

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

SDC

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from:

Bendix Carstensen Steno Diabetes Center, Gentofte, Denmark
& Department of Biostatistics, University of Copenhagen
b@bxc.dk
<http://BendixCarstensen.com>

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Chapter 1

Theory and technicalities

This vignette for the `Epi` package describes the probabilistic/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”, $S_D(t)$:

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

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 .

```
R version 3.3.2 (2016-10-31)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Ubuntu 14.04.5 LTS

attached base packages:
[1] splines      stats      graphics  grDevices  utils      datasets  methods    base

other attached packages:
[1] survival_2.40-1 Epi_2.10

loaded via a namespace (and not attached):
[1] cmprsk_2.2-7      MASS_7.3-45      Matrix_1.2-6     plyr_1.8.4
[5] parallel_3.3.2    tools_3.3.2      etm_0.6-2        Rcpp_0.12.5
[9] grid_3.3.2        data.table_1.9.6 numDeriv_2014.2-1 chron_2.3-47
[13] lattice_0.20-33
```

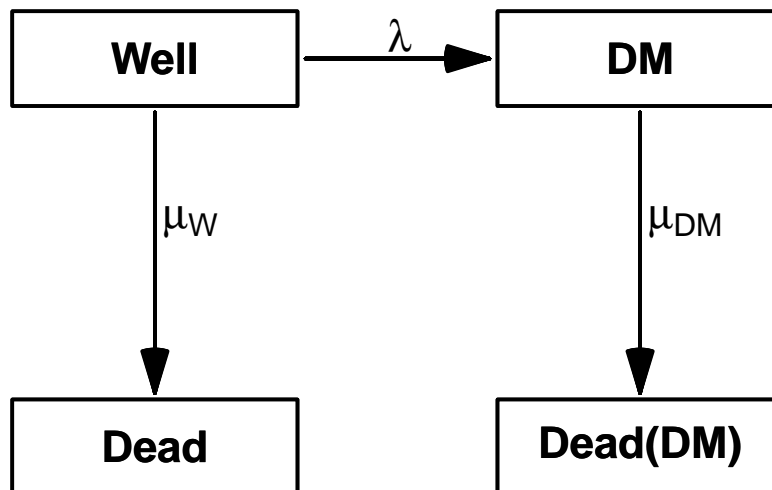


Figure 1.1: *Illness-death model describing diabetes incidence and -mortality.*

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:

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

1.3.1.1 Conditional survival functions

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

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

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):

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

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 $\lambda(a)$):

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

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 :

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

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:

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

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.

1.3.2.1 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:

$$\begin{aligned} P \{ \text{Well} | \text{Well at } A \} (a) &= \exp \left(- \int_A^a \mu_W(u) + \lambda(u) \, du \right) \\ P \{ \text{DM} | \text{Well at } A \} (a) &= \int_A^a \lambda(s) \exp \left(- \int_A^s \mu_W(u) + \lambda(u) \, du \right) \\ &\quad \times \exp \left(- \int_s^a \mu_D(u, u - s) \, du \right) \, ds \end{aligned}$$

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

1.4 Practical implementation

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

1.4.1 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)
{
  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)
}
<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)
}
<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 same 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))
    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])
        }
    }
    A1 <- A
}

```



```

    for (i in 1:length(A)) A1[i] <- max(surv$age[surv$age <=
      A[i]])
    colnames(surv)[-1] <- paste("A", c(age.in, A1), sep = "")
    return(surv)
}
<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")
  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)
}
<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"]
<environment: namespace:Epi>

```

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 )
> lls()
  name      mode      class      dim      size(Kb)
1 All.Dead list      glm lm      30      84,827.6
2 Cox.Dead list      coxph      22      17,157.4
3 CoxF      numeric  pState matrix 56 4      6.0
4 CoxM      numeric  pState matrix 56 4      6.0
5 DM.Dead   list      glm lm      30      70,981.2
6 DM.Ins    list      glm lm      30      70,981.2
7 DMepi     list      data.frame 4000 8      236.2
8 DMLate    list      data.frame 10000 7      548.6
9 Ins.Dead  list      glm lm      30      14,642.0
10 Nsim     numeric  numeric      1      0.0
11 PrF      numeric  pState matrix 56 4      6.0
12 PrM      numeric  pState matrix 56 4      6.0
13 Si       list      Lexis data.frame 115370 15      11,722.5
14 TM       numeric  matrix      4 4      1.0
15 Tr       list      list      2      156,605.3
16 Tr.c     list      list      2      105,296.8
17 Tr.p     list      list      2      240,637.2
18 aa       numeric  numeric      1      0.0
19 ad.kn    numeric  numeric      5      0.5
20 agehi    numeric  numeric     3129      24.5
21 ai.kn    numeric  numeric      5      0.5
22 clr      character character      2      0.2
23 clx      character character      4      0.3
24 dd       numeric  numeric      4      0.5
25 dd.kn    numeric  numeric      5      0.5
26 di.kn    numeric  numeric      5      0.5
```

```

27 dmi      list      Lexis data.frame 11690 15      1,237.9
28 dml      list      Lexis data.frame 9996 14      980.7
29 dnew     list      data.frame      121 7        8.0
30 ia       character character      1          0.1
31 ii       numeric   integer        1          0.0
32 ini      list      Lexis data.frame 2 9         4.8
33 nSt      numeric   table          56 4         5.1
34 nd       list      data.frame      121 4         4.8
35 nicC     list      Lexis data.frame 762 16        94.1
36 nicL     list      Lexis data.frame 679 15       113.0
37 nicS1    list      Lexis data.frame 2210 14      236.4
38 nicS2    list      Lexis data.frame 3129 14      333.4
39 nicS2C   list      Lexis data.frame 3203 14      353.7
40 nickel   list      data.frame      679 7        75.5
41 nk       numeric   numeric        1          0.0
42 pF       numeric   pState matrix  56 4         6.0
43 pM       numeric   pState matrix  56 4         6.0
44 pr.rates  numeric   array          121 4 4 2 3    99.5
45 rA       numeric   numeric        4          0.5
46 rD       numeric   numeric        4          0.5
47 rI       numeric   numeric        4          0.5
48 simC     list      Lexis data.frame 2742 10      176.2
49 simL     list      Lexis data.frame 2734 10      175.7
50 simP     list      Lexis data.frame 2768 10      177.8
51 ti.kn    numeric   numeric        5          0.5
52 what     character character      4          0.3
53 zz       list      MS              5          6.6

```

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':      4000 obs. of  8 variables:
 $ sex : Factor w/ 2 levels "M","F": 1 2 1 2 1 2 1 2 1 2 ...
 $ A   : num  0 0 1 1 2 2 3 3 4 4 ...
 $ P   : num  1996 1996 1996 1996 1996 1996 ...
 $ X   : num  1 9 4 7 7 2 6 5 9 4 ...
 $ D.nD: num  28 19 23 19 7 8 8 8 6 7 ...
 $ Y.nD: num  35454 33095 36451 34790 35329 ...
 $ D.DM: num  0 0 0 0 0 0 0 0 0 0 ...
 $ Y.DM: num  0.476 3.877 4.92 7.248 12.474 ...

> head( DMepi )
   sex A   P X D.nD   Y.nD D.DM   Y.DM
1  M 0 1996 1   28 35453.65    0 0.4757016
2  F 0 1996 9   19 33094.86    0 3.8767967
3  M 1 1996 4   23 36450.73    0 4.9199179
4  F 1 1996 7   19 34789.99    0 7.2484600
5  M 2 1996 7    7 35328.92    0 12.4743326
6  F 2 1996 2    8 33673.43    0 8.0951403

```

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	X	D.nD	Y.nD	D.DM	Y.DM	D.T	Y.T
63	M	31	1996	21	51	43909.32	0	291.4107	51	44200.73
64	F	31	1996	33	16	41376.91	2	287.4969	18	41664.41
65	M	32	1996	26	67	43159.94	0	299.6571	67	43459.59
66	F	32	1996	20	23	40706.49	1	275.2615	24	40981.75
67	M	33	1996	35	54	41251.06	4	321.0397	58	41572.10
68	F	33	1996	32	23	39102.29	1	277.4463	24	39379.74

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 )
```

	sex	D.nD	D.DM	X			
		M	F	M	F		
cut(A, c(30, a.kn, Inf))							
(30,40]		8899	4525	564	269	9912	8622
(40,51]		24686	15296	2886	1399	31668	20769
(51,62]		57747	38968	10276	4916	53803	34495
(62,73]		102877	78771	24070	13008	51000	38731
(73,84]		154804	153842	31006	25414	25444	26804
(84,95]		97698	175484	13972	21231	4726	7852
(95,Inf]		5800	20563	545	1522	74	238
Sum		452511	487449	83319	67759	176627	137511

```
> 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 )
```

	sex	D.nD	D.DM	X			
		M	F	M	F		
cut(P, c(1990, p.kn, Inf))							
(1990,1997]		51901	54162	6012	5378	12477	10030
(1997,2003]		145418	157768	21028	17976	43749	34255
(2003,2009]		133175	144717	25172	20595	56556	43891
(2009,2015]		122017	130802	31107	23810	63845	49335
(2015,Inf]		0	0	0	0	0	0
Sum		452511	487449	83319	67759	176627	137511

```

> 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 )

```

	sex	D.nD		D.DM		X	
		M	F	M	F	M	F
cut(P - A, c(-Inf, c.kn, Inf))							
(-Inf,1.91e+03]		19912	49797	1784	3731	536	1143
(1.91e+03,1.92e+03]		130691	190012	18160	23709	9765	13519
(1.92e+03,1.94e+03]		154227	146284	32435	24876	34897	32481
(1.94e+03,1.95e+03]		93397	67909	22921	11437	65012	44292
(1.95e+03,1.96e+03]		40948	26234	6724	3326	46155	29891
(1.96e+03,1.98e+03]		12534	6810	1245	654	19293	15311
(1.98e+03, Inf]		802	403	50	26	969	874
Sum		452511	487449	83319	67759	176627	137511

```

> # 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
15.363 0.003 15.374

```

```
> 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		11.7	10.8	9.8	9.7	7.8	8.2	5.6	6.3	3.4	3.9	1.5	1.6	0.0	0.0
	1997		11.5	10.6	9.7	9.4	7.7	7.9	5.6	6.1	3.4	3.9	1.4	1.6	0.0	0.0
	1998		11.3	10.3	9.6	9.2	7.6	7.7	5.5	5.9	3.4	3.8	1.4	1.5	0.0	0.0
	1999		11.1	10.0	9.4	9.0	7.5	7.5	5.4	5.7	3.3	3.7	1.4	1.5	0.0	0.0
	2000		10.9	9.8	9.3	8.7	7.4	7.3	5.4	5.6	3.3	3.6	1.4	1.5	0.0	0.0
	2001		10.7	9.5	9.1	8.5	7.3	7.1	5.3	5.4	3.3	3.4	1.4	1.4	0.0	0.0
	2002		10.5	9.2	9.0	8.3	7.1	6.9	5.2	5.2	3.2	3.3	1.3	1.4	0.0	0.0
	2003		10.3	9.0	8.8	8.1	7.0	6.7	5.1	5.1	3.1	3.2	1.3	1.3	0.0	0.0
	2004		10.0	8.8	8.6	7.8	6.8	6.5	5.0	4.9	3.1	3.1	1.3	1.3	0.0	0.0
	2005		9.7	8.5	8.4	7.6	6.6	6.3	4.8	4.8	3.0	3.0	1.2	1.3	0.0	0.0
	2006		9.4	8.3	8.1	7.5	6.5	6.2	4.7	4.6	2.9	2.9	1.2	1.2	0.0	0.0
	2007		9.1	8.1	7.9	7.3	6.3	6.0	4.6	4.5	2.8	2.8	1.1	1.2	0.0	0.0
	2008		8.9	7.9	7.7	7.1	6.1	5.9	4.4	4.3	2.7	2.7	1.1	1.1	0.0	0.0
	2009		8.6	7.7	7.5	6.9	6.0	5.7	4.3	4.2	2.7	2.6	1.1	1.1	0.0	0.0
	2010		8.4	7.5	7.3	6.8	5.9	5.6	4.2	4.1	2.6	2.5	1.1	1.1	0.0	0.0
	2011		8.3	7.3	7.2	6.7	5.8	5.5	4.2	4.0	2.6	2.5	1.0	1.0	0.0	0.0
	2012		8.1	7.2	7.1	6.5	5.7	5.4	4.1	4.0	2.6	2.4	1.0	1.0	0.0	0.0
	2013		8.0	7.1	7.0	6.4	5.6	5.3	4.1	3.9	2.5	2.4	1.0	1.0	0.0	0.0
	2014		7.8	6.9	6.9	6.3	5.6	5.3	4.1	3.8	2.5	2.3	1.0	0.9	0.0	0.0
	2015		7.7	6.8	6.8	6.2	5.5	5.2	4.0	3.8	2.5	2.2	1.0	0.9	0.0	0.0
	2016		7.6	6.7	6.7	6.1	5.5	5.1	4.0	3.7	2.5	2.2	1.0	0.9	0.0	0.0
Tot	1996		11.1	10.4	9.3	9.2	7.3	7.7	5.2	5.9	3.1	3.7	1.3	1.5	0.0	0.0
	1997		10.9	10.1	9.1	9.0	7.2	7.5	5.1	5.7	3.1	3.6	1.3	1.5	0.0	0.0
	1998		10.7	9.8	9.0	8.7	7.0	7.3	5.0	5.5	3.1	3.5	1.3	1.4	0.0	0.0
	1999		10.5	9.6	8.8	8.5	6.9	7.1	5.0	5.4	3.0	3.4	1.3	1.4	0.0	0.0
	2000		10.3	9.3	8.6	8.3	6.8	6.9	4.9	5.2	3.0	3.3	1.3	1.4	0.0	0.0
	2001		10.0	9.0	8.5	8.0	6.6	6.6	4.8	5.0	2.9	3.2	1.2	1.3	0.0	0.0
	2002		9.8	8.8	8.3	7.8	6.5	6.4	4.7	4.8	2.9	3.1	1.2	1.3	0.0	0.0
	2003		9.5	8.5	8.1	7.6	6.3	6.2	4.5	4.7	2.8	2.9	1.2	1.2	0.0	0.0
	2004		9.3	8.2	7.8	7.3	6.1	6.0	4.4	4.5	2.7	2.8	1.1	1.2	0.0	0.0
	2005		9.0	8.0	7.6	7.1	5.9	5.9	4.3	4.3	2.6	2.7	1.1	1.1	0.0	0.0

	2006	8.7	7.8	7.4	6.9	5.8	5.7	4.1	4.2	2.5	2.6	1.0	1.1	0.0	0.0
	2007	8.4	7.5	7.1	6.7	5.6	5.5	4.0	4.1	2.4	2.5	1.0	1.1	0.0	0.0
	2008	8.1	7.3	6.9	6.6	5.4	5.4	3.8	3.9	2.3	2.4	1.0	1.0	0.0	0.0
	2009	7.8	7.1	6.7	6.4	5.2	5.2	3.7	3.8	2.3	2.3	0.9	1.0	0.0	0.0
	2010	7.6	7.0	6.5	6.3	5.1	5.1	3.6	3.7	2.2	2.2	0.9	0.9	0.0	0.0
	2011	7.4	6.8	6.4	6.1	5.0	5.0	3.5	3.6	2.2	2.2	0.9	0.9	0.0	0.0
	2012	7.3	6.6	6.3	6.0	4.9	4.9	3.5	3.5	2.1	2.1	0.9	0.9	0.0	0.0
	2013	7.1	6.5	6.1	5.9	4.8	4.8	3.4	3.4	2.1	2.0	0.9	0.8	0.0	0.0
	2014	7.0	6.3	6.0	5.8	4.8	4.7	3.4	3.4	2.0	2.0	0.8	0.8	0.0	0.0
	2015	6.8	6.2	5.9	5.6	4.7	4.6	3.3	3.3	2.0	1.9	0.8	0.8	0.0	0.0
	2016	6.7	6.1	5.8	5.5	4.6	4.6	3.3	3.2	2.0	1.9	0.8	0.7	0.0	0.0
Sus	1996	10.7	10.1	8.9	9.0	7.1	7.6	5.2	5.9	3.2	3.8	1.4	1.6	0.0	0.0
	1997	10.5	9.8	8.8	8.8	7.0	7.4	5.1	5.7	3.2	3.7	1.4	1.5	0.0	0.0
	1998	10.3	9.6	8.7	8.5	6.9	7.2	5.1	5.5	3.2	3.6	1.4	1.5	0.0	0.0
	1999	10.2	9.3	8.5	8.3	6.8	7.0	5.0	5.4	3.1	3.5	1.4	1.5	0.0	0.0
	2000	10.0	9.0	8.4	8.1	6.7	6.8	4.9	5.2	3.1	3.4	1.4	1.4	0.0	0.0
	2001	9.7	8.8	8.2	7.8	6.5	6.6	4.8	5.0	3.1	3.3	1.3	1.4	0.0	0.0
	2002	9.5	8.5	8.1	7.6	6.4	6.4	4.7	4.9	3.0	3.2	1.3	1.4	0.0	0.0
	2003	9.2	8.3	7.8	7.4	6.2	6.2	4.6	4.7	2.9	3.1	1.3	1.3	0.0	0.0
	2004	8.9	8.0	7.6	7.2	6.0	5.9	4.5	4.5	2.9	3.0	1.2	1.3	0.0	0.0
	2005	8.6	7.7	7.3	6.9	5.8	5.8	4.3	4.4	2.8	2.8	1.2	1.2	0.0	0.0
	2006	8.3	7.5	7.1	6.7	5.6	5.6	4.2	4.2	2.7	2.7	1.1	1.2	0.0	0.0
	2007	8.0	7.2	6.8	6.5	5.4	5.4	4.0	4.1	2.6	2.6	1.1	1.1	0.0	0.0
	2008	7.7	7.0	6.6	6.3	5.2	5.2	3.9	3.9	2.5	2.5	1.1	1.1	0.0	0.0
	2009	7.4	6.8	6.4	6.2	5.1	5.1	3.8	3.8	2.4	2.4	1.0	1.1	0.0	0.0
	2010	7.3	6.6	6.2	6.0	5.0	5.0	3.7	3.7	2.4	2.4	1.0	1.0	0.0	0.0
	2011	7.1	6.5	6.2	5.9	4.9	4.9	3.7	3.7	2.4	2.3	1.0	1.0	0.0	0.0
	2012	7.0	6.4	6.1	5.8	4.9	4.9	3.6	3.6	2.3	2.3	1.0	1.0	0.0	0.0
	2013	7.0	6.3	6.0	5.8	4.9	4.8	3.6	3.6	2.3	2.2	1.0	0.9	0.0	0.0
	2014	6.9	6.3	6.0	5.7	4.9	4.8	3.6	3.5	2.3	2.2	1.0	0.9	0.0	0.0
	2015	6.8	6.2	6.0	5.7	4.9	4.8	3.6	3.5	2.3	2.1	1.0	0.9	0.0	0.0
	2016	6.8	6.1	6.0	5.6	4.9	4.7	3.6	3.5	2.3	2.1	1.0	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")
```

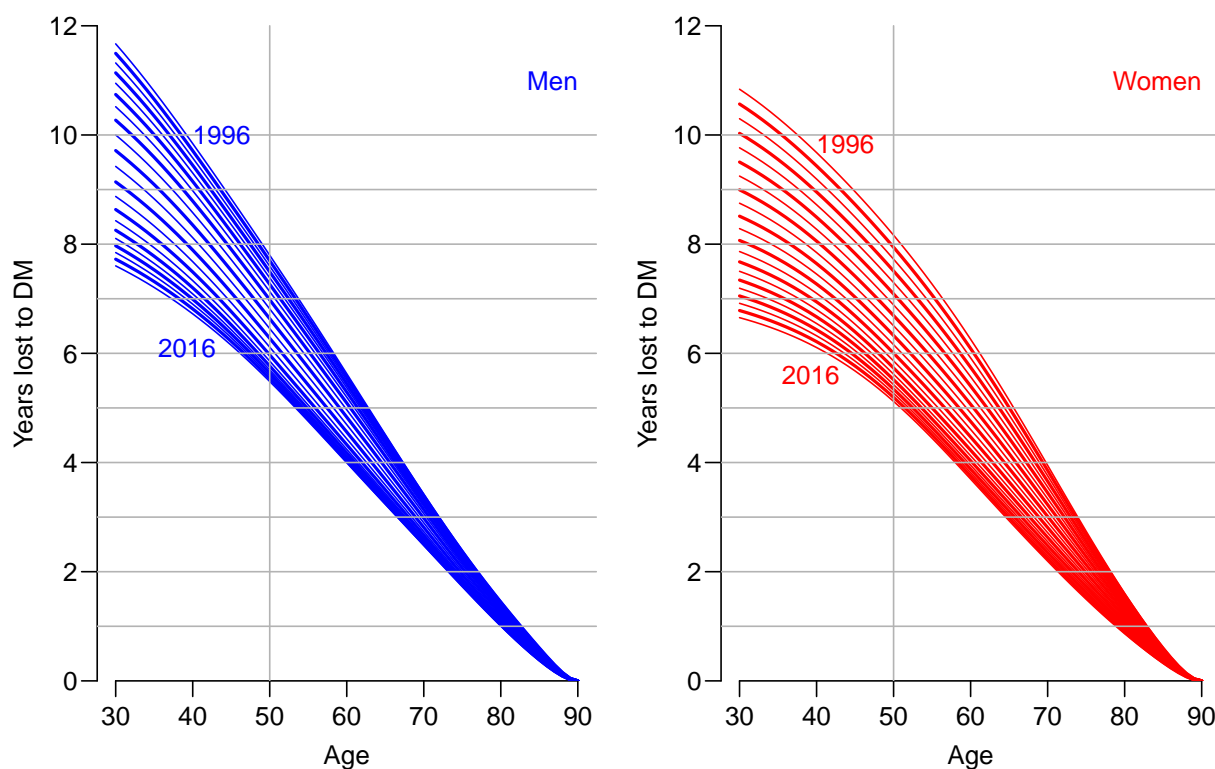


Figure 2.1: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, assuming the persons without diabetes at a given age remain free from diabetes (immunity assumption — not reasonable). The lines refer to date of evaluation;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

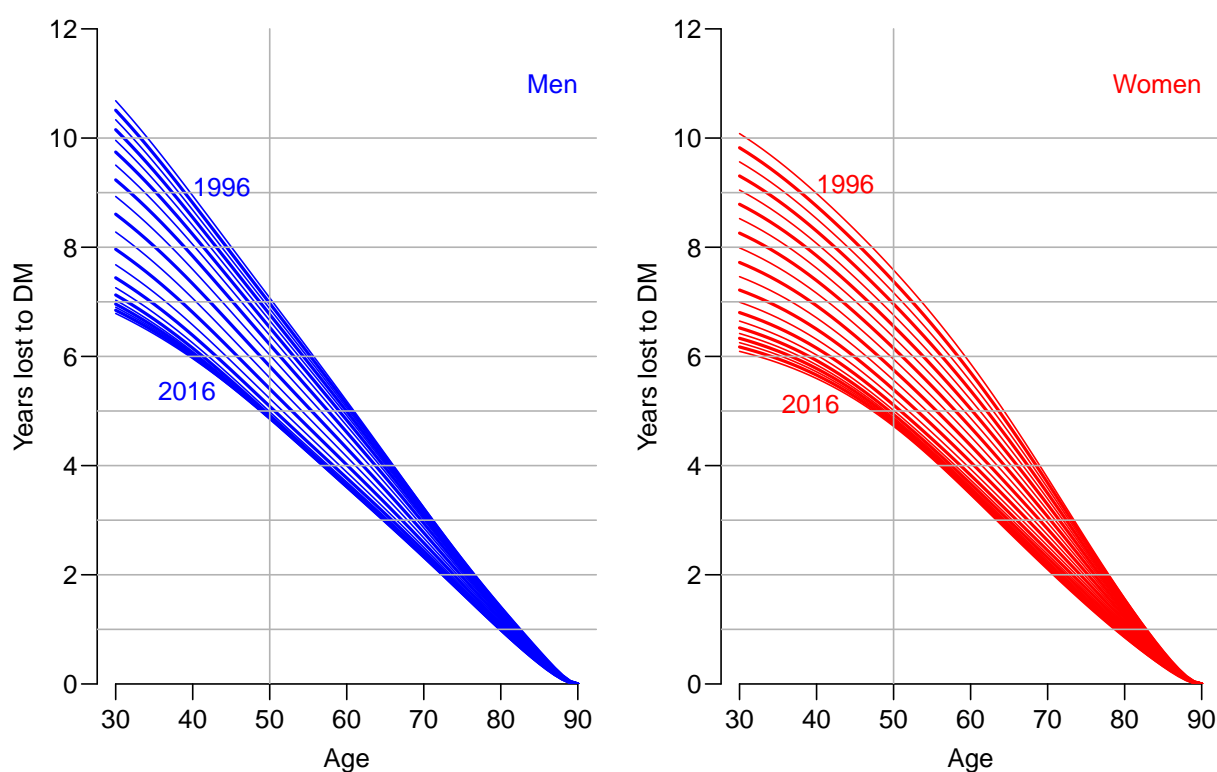


Figure 2.2: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes, allowing the persons without diabetes at a given to contract diabetes and thus be subject to higher mortality. The lines refer to date of evaluation; the top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

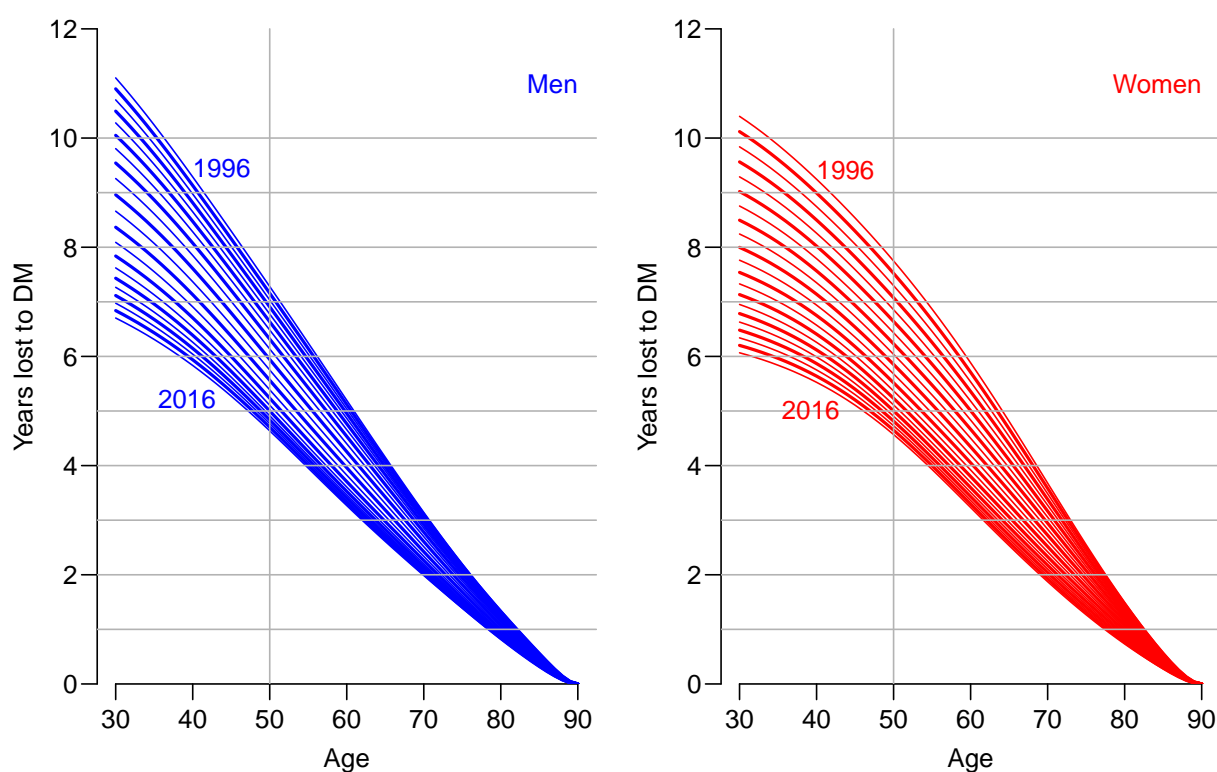


Figure 2.3: *Years of life lost to DM: the difference in expected residual life time at different ages between persons with and without diabetes. Allowance for susceptibility is approximated by using the total population mortality instead of non-DM mortality. The lines refer to date of evaluation; the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

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