects

```
> dlev <- c("D(no CVD)", "D(1 CVD)",  "D(2 CVD)",  "D(3+ CVD)")
> #
> m0 <- glm( (lex.Xst %in% dlev ) ~
+            Ns( tsb, knots=d.kn ) + lex.Cst + allocation,
+            offset = log(lex.dur),
+            family = poisson,
+            data = S1 )
> #
> m1  <- update( m0, . ~ . + sex + age )                    # the real model
> #
> m1i <- update( m1, . ~ . - allocation + allocation:lex.Cst )
> #
> # Test interaction
> anova( m1i, m1, test="Chisq" )
```

Modeling CVD rates in `Lexis` objects

```
> clev <- c("1st CVD","2nd CVD","3+ CVD")
> #
> c0 <- glm( ( (lex.Xst %in% clev) & (lex.Cst!=lex.Xst) ) ~
+            Ns( tsb, knots=d.kn ) + lex.Cst + allocation,
+            offset = log(lex.dur),
+            family = poisson,
+            data = subset( S1, lex.Cst!="3+ CVD" ) )
> #
> c1  <- update( c0, . ~ . + sex + age )
> #
> c1i <- update( c1, . ~ . - allocation + allocation:lex.Cst )
> #
> c1p <- update( c1, . ~ . + allocation:tsb )
> #
> # Test interaction & PH
> anova( c1i, c1, c1p, test="Chisq" )
```

Simulation: transition object

```
> TM1 <- list( "DM" = list( "D(no CVD)" = m1,
+                           "1st CVD" = c1 ),
+          "1st CVD" = list(  "D(1 CVD)" = m1,
+                           "2nd CVD" = c1 ),
+          "2nd CVD" = list(  "D(2 CVD)" = m1,
+                            "3+ CVD" = c1 ),
+           "3+ CVD" = list( "D(3+ CVD)" = m1 ) )
```

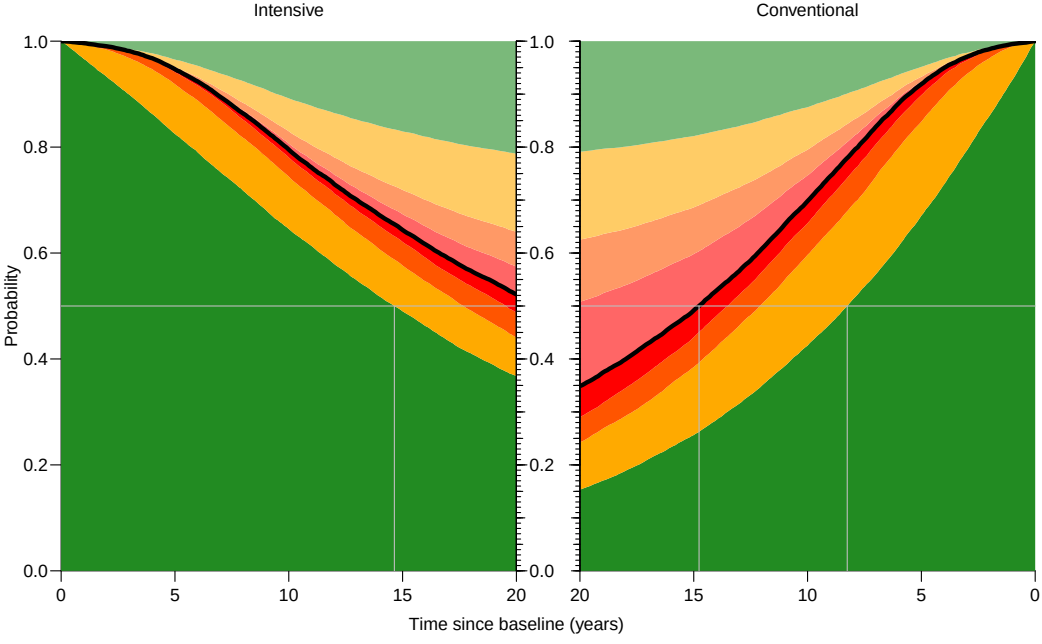
Simulation: baseline (init) object

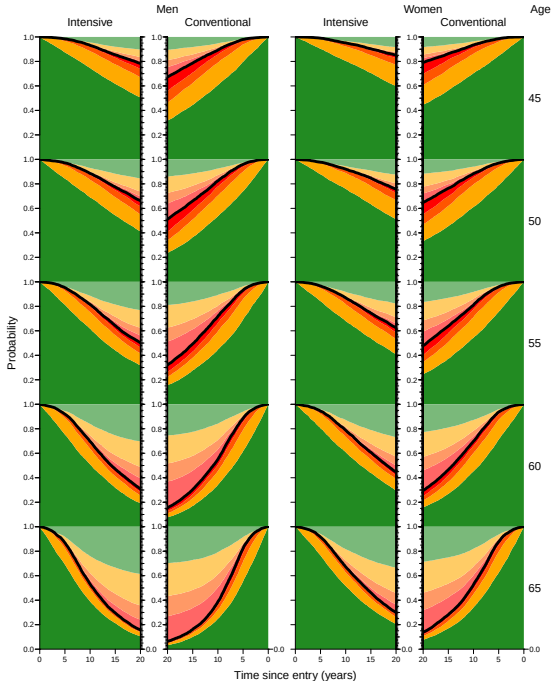
```
> St2 <- subset( L1, select = c(timeScales(L1),"lex.Cst","lex.dur",
+                               "allocation","sex") )
> levels(St2$lex.Cst) <- levels(S1$lex.Cst)
> nr <- nrow(St2)
> St2[1:nr,"tsb"] <- 0
> St2[1:nr,"lex.Cst"] <- levels(St2$lex.Cst)[1]
> St2[1:nr,"allocation"] <- levels(S1$allocation)[1]
> St2 <- rbind( St2, St2 )
> St2[1:nr,"allocation"] <- levels(S1$allocation)[2]
```

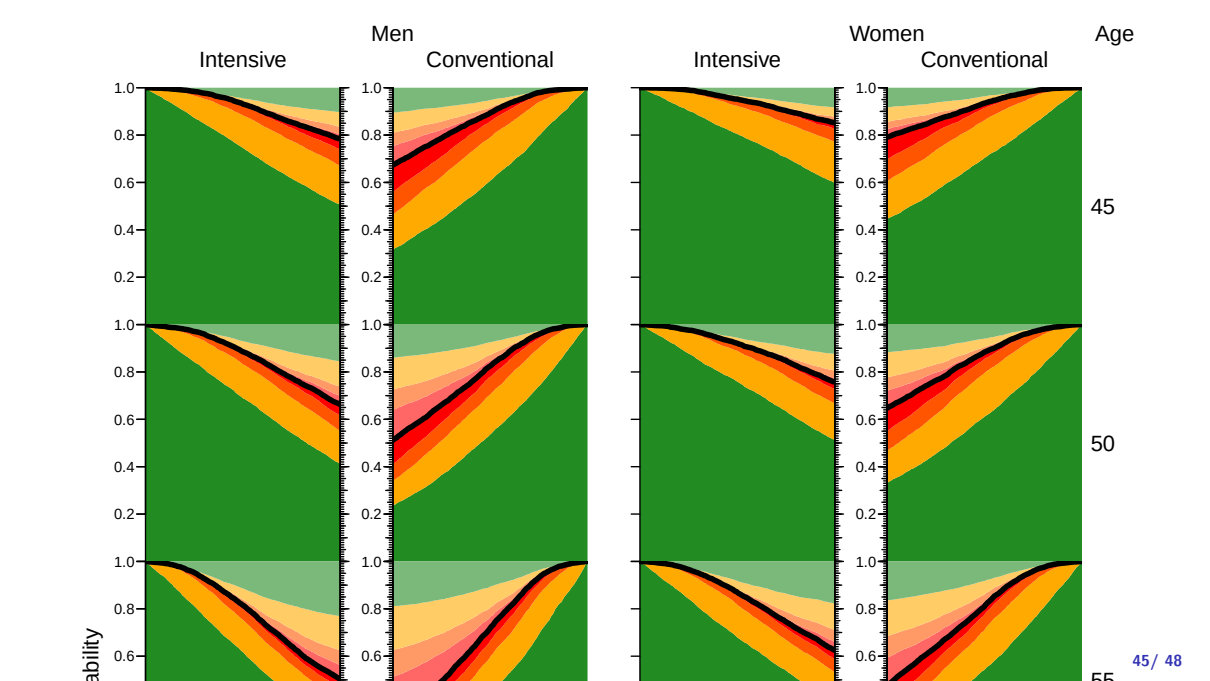
`St2` is a copy of the original date with `allocation="Intensive"` plus a copy of the original date with `allocation="Conventional"`

Simylating a follow up dataset

```
> sim2 <- simLexis( Tr = TM1,
+                  init = St2,
+                     N = 100,
+              time.pts = seq(0,21,0.1) )
> StC <- nState( subset(sim2,allocation=="Conventional"),
+                at=seq(0,20,0.1), from=0, time.scale="tsb" )
> StI <- nState( subset(sim2,allocation=="Intensive"),
+                at=seq(0,20,0.1), from=0, time.scale="tsb" )
> prm <- c(1:4,8:5)
> pC <- pState( StC, perm=prm )
> pI <- pState( StI, perm=prm )
```

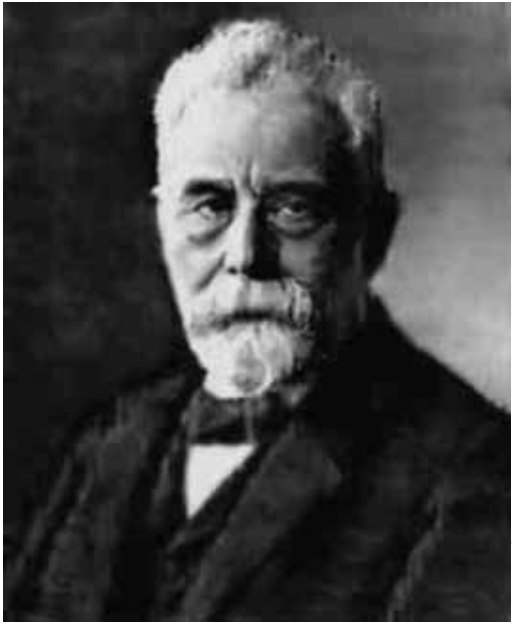

Intensive
Conventional
Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
Time since baseline (years)


Men
Women
Intensive
Conventional
Intensive
Conventional
Age
45
50
55
60
65
Probability
Time since entry (years)


Men
Women
Age
Intensive
Conventional
Intensive
Conventional
1.0
0.8
0.6
0.4
0.2
45
50
55
ability

History

- `Epi` package grew out of "Statistical Practice in Epidemiology with R", annually since 2002 in Tartu Estonia
- `Lexis` machinery conceived by Martyn Plummer, IARC
- Naming originally by David Clayton & Michael Hills, `stlexis` in Stata, later renamed `stsplit`
- David Claytion wrote a `lexis` function for the `Epi` package. Obsolete now.



THEORIE

DER

BEVÖLKERUNGSSTATISTIK

VON

W. LEXIS

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

STRASSBURG

KARL J. TRÜBNER

1875.

Summary

- Proper representation of multistate data essential:
  States, transitions, risk time
- Readable modeling code
- Calculation of state probabilities requires a simulation in any realistic situation
- Examples of use in:
  `http://bendixcarstensen.com/AdvCoh/Lexis-ex/`

Thanks for your attention