Years of Life Lost (YLL) to disease
Diabetes in DK as example

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Chapter 1

Theory and technicalities

This vignette for the `Epi` package describes the probabilistic and demographic background for and technical implementation of the `erl` and `yll` functions that computes the expected residual life time and years of life lost in an illness-death model.

1.1 Years of life lost (YLL)

...to diabetes or any other disease for that matter.

The general concept in calculation of "years lost to..." is the comparison of the expected lifetime between two groups of persons; one with and one without disease (in this example DM). The expected lifetime is the area under the survival curve, so basically the exercise requires that two survival curves that are deemed relevant be available.

The years of life lost is therefore just the area between the survival curves for those "Well", $S_W(t)$, and for those "Diseased", $S_D(t)$:

$$\text{YLL} = \int_0^\infty S_W(t) - S_D(t) \, \mathrm{d}t$$

The time t could of course be age, but it could also be "time after age 50" and the survival curves compared would then be survival curves *conditional* on survival till age 50, and the YLL would be the years of life lost for a 50-year old person with diabetes.

If we are referring to the expected lifetime we will more precisely use the label expected residual lifetime, ERL.

1.2 Constructing the survival curves

YLL can be computed in two different ways, depending on the way the survival curve and hence the expected lifetime of a person *without* diabetes is computed:

- Assume that the "Well" persons are *immune* to disease — using only the non-DM mortality rates throughout for calculation of expected life time.

- Assume that the "Well" persons *can* acquire the disease and thereby see an increased mortality, thus involving all three rates shown in figure 1.1.

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The former gives a higher YLL because the comparison is to persons assumed immune to DM (and yet with the same mortality as non-immune prior to diagnosis), the latter gives a more realistic picture of the comparison of group of persons with and without diabetes at a given age that can be interpreted in the real world.

The differences can be illustrated by figure 1.1; the immune approach corresponds to an assumption of $\lambda(t) = 0$ in the calculation of the survival curve for a person in the "Well" state.

Calculation of the survival of a diseased person already in the "DM" state is unaffected by assumptions about λ.
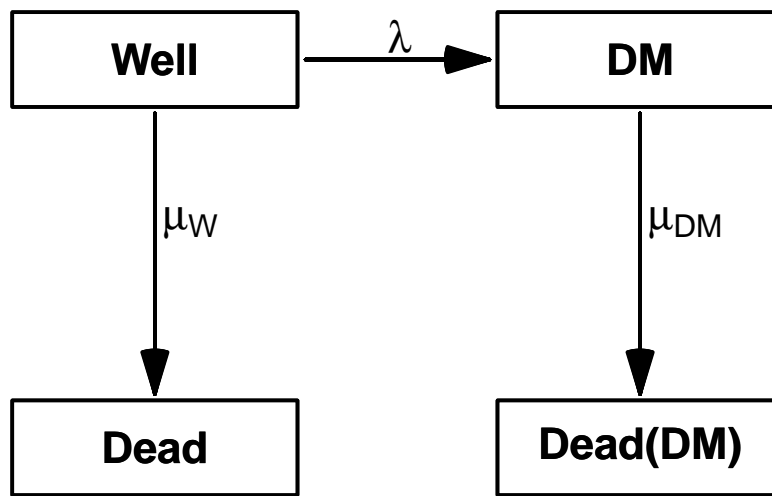
Figure 1.1: *Illness-death model describing diabetes incidence and -mortality.* `./yll-states`

1.2.1 Total mortality — a shortcut?

A practical crude shortcut could be to compare the ERL in the diabetic population to the ERL for the *entire* population (that is use the total mortality ignoring diabetes status).

Note however that this approach also counts the mortality of persons that acquired the disease earlier, thus making the comparison population on average more ill than the population we aim at, namely those well at a given time, which only then become more gradually ill.

How large these effects are can however be empirically explored, as we shall do later.

1.2.2 Disease duration

In the exposition above there is no explicit provision for the effect of disease duration, but if we were able to devise mortality rates for any combination of age and duration, this could be taken into account.

There are however severe limitations in this as we in principle would want to have duration effects as long as the age-effects — in principle for all (a, d) where $d \leq A$, where A is the age at which we condition. So even if we were only to compute ERL from age, say, 40 we would still need duration effects up to 60 years (namely to age 100).

The incorporation of duration effects is in principle trivial from a computational point of view, but we would be forced to entertain models predicting duration effects way beyond what is actually observed disease duration in any practical case.

1.2.3 Computing integrals

The practical calculations of survival curves, ERL and YLL involves calculation of (cumulative) integrals of rates and functions of these as we shall see below. This is easy if we have a closed form expression of the function, so its value may be computed at any time point — this will be the case if we model rates by smooth parametric functions.

Computing the (cumulative) integral of a function is done as follows:

- Compute the value of the function (mortality rate for example) at the midpoints of a sequence of narrow equidistant intervals — for example one- or three month intervals of age, say.

- Take the cumulative sum of these values multiplied by the interval length — this will be a very close approximation to the cumulative integral evaluated at the end of each interval.

- If the intervals are really small (like 1/100 year), the distinction between the value at the middle and at the end of each interval becomes irrelevant.

Note that in the above it is assumed that the rates are given in units corresponding to the interval length — or more precisely, as the cumulative rates over the interval.

1.3 Survival functions in the illness-death model

The survival functions for persons in the "Well" state can be computed under two fundamentally different scenarios, depending on whether persons in the "Well" state are assumed to be immune to the disease ($\lambda(a) = 0$) or not.

1.3.1 Immune approach

In this case both survival functions for person in the two states are the usual simple transformation of the cumulative mortality rates:

$$S_W(a) = \exp\left(-\int_0^a \mu_W(u)\,\mathrm{d}u\right), \qquad S_D(a) = \exp\left(-\int_0^a \mu_D(u)\,\mathrm{d}u\right)$$

Conditional survival functions

If we want the *conditional* survival functions given survival to age A, say, they are just:

$$S_W(a|A) = S_W(a)/S_W(A), \qquad S_D(a|A) = S_D(a)/S_D(A)$$

1.3.2   Non-immune approach

For a diseased person, the survival function in this states is the same as above, but the survival function for a person without disease (at age 0) is (see figure 1.1):

$$S(a) = \text{P\{Well\}}(a) + \text{P\{DM\}}(a)$$

In the appendix of the paper [2] is an indication of how to compute the probability of being in any of the four states shown in figure 1.1, which I shall repeat here:

In terms of the rates, the probability of being in the "Well" box is simply the probability of escaping both death (at a rate of $\mu_W(a)$) and diabetes (at a rate of $\lambda(a)$):

$$\text{P\{Well\}}(a) = \exp\left(-\int_0^a \mu_W(u) + \lambda(u)\right)\,\mathrm{d}u$$

The probability of being alive with diabetes at age a, is computed given that diabetes occurred at age s $(s < a)$ and then integrated over s from 0 to a:

$$\begin{aligned}
\text{P\{DM\}}(a) &= \int_0^a \text{P\{survive to } s\text{, DM diagnosed at } s\} \\
&\quad \times \text{P\{survive with DM from } s \text{ to } a\}\,\mathrm{d}s \\
&= \int_0^a \lambda(s) \exp\left(-\int_0^s \mu_W(u) + \lambda(u)\,\mathrm{d}u\right) \\
&\quad \times \exp\left(-\int_s^a \mu_D(u)\,\mathrm{d}u\right)\,\mathrm{d}s
\end{aligned}$$

Sometimes we will use a version where the mortality among diabetes patients depend both on age a and duration of diabetes, d, $\mu_D(a, d)$, in which case we get:

$$\begin{aligned}
\text{P\{DM\}}(a) &= \int_0^a \lambda(s) \exp\left(-\int_0^s \mu_W(u) + \lambda(u)\,\mathrm{d}u\right) \\
&\quad \times \exp\left(-\int_s^a \mu_D(u, u - s)\,\mathrm{d}u\right)\,\mathrm{d}s
\end{aligned}$$

because the integration variable u is the age-scale and the second integral refers to mortality among persons diagnosed at age s, that is, with duration $u - s$ at age u.

The option of using duration-dependent mortality rates among diseased individuals is not implemented yet.

Conditional survival functions

Unlike the immune approach, the conditional survival function in the more realistic case is not just a ratio of the unconditional to the value at the conditioning age, A, say. This would amount to conditioning on being merely *alive* at age A, but what we want is to condition on being in the "Well" state at age A.

The formulae for the conditional probabilities of being either in "Well" or "DM", given being in "Well" at age A are basically replicates of the unconditional, albeit with changes in

integration limits:

$$P\{\text{Well}|\text{Well at } A\}(a) = \exp\left(-\int_A^a \mu_W(u) + \lambda(u)\right) du$$

$$P\{\text{DM}|\text{Well at } A\}(a) = \int_A^a \lambda(s) \exp\left(-\int_A^s \mu_W(u) + \lambda(u)\, du\right)$$

$$\times \exp\left(-\int_s^a \mu_D(u, u - s)\, du\right) ds$$

The calculation of these conditional survival functions is implemented but not allowing for duration-dependence. Thus it is only implemented assuming $\mu_D(a, d) = \mu_D(a)$.

Chapter 2

Analyses for DM in Denmark

The rates we use as basis for the following calculations are derived from the NDR, where we have omitted the blood-glucose criteria, because there is compelling evidence that these have quite a low specificity (particularly in the younger ages among women), and do not substantially contribute to the sensitivity.

As noted above the calculations of YLL requires access to (age-specific) rates of incidence of DM and mortality for persons with and without DM.

2.1   Modeling mortality and incidence data

We read in the dataset of DM and population mortality and incidence, `DMepi`:

```
> data( DMepi )
```

The dataset `DMepi` contains diabetes events, deaths and person-years for persons without diabetes and deaths and person-years for persons with diabetes:

```
> str( DMepi )
'data.frame':        4200 obs. of  8 variables:
 $ sex : Factor w/ 2 levels "M","F": 1 1 1 1 1 1 1 1 1 1 ...
 $ A   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ P   : num  1996 1997 1998 1999 2000 ...
 $ D.DM: num  0 0 0 0 0 0 0 0 0 0 ...
 $ Y.DM: num  0.484 0.64 1.641 0.552 2.507 ...
 $ X   : num  1 2 4 4 4 1 1 3 4 1 ...
 $ D.nD: num  28 19 20 11 21 16 21 15 16 16 ...
 $ Y.nD: num  35469 35085 34240 34056 34002 ...
> head( DMepi )
  sex A    P D.DM       Y.DM X D.nD      Y.nD
2   M 0 1996    0 0.4839151 1   28 35468.92
3   M 0 1997    0 0.6399726 2   19 35085.18
4   M 0 1998    0 1.6406571 4   20 34240.14
5   M 0 1999    0 0.5523614 4   11 34055.52
6   M 0 2000    0 2.5065024 4   21 34002.22
7   M 0 2001    0 0.1184120 1   16 34177.39
```

For each combination of sex, age, period and date of birth in 1 year age groups, we have the person-years in the "Well" (`Y.nD`) and the "DM" (`Y.DM`) states, as well as the number of

deaths from these (`D.nD`, `D.DM`) and the number of incident diabetes cases from the "Well" state (`X`).

In order to compute the years of life lost to diabetes and how this has changed over time, we fit models for the mortality and incidence of both groups (and of course, separately for men and women). The models we use will be age-period-cohort models [1] providing estimated mortality rates for ages 0–99 and dates 1.1.1996–1.1.2016.

First we transform the age and period variables to reflect the mean age and period in each of the Lexis triangles. We also compute the total number of deaths and amount of risk time, as we are going to model the total mortality as well. Finally we restrict the dataset to ages over 30 only:

```
> DMepi <- transform( subset( DMepi, A>30 ),
+                     D.T = D.nD + D.DM,
+                     Y.T = Y.nD + Y.DM )
> head(DMepi)
    sex  A    P D.DM     Y.DM  X D.nD     Y.nD D.T      Y.T
684   M 31 1996    0 305.9671 29   51 44161.83  51 44467.80
685   M 31 1997    2 326.2074 31   54 45508.64  56 45834.85
686   M 31 1998    2 340.1759 34   46 44954.45  48 45294.63
687   M 31 1999    5 330.9918 24   39 41148.97  44 41479.96
688   M 31 2000    1 332.0876 41   26 39027.30  27 39359.39
689   M 31 2001    2 310.8467 35   33 37975.78  35 38286.63
```

With the correct age and period coding in the Lexis triangles, we fit models for the mortalities and incidences. Note that we for comparative purposes also fit a model for the *total* mortality, ignoring the

```
> # Knots used in all models
> ( a.kn <- seq(40,95,,6) )
[1] 40 51 62 73 84 95

> ( p.kn <- seq(1997,2015,,4) )
[1] 1997 2003 2009 2015

> ( c.kn <- seq(1910,1976,,6) )
[1] 1910.0 1923.2 1936.4 1949.6 1962.8 1976.0

> # Check the number of events between knots
> ae <- xtabs( cbind(D.nD,D.DM,X) ~ cut(A,c(30,a.kn,Inf)) + sex, data=DMepi )
> ftable( addmargins(ae,1), col.vars=3:2 )
```

		D.nD		D.DM		X	
	sex	M	F	M	F	M	F
cut(A, c(30, a.kn, Inf))							
(30,40]		9135	4650	597	277	12080	9648
(40,51]		25535	15784	2947	1439	35445	23925
(51,62]		59698	40171	10838	5253	60539	40034
(62,73]		106519	81253	26197	14299	55908	44221
(73,84]		158365	156678	34510	28834	27985	30381
(84,95]		100880	179466	16194	25317	5272	8967
(95,Inf]		6095	21414	640	1928	90	288
Sum		466227	499416	91923	77347	197319	157464

```
> pe <- xtabs( cbind(D.nD,D.DM,X) ~ cut(P,c(1990,p.kn,Inf)) + sex, data=DMepi )
> ftable( addmargins(pe,1), col.vars=3:2 )
```

```
                              D.nD            D.DM              X
                    sex     M       F       M       F       M       F
cut(P, c(1990, p.kn, Inf))
(1990,1997]                51569   53567    6407    5990   13175   10960
(1997,2003]               144136  155695   22390   19922   49805   41277
(2003,2009]               131159  141782   26079   22249   60554   48066
(2009,2015]               119812  127714   31285   24704   63440   49457
(2015,Inf]                 19551   20658    5762    4482   10345    7704
Sum                       466227  499416   91923   77347  197319  157464

> ce <- xtabs( cbind(D.nD,D.DM,X) ~ cut(P-A,c(-Inf,c.kn,Inf)) + sex, data=DMepi )
> ftable( addmargins(ce,1), col.vars=3:2 )
                              D.nD            D.DM              X
                    sex     M       F       M       F       M       F
cut(P - A, c(-Inf, c.kn, Inf))
(-Inf,1.91e+03]            19679   49020    2004    4446     599    1416
(1.91e+03,1.92e+03]      129799  189192   19780   26870   10665   15275
(1.92e+03,1.94e+03]      158953  152454   35667   28471   37850   36659
(1.94e+03,1.95e+03]       99058   72432   25494   13074   71489   50631
(1.95e+03,1.96e+03]       44129   28315    7534    3731   51750   34255
(1.96e+03,1.98e+03]       13598    7484    1373     720   22942   17689
(1.98e+03, Inf]            1011     519      71      35    2024    1539
Sum                       466227  499416   91923   77347  197319  157464

> # Fit an APC-model for all transitions, seperately for men and women
> mW.m <- glm( D.nD ~ -1 + Ns(A  ,knots=a.kn,int=TRUE) +
+                         Ns(  P,knots=p.kn,ref=2005) +
+                         Ns(P-A,knots=c.kn,ref=1950),
+          offset = log(Y.nD),
+          family = poisson,
+            data = subset( DMepi, sex=="M" ) )
> mD.m <- update( mW.m,  D.DM ~ . , offset=log(Y.DM) )
> mT.m <- update( mW.m,  D.T  ~ . , offset=log(Y.T ) )
> lW.m <- update( mW.m,  X ~ . )
> # Model for women
> mW.f <- update( mW.m, data = subset( DMepi, sex=="F" ) )
> mD.f <- update( mD.m, data = subset( DMepi, sex=="F" ) )
> mT.f <- update( mT.m, data = subset( DMepi, sex=="F" ) )
> lW.f <- update( lW.m, data = subset( DMepi, sex=="F" ) )
```

2.2   Residual life time and years lost to DM

We now collect the estimated years of life lost classified by method (immune assumption or
not), sex, age and calendar time:

```
> a.ref <- 30:90
> p.ref <- 1996:2016
> aYLL <- NArray( list( type = c("Imm","Tot","Sus"),
+                        sex = levels( DMepi$sex ),
+                        age = a.ref,
+                       date = p.ref ) )
> str( aYLL )
 logi [1:3, 1:2, 1:61, 1:21] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 4
  ..$ type: chr [1:3] "Imm" "Tot" "Sus"
  ..$ sex : chr [1:2] "M" "F"
```

```
    ..$ age : chr [1:61] "30" "31" "32" "33" ...
    ..$ date: chr [1:21] "1996" "1997" "1998" "1999" ...

> system.time(
+ for( ip in p.ref )
+    {
+    nd <- data.frame( A = seq(30,90,0.2)+0.1,
+                      P = ip,
+                  Y.nD = 1,
+                  Y.DM = 1,
+                  Y.T  = 1 )
+    muW.m <- ci.pred( mW.m, nd )[,1]
+    muD.m <- ci.pred( mD.m, nd )[,1]
+    muT.m <- ci.pred( mT.m, nd )[,1]
+    lam.m <- ci.pred( lW.m, nd )[,1]
+    muW.f <- ci.pred( mW.f, nd )[,1]
+    muD.f <- ci.pred( mD.f, nd )[,1]
+    muT.f <- ci.pred( mT.f, nd )[,1]
+    lam.f <- ci.pred( lW.f, nd )[,1]
+    aYLL["Imm","M",,paste(ip)] <- yll( int=0.2, muW.m, muD.m, lam=NULL,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    aYLL["Imm","F",,paste(ip)] <- yll( int=0.2, muW.f, muD.f, lam=NULL,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    aYLL["Tot","M",,paste(ip)] <- yll( int=0.2, muT.m, muD.m, lam=NULL,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    aYLL["Tot","F",,paste(ip)] <- yll( int=0.2, muT.f, muD.f, lam=NULL,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    aYLL["Sus","M",,paste(ip)] <- yll( int=0.2, muW.m, muD.m, lam=lam.m,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    aYLL["Sus","F",,paste(ip)] <- yll( int=0.2, muW.f, muD.f, lam=lam.f,
+                                       A=a.ref, age.in=30, note=FALSE )[-1]
+    } )
   user  system elapsed
 17.881   8.404  15.899
> round( ftable( aYLL[,,seq(1,61,10),], col.vars=c(3,2) ), 1 )
```

		age 30		40		50		60		70		80		90	
		sex M	F	M	F	M	F	M	F	M	F	M	F	M	F
type	date														
Imm	1996	11.3	10.2	9.4	9.1	7.4	7.6	5.4	5.9	3.4	3.8	1.5	1.6	0.0	0.0
	1997	11.1	9.9	9.2	8.9	7.3	7.4	5.3	5.7	3.3	3.7	1.4	1.5	0.0	0.0
	1998	10.9	9.7	9.1	8.6	7.2	7.2	5.3	5.5	3.3	3.6	1.4	1.5	0.0	0.0
	1999	10.7	9.4	9.0	8.4	7.1	7.0	5.2	5.3	3.3	3.5	1.4	1.5	0.0	0.0
	2000	10.5	9.1	8.8	8.2	6.9	6.8	5.1	5.1	3.2	3.4	1.4	1.4	0.0	0.0
	2001	10.3	8.9	8.6	7.9	6.8	6.6	5.0	5.0	3.1	3.2	1.3	1.4	0.0	0.0
	2002	10.0	8.6	8.4	7.7	6.6	6.3	4.9	4.8	3.1	3.1	1.3	1.3	0.0	0.0
	2003	9.7	8.3	8.2	7.4	6.4	6.1	4.7	4.6	3.0	3.0	1.3	1.3	0.0	0.0
	2004	9.4	8.0	7.9	7.1	6.2	5.9	4.5	4.4	2.8	2.8	1.2	1.2	0.0	0.0
	2005	9.0	7.6	7.6	6.9	6.0	5.6	4.4	4.1	2.7	2.6	1.1	1.1	0.0	0.0
	2006	8.6	7.3	7.4	6.6	5.8	5.4	4.2	3.9	2.6	2.5	1.1	1.1	0.0	0.0
	2007	8.3	7.0	7.1	6.3	5.5	5.2	4.0	3.8	2.5	2.4	1.0	1.0	0.0	0.0
	2008	8.0	6.8	6.8	6.1	5.4	5.0	3.8	3.6	2.4	2.2	1.0	0.9	0.0	0.0
	2009	7.7	6.6	6.6	6.0	5.2	4.9	3.7	3.5	2.3	2.1	0.9	0.9	0.0	0.0
	2010	7.5	6.4	6.5	5.8	5.1	4.8	3.7	3.4	2.2	2.1	0.9	0.9	0.0	0.0
	2011	7.4	6.3	6.4	5.8	5.1	4.7	3.6	3.4	2.2	2.0	0.9	0.8	0.0	0.0
	2012	7.3	6.3	6.4	5.7	5.1	4.7	3.6	3.3	2.2	2.0	0.9	0.8	0.0	0.0
	2013	7.3	6.2	6.4	5.7	5.1	4.7	3.6	3.3	2.2	2.0	0.9	0.8	0.0	0.0
	2014	7.3	6.2	6.4	5.7	5.1	4.7	3.7	3.4	2.2	2.0	0.9	0.8	0.0	0.0

```
        2015      7.3  6.2  6.4  5.7  5.2  4.8  3.7  3.4  2.3  2.0  0.9  0.8  0.0  0.0
        2016      7.3  6.2  6.4  5.7  5.2  4.8  3.8  3.4  2.3  2.0  0.9  0.8  0.0  0.0
Tot     1996     10.7  9.8  8.8  8.7  6.9  7.2  5.0  5.5  3.1  3.5  1.3  1.4  0.0  0.0
        1997     10.5  9.5  8.6  8.4  6.7  7.0  4.9  5.3  3.0  3.4  1.3  1.4  0.0  0.0
        1998     10.3  9.2  8.5  8.2  6.6  6.8  4.8  5.1  3.0  3.3  1.3  1.4  0.0  0.0
        1999     10.0  8.9  8.3  7.9  6.5  6.5  4.7  4.9  2.9  3.2  1.3  1.3  0.0  0.0
        2000      9.8  8.7  8.1  7.7  6.3  6.3  4.6  4.7  2.9  3.1  1.2  1.3  0.0  0.0
        2001      9.6  8.4  7.9  7.4  6.2  6.1  4.5  4.6  2.8  2.9  1.2  1.2  0.0  0.0
        2002      9.3  8.1  7.7  7.2  6.0  5.9  4.3  4.4  2.7  2.8  1.2  1.2  0.0  0.0
        2003      9.0  7.8  7.5  6.9  5.8  5.6  4.2  4.2  2.6  2.7  1.1  1.1  0.0  0.0
        2004      8.6  7.5  7.2  6.6  5.6  5.4  4.0  4.0  2.5  2.5  1.1  1.1  0.0  0.0
        2005      8.3  7.1  6.9  6.4  5.3  5.1  3.8  3.7  2.4  2.4  1.0  1.0  0.0  0.0
        2006      7.9  6.8  6.6  6.1  5.1  4.9  3.6  3.6  2.2  2.2  0.9  0.9  0.0  0.0
        2007      7.6  6.5  6.4  5.9  4.9  4.7  3.4  3.4  2.1  2.1  0.9  0.9  0.0  0.0
        2008      7.3  6.3  6.1  5.6  4.7  4.5  3.3  3.2  2.0  2.0  0.8  0.8  0.0  0.0
        2009      7.0  6.1  5.9  5.5  4.5  4.4  3.2  3.1  1.9  1.9  0.8  0.8  0.0  0.0
        2010      6.8  5.9  5.8  5.4  4.4  4.3  3.1  3.0  1.8  1.8  0.8  0.7  0.0  0.0
        2011      6.7  5.8  5.7  5.3  4.4  4.3  3.0  3.0  1.8  1.7  0.7  0.7  0.0  0.0
        2012      6.6  5.8  5.6  5.2  4.3  4.2  3.0  2.9  1.8  1.7  0.7  0.7  0.0  0.0
        2013      6.5  5.7  5.6  5.2  4.3  4.2  3.0  2.9  1.8  1.7  0.7  0.7  0.0  0.0
        2014      6.5  5.7  5.6  5.2  4.4  4.2  3.0  2.9  1.8  1.7  0.7  0.7  0.0  0.0
        2015      6.4  5.6  5.6  5.2  4.4  4.2  3.1  2.9  1.8  1.7  0.7  0.7  0.0  0.0
        2016      6.4  5.6  5.6  5.2  4.4  4.3  3.1  3.0  1.8  1.7  0.8  0.7  0.0  0.0
Sus     1996     10.3  9.4  8.4  8.4  6.6  7.0  5.0  5.5  3.2  3.6  1.4  1.5  0.0  0.0
        1997     10.1  9.2  8.3  8.2  6.5  6.8  4.9  5.3  3.1  3.5  1.4  1.5  0.0  0.0
        1998      9.9  8.9  8.1  7.9  6.4  6.6  4.8  5.1  3.1  3.4  1.4  1.5  0.0  0.0
        1999      9.7  8.6  8.0  7.7  6.3  6.4  4.7  4.9  3.1  3.3  1.4  1.4  0.0  0.0
        2000      9.4  8.3  7.8  7.4  6.1  6.2  4.6  4.7  3.0  3.2  1.3  1.4  0.0  0.0
        2001      9.2  8.1  7.6  7.2  6.0  5.9  4.5  4.5  2.9  3.0  1.3  1.3  0.0  0.0
        2002      8.9  7.8  7.4  6.9  5.8  5.7  4.4  4.4  2.8  2.9  1.3  1.3  0.0  0.0
        2003      8.6  7.5  7.2  6.7  5.6  5.5  4.2  4.2  2.7  2.8  1.2  1.2  0.0  0.0
        2004      8.3  7.1  6.9  6.4  5.4  5.3  4.0  4.0  2.6  2.6  1.2  1.2  0.0  0.0
        2005      7.9  6.8  6.6  6.1  5.2  5.0  3.8  3.8  2.5  2.5  1.1  1.1  0.0  0.0
        2006      7.5  6.5  6.3  5.9  5.0  4.8  3.7  3.6  2.4  2.3  1.0  1.0  0.0  0.0
        2007      7.2  6.3  6.1  5.6  4.7  4.6  3.5  3.4  2.3  2.2  1.0  1.0  0.0  0.0
        2008      6.9  6.0  5.9  5.5  4.6  4.5  3.4  3.3  2.2  2.1  0.9  0.9  0.0  0.0
        2009      6.7  5.8  5.7  5.3  4.4  4.3  3.3  3.2  2.1  2.0  0.9  0.9  0.0  0.0
        2010      6.5  5.7  5.6  5.2  4.4  4.3  3.2  3.1  2.0  1.9  0.9  0.8  0.0  0.0
        2011      6.4  5.6  5.5  5.1  4.3  4.2  3.2  3.1  2.0  1.9  0.9  0.8  0.0  0.0
        2012      6.4  5.6  5.5  5.1  4.4  4.2  3.2  3.1  2.0  1.9  0.9  0.8  0.0  0.0
        2013      6.4  5.6  5.5  5.1  4.4  4.3  3.2  3.1  2.0  1.9  0.9  0.8  0.0  0.0
        2014      6.4  5.6  5.5  5.2  4.5  4.3  3.3  3.1  2.1  1.9  0.9  0.8  0.0  0.0
        2015      6.4  5.6  5.6  5.2  4.5  4.4  3.3  3.1  2.1  1.9  0.9  0.8  0.0  0.0
        2016      6.4  5.6  5.6  5.2  4.6  4.4  3.4  3.2  2.1  1.9  0.9  0.8  0.0  0.0
```

We now have the relevant points for the graph showing YLL to diabetes for men and women by age, and calendar year, both under the immunity and susceptibility models for the calculation of YLL.

```
> plyll <- function(wh){
+ par( mfrow=c(1,2), mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
+
+ matplot( a.ref, aYLL[wh,"M",,],
+         type="l", lty=1, col="blue", lwd=1:2,
+         ylim=c(0,12), xlab="Age",
+         ylab="Years lost to DM", yaxs="i" )
+ abline(v=50,h=1:10,col=gray(0.7))
```

```
+ text( 90, 11, "Men", col="blue", adj=1 )
+ text( 40, aYLL[wh,"M","40","1996"], "1996", adj=c(0,0), col="blue" )
+ text( 43, aYLL[wh,"M","44","2016"], "2016", adj=c(1,1), col="blue" )
+
+ matplot( a.ref, aYLL[wh,"F",,],
+          type="l", lty=1, col="red", lwd=1:2,
+          ylim=c(0,12), xlab="Age",
+          ylab="Years lost to DM", yaxs="i" )
+ abline(v=50,h=1:10,col=gray(0.7))
+ text( 90, 11, "Women", col="red", adj=1 )
+ text( 40, aYLL[wh,"F","40","1996"], "1996", adj=c(0,0), col="red" )
+ text( 43, aYLL[wh,"F","44","2016"], "2016", adj=c(1,1), col="red" )
+ }
> plyll("Imm")

> plyll("Tot")

> plyll("Sus")
```
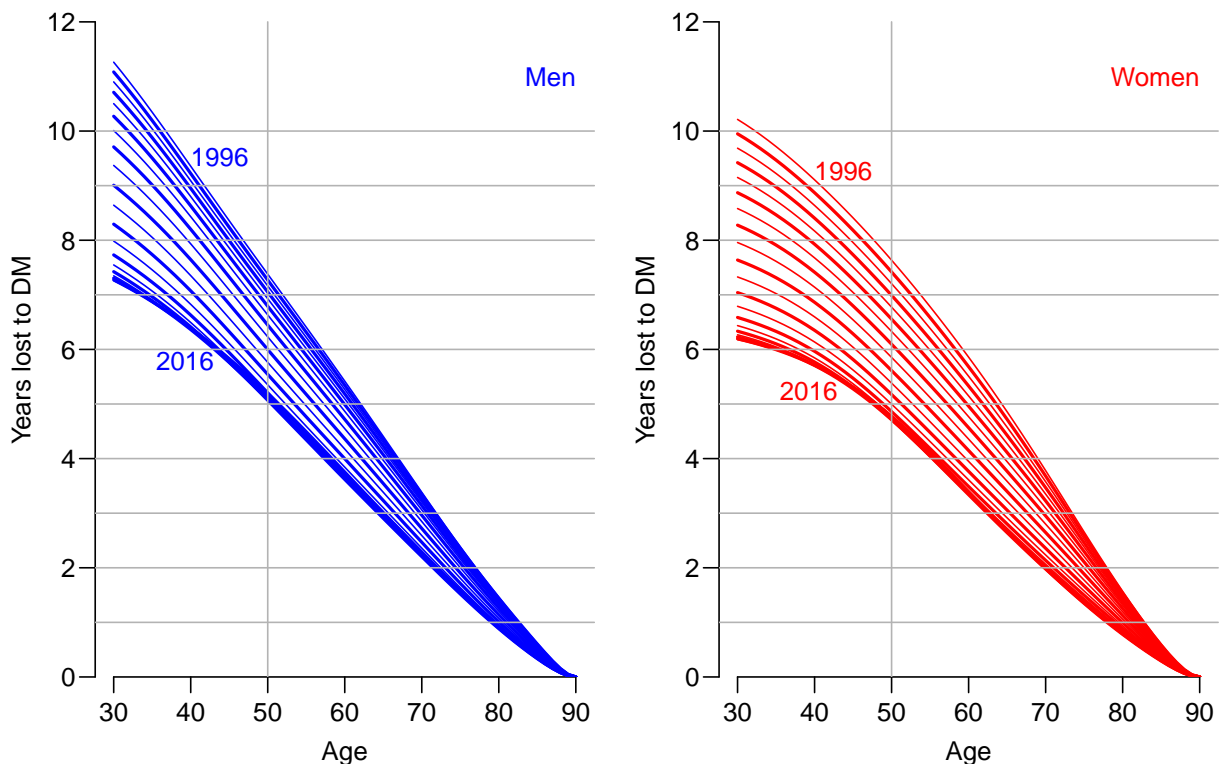

Figure 2.1: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, assuming the persons without diabetes at a given age remain free from diabetes (immunity assumption — not reasonable). The lines refer to date of evaluation; the top lines refer to 1.1.1996 the bottom ones to 1.1.2016. Blue curves are men, red women.*

From figure 2.2 we see that for men aged 50 the years lost to diabetes has decreased from a bit over 8 to a bit less than 6 years, and for women from 8.5 to 5 years; so a greater improvement for women.
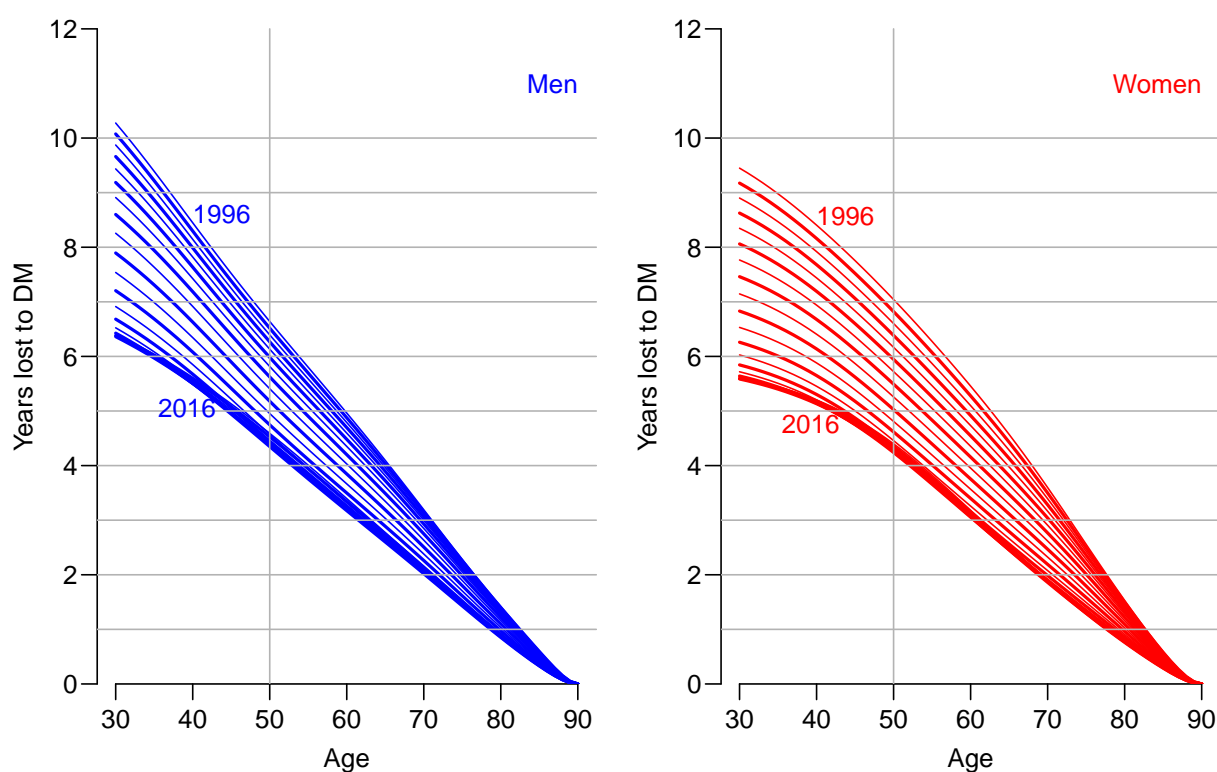
Figure 2.2: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, allowing the persons without diabetes at a given to contract diabetes and thus be subject to higher mortality. The lines refer to date of evaluation; the top lines refer to 1.1.1996 the bottom ones to 1.1.2016. Blue curves are men, red women.*
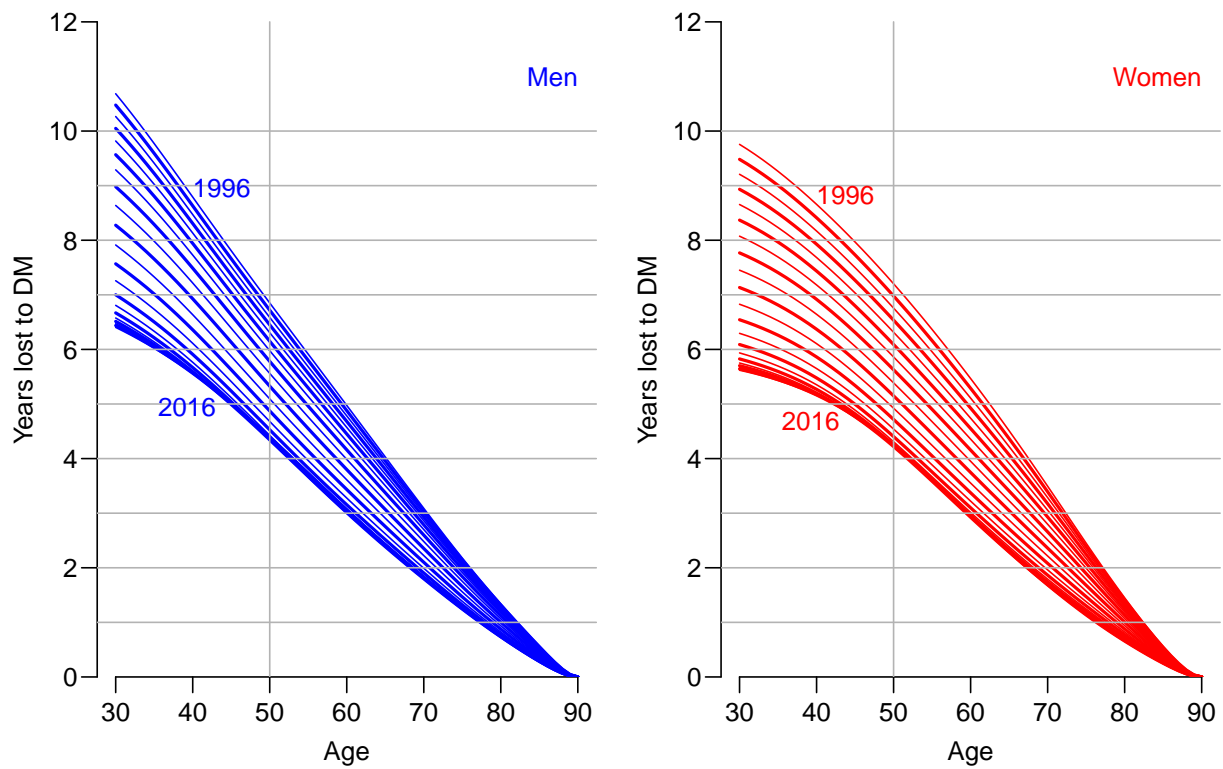
Figure 2.3: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes. Allowance for susceptibility is approximated by using the total population mortality instead of non-DM mortality. The lines refer to date of evaluation; the top lines refer to 1.1.1996 the bottom ones to 1.1.2016. Blue curves are men, red women.*

Chapter 3

Practical implementation

We have devised functions that wraps these formulae up for practical use.

3.1 Function definitions

When using the functions it is assumed that the functions μ_W, μ_D and λ are given as vectors corresponding to equidistantly (usually tightly) spaced ages from 0 to K where K is the age where everyone can safely be assumed dead.

surv1 is a simple function that computes the survival function from a vector of mortality rates, and optionally the conditional survival given being alive at prespecified ages:

```
> surv1
function (int, mu, age.in = 0, A = NULL)
{
    if (any(is.na(mu))) {
        mu[is.na(mu)] <- 0
        warning("NAs in agument 'mu' set to 0")
    }
    age <- 0:length(mu) * int + age.in
    Mu <- c(0, cumsum(mu) * int)
    Sv <- exp(-Mu)
    surv <- data.frame(age = age, surv = Sv)
    if (cond <- !is.null(A)) {
        j <- 0
        cage <- NULL
        for (ia in A) {
            j <- j + 1
            cA <- which(diff(age > ia) == 1)
            surv <- cbind(surv, pmin(1, surv$surv/(surv$surv[cA])))
            cage[j] <- surv$age[cA]
        }
    }
    names(surv)[-1] <- paste("A", c(age.in, if (cond) cage else NULL),
        sep = "")
    rownames(surv) <- NULL
    return(surv)
}
<bytecode: 0x9ab9220>
<environment: namespace:Epi>
```

erl1 basically just expands the result of **surv1** with a column of expected residual life times:

```
> erl1
function (int, mu, age.in = 0)
{
    age <- 0:length(mu) * int + age.in
    musmuc <- function(x) rev(cumsum(rev(x)))
    surv <- surv1(int = int, mu = mu, age.in = age.in)[, 2]
    cbind(age = age, surv = surv, erl = c(musmuc((surv[-1] -
        diff(surv)/2))/surv[-length(surv)], 0) * int)
}
<bytecode: 0x92a0478>
<environment: namespace:Epi>
```

We also define a function, **surv2**, that computes the survival function for a non-diseased person that may become diseased with rate **lam** and after that die at a rate of **muD** (corresponding to the formulae above). This is the sane way of handling years of life lost to a particular illness:

```
> surv2
function (int, muW, muD, lam, age.in = 0, A = NULL)
{
    if (length(muW) != length(muD) | length(muD) != length(lam))
        stop("Vectors with rates must have same length:\n", "length(muW)=",
            length(muW), ", length(muD)=", length(muD), ", length(lam)=",
            length(lam))
    if (!is.null(lam)) {
        if (any(is.na(lam))) {
            lam[is.na(lam)] <- 0
            warning("NAs in agument 'lam' set to 0")
        }
    }
    if (any(is.na(muD))) {
        muD[is.na(muD)] <- 0
        warning("NAs in agument 'muD' set to 0")
    }
    if (any(is.na(muW))) {
        muW[is.na(muW)] <- 0
        warning("NAs in agument 'muW' set to 0")
    }
    wsurv2 <- function(int, muW, muD, lam, age.in = 0, A = 0) {
        age <- 0:length(muW) * int + age.in
        MuW <- cumsum(c(0, muW) * (age > A)) * int
        MuD <- cumsum(c(0, muD) * (age > A)) * int
        Lam <- cumsum(c(0, lam) * (age > A)) * int
        pW <- exp(-(Lam + MuW))
        Dis <- c(0, lam) * (age > A) * exp(-(Lam + MuW)) * int
        pDM <- Dis * 0
        for (ia in 1:length(age)) pDM[ia] <- sum(Dis[1:ia] *
            exp(-(MuD[ia] - MuD[1:ia])))
        surv <- data.frame(age = age, surv = pDM + pW)
        return(surv)
    }
    surv <- wsurv2(int, muW, muD, lam, age.in = age.in, A = 0)
    if (!is.null(A)) {
        for (j in 1:length(A)) {
```

```
            surv <- cbind(surv, wsurv2(int, muW, muD, lam, age.in = age.in,
                A = A[j])[, 2])
        }
    }
    Al <- A
    for (i in 1:length(A)) Al[i] <- max(surv$age[surv$age <=
        A[i]])
    colnames(surv)[-1] <- paste("A", c(age.in, Al), sep = "")
    return(surv)
}
<bytecode: 0x9504ea8>
<environment: namespace:Epi>
```

Finally we devised a function using these to compute the expected residual lifetime at select ages:

```
> erl
function (int, muW, muD, lam = NULL, age.in = 0, A = NULL, immune = is.null(lam),
    yll = TRUE, note = TRUE)
{
    trsum <- function(x) {
        x[c(diff(x) == 0, TRUE)] <- NA
        sum((x[-length(x)] + x[-1])/2, na.rm = TRUE)
    }
    if (!immune & is.null(lam))
        stop("'lam' is required when immune=FALSE\n")
    if (!is.null(lam)) {
        if (any(is.na(lam))) {
            lam[is.na(lam)] <- 0
            warning("NAs in agument 'lam' set to 0")
        }
    }
    if (any(is.na(muD))) {
        muD[is.na(muD)] <- 0
        warning("NAs in agument 'muD' set to 0")
    }
    if (any(is.na(muW))) {
        muW[is.na(muW)] <- 0
        warning("NAs in agument 'muW' set to 0")
    }
    sD <- surv1(int = int, muD, age.in = age.in, A = A)
    if (immune)
        sW <- surv1(int = int, muW, age.in = age.in, A = A)
    else sW <- surv2(int = int, muW, muD, lam, age.in = age.in,
        A = A)
    erl <- cbind(apply(sW[, -1], 2, trsum), apply(sD[, -1], 2,
        trsum)) * int
    colnames(erl) <- c("Well", "Dis")
    rownames(erl) <- colnames(sW)[-1]
    if (yll)
        erl <- cbind(erl, YLL = erl[, "Well"] - erl[, "Dis"])
    if (immune) {
        attr(erl, "NOTE") <- "Calculations assume that Well persons cannot get Ill (quite s
        if (note)
            cat("NOTE:", attr(erl, "NOTE"), "\n")
    }
    return(erl)
```

```
}
<bytecode: 0x9ac1e20>
<environment: namespace:Epi>
```

. . . and a wrapper for this if we only want the years of life lost returned:

```
> yll
function (int, muW, muD, lam = NULL, age.in = 0, A = NULL, immune = is.null(lam),
    note = TRUE)
erl(int = int, muW = muW, muD = muD, lam = lam, age.in = age.in,
    A = A, immune = immune, yll = TRUE, note = note)[, "YLL"]
<bytecode: 0xb865200>
<environment: namespace:Epi>
```

Bibliography

[1] B Carstensen. Age-Period-Cohort models for the Lexis diagram. *Statistics in Medicine*, 26(15):3018–3045, 2007.

[2] B Carstensen, JK Kristensen, P Ottosen, and K Borch-Johnsen. The Danish National Diabetes Register: Trends in incidence, prevalence and mortality. *Diabetologia*, 51:2187–2196, 2008.