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

SDC

November 2017

http://bendixcarstensen.com/Epi

February 1.2

Compiled Wednesday 6th April, 2022, 07:54

from: /home/bendix/stat/R/lib.src/Epi/pkg/vignettes/yll.tex

Bendix Carstensen Steno Diabetes Center, Gentofte, Denmark

& Department of Biostatistics, University of Copenhagen

b@bxc.dk

http://BendixCarstensen.com

Contents

1	$\mathrm{Th}\epsilon$	heory and technicalities		
	1.1	Years	of life lost (YLL)	1
1.2		Constructing the survival curves		
		1.2.1	Total mortality — a shortcut?	2
		1.2.2	Disease duration	2
		1.2.3	Computing integrals	3
	1.3	Surviv	val functions in the illness-death model	3
		1.3.1	Immune approach	3
			Conditional survival functions	3
		1.3.2	Non-immune approach	4
			Conditional survival functions	4
2	Analyses for DM in Denmark			
	2.1	Model	ling mortality and incidence data	6
	2.2			8
R	oforo	ncos		11

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", $S_D(t)$:

$$YLL = \int_0^\infty S_W(t) - S_D(t) dt$$

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:

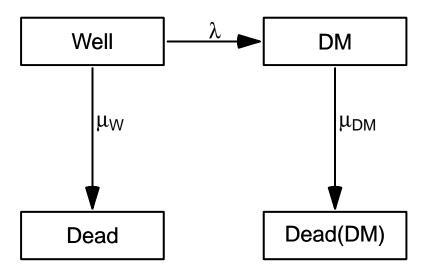
- Assume that the "Well" persons are *immune* to disease using only the non-DM mortality rates throughout for calculation of expected life time.
- Assume that the "Well" persons *can* acquire the disease and thereby see an increased mortality, thus involving all three rates shown in figure 1.1.

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 .

We can edit the output from boxes



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:

$$S_W(a) = \exp\left(-\int_0^a \mu_W(u) du\right), \qquad S_D(a) = \exp\left(-\int_0^a \mu_D(u) du\right)$$

Conditional survival functions

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

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

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):

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

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 $\lambda(a)$):

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

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:

P{DM}
$$(a) = \int_0^a P\{\text{survive to } s, \text{ DM diagnosed at } s\}$$

$$\times P\{\text{survive with DM from } s \text{ to } a\} \text{ ds}$$

$$= \int_0^a \lambda(s) \exp\left(-\int_0^s \mu_W(u) + \lambda(u) \, du\right)$$

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

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:

$$P\{DM\}(a) = \int_0^a \lambda(s) \exp\left(-\int_0^s \mu_W(u) + \lambda(u) du\right)$$
$$\times \exp\left(-\int_s^a \mu_D(u, u - s) du\right) ds$$

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:

$$\begin{aligned} \text{P\{Well|Well at } A\}\left(a\right) &= \exp\left(-\int_{A}^{a} \mu_{W}(u) + \lambda(u)\right) \, \mathrm{d}u \\ \text{P\{DM|Well at } A\}\left(a\right) &= \int_{A}^{a} \lambda(s) \exp\left(-\int_{A}^{s} \mu_{W}(u) + \lambda(u) \, \mathrm{d}u\right) \\ &\times \exp\left(-\int_{s}^{a} \mu_{D}(u, u - s) \, \mathrm{d}u\right) \, \mathrm{d}s \end{aligned}$$

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 ...
      : num 0000000000...
      : num 1996 1997 1998 1999 2000 ...
 $ D.DM: num 0 0 0 0 0 0 0 0 0 ...
 $ Y.DM: num
             0.484 0.64 1.641 0.552 2.507 ...
             1 2 4 4 4 1 1 3 4 1 ...
      : num
 $ D.nD: num
             28 19 20 11 21 16 21 15 16 16 ...
$ Y.nD: num 35469 35085 34240 34056 34002 ...
> head(DMepi)
          P D.DM
                      Y.DM X D.nD
 sex A
                                      Y.nD
   M 0 1996
               0 0.4839151 1
                             28 35468.92
   M 0 1997
               0 0.6399726 2
                               19 35085.18
   M 0 1998
               0 1.6406571 4
                               20 34240.14
5
               0 0.5523614 4
   M 0 1999
                               11 34055.52
   M 0 2000
               0 2.5065024 4
                               21 34002.22
   M 0 2001
                               16 34177.39
               0 0.1184120 1
```

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
        Α
              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
                                           F
                                                          F
                                                                         F
                                   M
                                                  M
                                                                 Μ
                          sex
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
                              158365 156678
(73,84]
                                              34510
                                                      28834
                                                             27985
                                                                     30381
(84,95]
                              100880 179466
                                              16194
                                                      25317
                                                              5272
                                                                      8967
(95, Inf]
                                 6095
                                                640
                                                       1928
                                                                90
                                                                       288
                                       21414
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
                                                                        Μ
                                                                               F
                                                        М
                              sex
cut(P, c(1990, p.kn, Inf))
(1990, 1997]
                                    51569
                                           53567
                                                     6407
                                                            5990
                                                                   13175
(1997, 2003]
                                   144136 155695
                                                   22390
                                                           19922
                                                                   49805
                                                                           41277
(2003, 2009]
                                   131159 141782
                                                   26079
                                                           22249
                                                                   60554
(2009, 2015]
                                                   31285
                                                           24704
                                                                   63440
                                   119812 127714
(2015, Inf]
                                    19551
                                           20658
                                                     5762
                                                            4482
                                                                   10345
                                   466227 499416
                                                   91923
                                                          77347 197319 157464
Sum
> ce <- xtabs(cbind(D.nD, D.DM, X) ~ cut(P-A, c(-Inf, c.kn, Inf)) + sex, data=DMepi)</pre>
> ftable(addmargins(ce, 1), col.vars=3:2)
                                         D.nD
                                                         D.DM
                                                            M
                                                                            М
                                                                                    F
                                   sex
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
                                                        25494
                                                                                50631
(1.94e+03,1.95e+03]
                                        99058
                                                72432
                                                                13074
                                                                        71489
(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
                                       466227 499416
Sum
                                                        91923
                                                                77347 197319 157464
> # Fit an APC-model for all transitions, seperately for men and women
> mW.m <- glm(D.nD \sim -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 \tilde{\ } . , offset=log(Y.DM)) > mT.m <- update(mW.m, D.T \tilde{\ } . , offset=log(Y.T))
                          x ~ .)
> lW.m <- update(mW.m,</pre>
> # Model for women
> mW.f <- update(mW.m, data = subset(DMepi, sex=="F"))</pre>
> mD.f <- update(mD.m, data = subset(DMepi, sex=="F"))</pre>
> mT.f <- update(mT.m, data = subset(DMepi, sex=="F"))</pre>
> lW.f <- update(lW.m, data = subset(DMepi, sex=="F"))</pre>
```

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:

```
..$ age : chr [1:61] "30" "31" "32" "33"
  ..$ date: chr [1:21] "1996" "1997" "1998" "1999" ...
> system.time(
  for(ip in p.ref)
     {
+
     nd \leftarrow 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]</pre>
     muD.m <- ci.pred(mD.m, nd)[, 1]
     muT.m <- ci.pred(mT.m, nd)[, 1]</pre>
     lam.m <- ci.pred(lW.m, nd)[, 1]</pre>
+
     muW.f <- ci.pred(mW.f, nd)[, 1]</pre>
     muD.f <- ci.pred(mD.f, nd)[, 1]</pre>
+
+
     muT.f \leftarrow ci.pred(mT.f, nd)[, 1]
     lam.f <- ci.pred(lW.f, nd)[, 1]</pre>
     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
 17.831
          8.190 15.992
> round(ftable(aYLL[, , seq(1, 61, 10), ], col.vars=c(3, 2)), 1)
                 30
                            40
                                       50
                                                  60
                                                             70
                                                                        80
                                                                                  90
                        F
                             M
                                  F
                                        Μ
                                             F
                                                   М
                                                        F
                                                              M
                                                                   F
                                                                         M
                                                                              F
           sex
type date
               11.3 10.2
                           9.4
                                      7.4
                                           7.6
                                                 5.4
                                                      5.9
                                                            3.4
    1996
                                9.1
                                                                 3.8
                                                                      1.5
                                                                            1.6
                                                                                 0.0
                                                                                       0.0
Tmm
                           9.2
                                8.9
                                      7.3
                                           7.4
                                                      5.7
     1997
               11.1
                     9.9
                                                 5.3
                                                            3.3
                                                                 3.7
                                                                       1.4
                                                                            1.5
                                                                                 0.0
                                                                                       0.0
                                                      5.5
     1998
               10.9
                     9.7
                           9.1
                                8.6
                                      7.2
                                           7.2
                                                 5.3
                                                            3.3
                                                                 3.6
                                                                      1.4
                                                                            1.5
                                                                                 0.0
                                                                                       0.0
               10.7
                           9.0
                                8.4
                                      7.1
                                           7.0
                                                 5.2
                                                      5.3
                                                           3.3
                                                                 3.5
     1999
                     9.4
                                                                       1.4
                                                                            1.5
                                                                                       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
                                7.9
                     8.9
                                                 5.0
                                                            3.1
     2001
               10.3
                           8.6
                                      6.8
                                           6.6
                                                      5.0
                                                                 3.2
                                                                       1.3
                                                                            1.4
                                                                                 0.0
                                                                                       0.0
                                7.7
     2002
               10.0
                     8.6
                           8.4
                                      6.6
                                           6.3
                                                 4.9
                                                      4.8
                                                                 3.1
                                                                       1.3
                                                                            1.3
                                                                                 0.0
                                                           3.1
                                                                                       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
                           7.9
                                7.1
                                      6.2
                                           5.9
                                                 4.5
                                                      4.4
                                                            2.8
                                                                 2.8
                                                                       1.2
                                                                            1.2
                     8.0
                                                                                 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
                                           5.2
     2007
                8.3
                     7.0
                           7.1
                                6.3
                                      5.5
                                                 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
     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
                           6.4
                7.4
                     6.3
                                      5.1
                                           4.7
                                                 3.6
                                                      3.4
                                                            2.2
                                                                 2.0
     2011
                                5.8
                                                                      0.9
                                                                            0.8
                                                                                 0.0
                                                                                       0.0
                7.3
                     6.3
                           6.4
                                5.7
                                      5.1
                                           4.7
                                                 3.6
                                                      3.3
                                                            2.2
                                                                 2.0
                                                                      0.9
                                                                            0.8
     2012
                                                                                 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
                           6.4 5.7
                                      5.1 4.7
                                                3.7
                                                      3.4 2.2
                     6.2
                                                                 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
                                                                                   1.4
      1997
                10.5
                       9.5
                             8.6
                                   8.4
                                         6.7
                                               7.0
                                                     4.9
                                                           5.3
                                                                 3.0
                                                                       3.4
                                                                             1.3
                                                                                         0.0
                                                                                               0.0
                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
      1998
                                                                                               0.0
                10.0
                       8.9
                             8.3
                                   7.9
                                         6.5
                                               6.5
                                                     4.7
                                                           4.9
                                                                 2.9
                                                                       3.2
                                                                             1.3
      1999
                                                                                   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
                             7.9
                                   7.4
                                                     4.5
                                                                 2.8
                                                                             1.2
      2001
                  9.6
                       8.4
                                         6.2
                                               6.1
                                                           4.6
                                                                       2.9
                                                                                   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
                       7.8
                             7.5
                                               5.6
                                                     4.2
                                                           4.2
                                                                 2.6
                                                                       2.7
      2003
                  9.0
                                   6.9
                                         5.8
                                                                             1.1
                                                                                   1.1
                                                                                         0.0
                                                                                               0.0
                       7.5
                                         5.6
                                                                       2.5
                             7.2
                                               5.4
                                                     4.0
                                                           4.0
                                                                 2.5
      2004
                  8.6
                                   6.6
                                                                             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
                                                                             0.9
                                                                                   0.9
                  7.6
                       6.5
                             6.4
                                   5.9
                                         4.9
                                               4.7
                                                     3.4
                                                           3.4
                                                                 2.1
                                                                       2.1
      2007
                                                                                         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
                                   5.5
                                                     3.2
      2009
                  7.0
                       6.1
                             5.9
                                         4.5
                                               4.4
                                                           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
                             5.7
                                               4.3
                                                     3.0
      2011
                  6.7
                       5.8
                                   5.3
                                         4.4
                                                           3.0
                                                                 1.8
                                                                       1.7
                                                                             0.7
                                                                                   0.7
                                                                                         0.0
                                                                                               0.0
                       5.8
                                         4.3
                                               4.2
                                                     3.0
                                                           2.9
                                                                                   0.7
      2012
                  6.6
                             5.6
                                   5.2
                                                                 1.8
                                                                       1.7
                                                                             0.7
                                                                                         0.0
                                                                                               0.0
                                   5.2
                                               4.2
                                                     3.0
                                                           2.9
      2013
                  6.5
                       5.7
                             5.6
                                         4.3
                                                                 1.8
                                                                       1.7
                                                                             0.7
                                                                                   0.7
                                                                                         0.0
                                                                                               0.0
                                   5.2
                                               4.2
                                                     3.0
                                                           2.9
      2014
                  6.5
                       5.7
                             5.6
                                         4.4
                                                                 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
                10.3
                       9.4
                                   8.4
                                         6.6
                                               7.0
                                                     5.0
                                                                 3.2
                                                                       3.6
                                                                             1.4
Sus
      1996
                             8.4
                                                           5.5
                                                                                   1.5
                                                                                         0.0
                                                                                               0.0
                                                                             1.4
                       9.2
                             8.3
                                   8.2
                                         6.5
                                               6.8
                                                           5.3
                                                                       3.5
                                                                                         0.0
      1997
                10.1
                                                     4.9
                                                                 3.1
                                                                                   1.5
                                                                                               0.0
                                               6.6
                  9.9
                       8.9
                                   7.9
                                                     4.8
                                                                             1.4
      1998
                             8.1
                                         6.4
                                                           5.1
                                                                 3.1
                                                                       3.4
                                                                                   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
                             7.6
      2001
                  9.2
                       8.1
                                   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
                       7.5
                             7.2
                                                     4.2
                                                           4.2
                                                                 2.7
                                                                       2.8
                                                                             1.2
                                                                                   1.2
      2003
                  8.6
                                   6.7
                                         5.6
                                               5.5
                                                                                         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
                                                     3.8
      2005
                  7.9
                       6.8
                             6.6
                                   6.1
                                         5.2
                                               5.0
                                                           3.8
                                                                 2.5
                                                                       2.5
                                                                             1.1
                                                                                   1.1
                                                                                         0.0
                                                                                               0.0
                 7.5
                       6.5
                             6.3
                                   5.9
                                         5.0
                                               4.8
                                                     3.7
                                                           3.6
                                                                 2.4
                                                                       2.3
                                                                             1.0
                                                                                   1.0
      2006
                                                                                         0.0
                                                                                               0.0
                  7.2
                                               4.6
                                                     3.5
                                                                 2.3
                                                                       2.2
      2007
                       6.3
                             6.1
                                   5.6
                                         4.7
                                                           3.4
                                                                             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
                                               4.3
                                                     3.2
                                                                 2.0
      2010
                  6.5
                       5.7
                             5.6
                                   5.2
                                         4.4
                                                           3.1
                                                                       1.9
                                                                             0.9
                                                                                   0.8
                                                                                         0.0
                                                                                               0.0
                                               4.2
                                                     3.2
                                                                 2.0
                                                                                   0.8
      2011
                  6.4
                       5.6
                             5.5
                                   5.1
                                         4.3
                                                           3.1
                                                                       1.9
                                                                             0.9
                                                                                         0.0
                                                                                               0.0
                             5.5
                                               4.2
                                                     3.2
                  6.4
                       5.6
                                   5.1
                                         4.4
                                                           3.1
                                                                 2.0
                                                                       1.9
                                                                             0.9
                                                                                   0.8
                                                                                         0.0
      2012
                                                                                               0.0
                                               4.3
      2013
                  6.4
                       5.6
                             5.5
                                   5.1
                                         4.4
                                                     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))</pre>
```

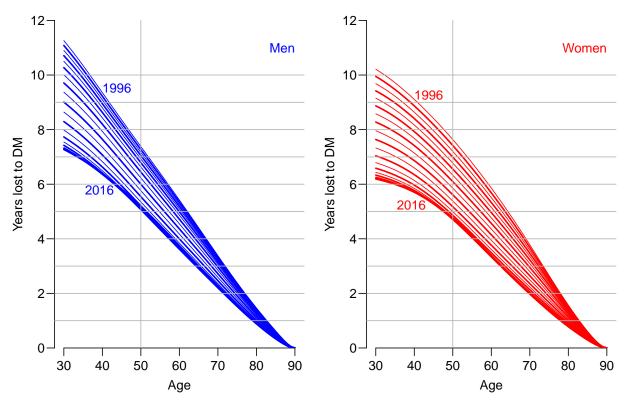


Figure 2.1: Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, assuming the persons without diabetes at a given age remain free from diabetes (immunity assumption — not reasonable). The lines refer to date of evaluation; 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.

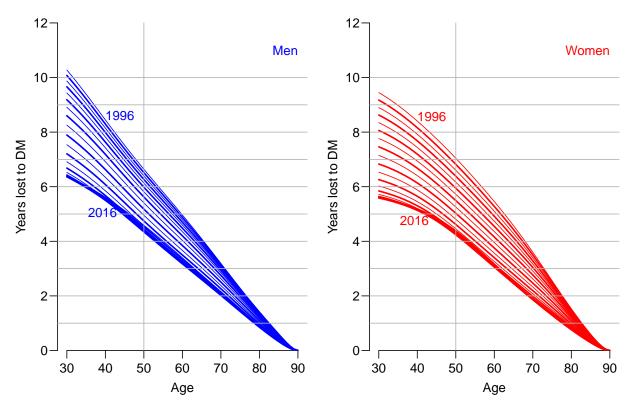


Figure 2.2: Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, allowing the persons without diabetes at a given to contract diabetes and thus be subject to higher mortality. The lines refer to date of evaluation; the top lines refer to 1.1.1996 the bottom ones to 1.1.2016. Blue curves are men, red women.

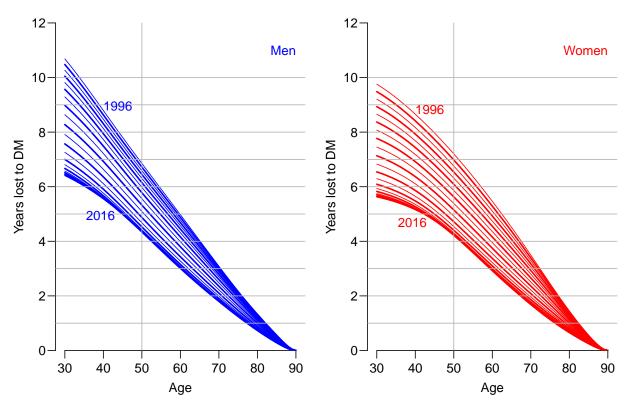


Figure 2.3: Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes. Allowance for susceptibility is approximated by using the total population mortality instead of non-DM mortality. The lines refer to date of evaluation; the top lines refer to 1.1.1996 the bottom ones to 1.1.2016. Blue curves are men, red women.

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.