Danish data (–2016) and results for the Daffodil project

SDC
September 2018
http://bendixcarstensen.com/SDC/daf
Version 41

Compiled Sunday 16th September, 2018, 17:56
from: `/home/bendix/sdc/proj/daffodil/rep/DKdat.tex`

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Contents

Chapter 1

Analysis of SGLT-2i vs. SU

1.1 Dataset for analysis od SGLT-2i vs SU

First load the relevant package:

```
> options( width=95 )
> library( Epi )
> library( splines )
> library( haven )
> library( Matching )
> clear()
> print( sessionInfo(), l=F )
R version 3.5.0 (2018-04-23)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] Matching_4.9-3 MASS_7.3-49    haven_1.1.1    Epi_2.30

loaded via a namespace (and not attached):
 [1] Rcpp_0.12.16      lattice_0.20-35   zoo_1.8-1         grid_3.5.0        plyr_1.8.4
 [6] magrittr_1.5      etm_0.6-2         pillar_1.2.2      rlang_0.2.0       Matrix_1.2-14
[11] forcats_0.3.0     tools_3.5.0       cmprsk_2.2-7      numDeriv_2016.8-1 survival_2.41-3
[16] parallel_3.5.0    compiler_3.5.0    tibble_1.4.2
```

Then we can read the data:

```
> system.time(
+ mset <- read_sas( "../data/episodes.sas7bdat" ) )
   user  system elapsed
   6.82    0.18   18.72
```

```
> dim( mset )
```

```
[1] 244715     98
```

```
> names( mset )
```

```
                                               ...now input from ../rep/matchSGSU.tex
 [1] "druggr"       "pnr"          "eksd"         "ATC"          "doDM"         "epiN"
 [7] "doIx"         "Ixdr"         "Ixatc"        "lastpr"       "doTm"         "doFL"
[13] "FLdr"         "FLatc"        "deCVDD"       "coD"          "doTIA"        "doAngina"
[19] "doBleed"      "doCOPD"       "doPAD"        "doHF"         "doCancer"     "doDMcompl"
[25] "doNeuro"      "doDKD"        "doDiaEye"     "doHypo"       "doAtrFib"     "doMI"
[31] "doUnstAng"    "doHmStr"      "doDiaFoot"    "doOther"      "doPeriAng"    "doIscStr"
[37] "doAmp"        "doCKD"        "doPCIsten"    "doCABG"       "doKeto"       "doDial"
[43] "doBari"       "sex"          "doBth"        "whBth"        "doDth"        "dSrc"
[49] "dolACE"       "dolSta"       "dolBBl"       "dolARB"       "dolAlA"       "dolDHP"
[55] "dolWtL"       "dolRPA"       "dolWrf"       "dolAsp"       "dolHCD"       "dolTHZ"
[61] "dolCcs"       "dolDXI"       "dolDgo"       "dolAPl"       "dolAmi"       "dolDTI"
[67] "dolNHP"       "dolFla"       "dolMetformin" "dolGLP1"      "dolMetxSGLT2" "dolMetxDPP4"
[73] "dolSGLT2"     "dollongIns"   "dolmixIns"    "dolDPP4"      "dolSU"        "dolintIns"
[79] "dolfastIns"   "dolTZD"       "dolAcarbose"  "dolTZDxDPP4"  "maxH"         "frail"
[85] "recnum"       "C_ADIAG"      "compl"        "C_OPR"        "D_INDDTO"     "V_SENGDAGE"
[91] "deHF"         "deMACE"       "deMI"         "deStr"        "deIscStr"     "deAF"
[97] "deHH"         "deDKD"
```

We subset to SGLT-2i / SU and on the fly convert all dates to fractions of years to facilitate programming:

```
> mset <- cal.yr( subset( as.data.frame( mset ), Ixdr %in% c("SGLT2","SU") ) )
```

We then select the first of these episodes from each person, and exclude those with the other in the baseline. Note that persons where both drugs are initiated the same day, will be excluded entirely, because drugs initiated on the index day are coded as baseline drug with the same date.

```
> nrow( mset )
[1] 36777
```

```
> mset <- mset[order(mset$pnr,mset$doIx),]
> mset <- mset[!duplicated(mset$pnr),]
> mset <- subset( mset, ( Ixdr=="SGLT2" & is.na(dolSU    ) ) |
+                       ( Ixdr=="SU"    & is.na(dolSGLT2) ) )
> with( mset, table(table(pnr)) )

    1
29922
```

Thus we see that we have precisely one episode per person after these exclusions.

To make `FLdr` and `Ixdr` into factors we need some sensible levels:

```
> ( drlab <- read.table( "drlab.txt", header=TRUE, as.is=TRUE ) )
        gr  lab     longlab
1       11  Met   Metformin
2       12   SU Sulfonylurea
3       13  TZD         TZD
4       14  DPP       DPP-4
5       15  GLP       GLP-1
6       16  SGL       SGLT2
7  fastIns fIns     fastIns
8   intIns iIns      intIns
9   mixIns mIns      mixIns
10 longIns lIns     longIns
11      18  Aca    Acarbose
12      19  Meg  Meglitinide
```

```
13     212  M+U       Met+SU
14     213  M+T      Met+TZD
15     214  M+D     Met+DPP4
16     216  M+S    Met+SGLT2
17     218  M+A Met+Acarbose
18     223  U+T       SU+TZD
19     234  D+T     TZD+DPP4
20     246  D+S   DPP4+SGLT2
```

Then we can define the first line and the index drug variables as factors:

```
> mset <- transform( mset, FLdr = factor( FLdr,
+                                          levels = drlab$gr,
+                                          labels = drlab$lab ),
+                           Ixdr = factor( Ixdr ) )
```

We tabulate the index drug versus the first-line drug separately for those where the index date and first-line dates are the same:

```
> print( ftable( with( mset, addmargins(
+                 table( "doIx=doFL"=abs(doIx-doFL)<0.1, FLdr, Ixdr ), 1:2 ) ),
+                 col.vars=c(3,1) ),
+        zero = "." )
     Ixdr      SGLT2                SU
     doIx=doFL FALSE  TRUE   Sum FALSE  TRUE   Sum
FLdr
Met             9175   130  9305 12122   990 13112
SU              2311     .  2311  3078   892  3970
TZD                3     .     3     5     .     5
DPP               33     1    34    46     9    55
GLP               23     2    25    12     .    12
SGL                .    92    92     .     .     .
fIns             182     .   182   124     4   128
iIns             140     .   140    79     3    82
mIns             104     1   105   106     2   108
lIns              20     .    20    16     2    18
Aca                8     .     8    18     .    18
Meg                .     .     .     .     .     .
M+U                .     .     .     .     .     .
M+T               15     .    15    12     .    12
M+D               64     1    65    60    14    74
M+S                .    23    23     .     .     .
M+A                .     .     .     .     .     .
U+T                .     .     .     .     .     .
D+T                .     .     .     .     .     .
D+S                .     .     .     .     .     .
Sum            12078   250 12328 15678  1916 17594
```

We see that among those where the two dates are equal, there are still some where the first line and Index drug are not the same. This is because each initiating drug generates its own episode.

1.2 Baseline tables for all new-starters

We produce an overview of the the exposure status, but first we need a few derived variables, including the indicator of *any* previous CVD:

```
> mset <- transform( mset, age = doIx - doBth,
+                          tff = doIx - doFL,
+                          sex = factor( sex, labels=c("M","F") ),
+                        frail = pmax( frail, 0, na.rm=TRUE ),
+                         maxH = pmax( 0, maxH, na.rm=TRUE ) )
> with( mset, addmargins( table( Ixatc, Ixdr ), 1 ) )
         Ixdr
Ixatc     SGLT2    SU
  A10BB01     0   960
  A10BB03     0   290
  A10BB07     0   753
  A10BB09     0  1753
  A10BB12     0 13490
  A10BD15   313     0
  A10BD16    11     0
  A10BD20   378     0
  A10BK01  7238     0
  A10BK02   357     0
  A10BK03  4031     0
  A10BX02     0   347
  A10BX03     0     1
  Sum     12328 17594
```

We now produce the baseline baseline tables for the entire set of new users, the result is in three tables, `dt.tab` (demographics for `total` sample), `ct.tab` (comobidites for `total` sample) and `mt.tab` (medication for `total` sample).

```
> ptab <- function( var ) cbind( tt <- table( var, mset$Ixdr ),
+                                round( prop.table( tt, 2 ) * 100, 1 ) )
```

1.2.1 Demographics

First the tabulations of the baseline demographics:

```
> t.sex <- with( mset, ptab(sex) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0
                   SGLT2   SU SGLT2   SU
Index = First Line   156 1203   1.3 6.8
```

```
> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                      tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0
                        [,1] [,2] [,3] [,4]
Index not FL: Mean / SD  8.5  6.2  5.3    5
```

```
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
+                                tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age
```

```
                [,1] [,2] [,3] [,4]
Age: Mean / SD 59.8 63.9   11   13
```

```
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )
```

```
       SGLT2   SU SGLT2   SU
2012.5    11  412   0.1  2.3
2013     588 2800   4.8 15.9
2013.5   765 2330   6.2 13.2
2014     930 2486   7.5 14.1
2014.5  1139 1991   9.2 11.3
2015    1616 2229  13.1 12.7
2015.5  1717 1907  13.9 10.8
2016    2848 1927  23.1 11.0
2016.5  2714 1512  22.0  8.6
```

```
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dt.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dt.tab
```

```
                          SGLT2      SU SGLT2   SU
Sex M                    7525.0 10348.0  61.0 58.8
F                        4803.0  7246.0  39.0 41.2
Index = First Line        156.0  1203.0   1.3  6.8
Index not FL: Mean / SD     8.5     6.2   5.3  5.0
Age at index <40          509.0   637.0   4.1  3.6
40                       1782.0  1993.0  14.5 11.3
50                       3787.0  3912.0  30.7 22.2
60                       4007.0  5147.0  32.5 29.3
70                       1960.0  4092.0  15.9 23.3
80+                       283.0  1813.0   2.3 10.3
Age: Mean / SD             59.8    63.9  11.0 13.0
Index date 2012            11.0   412.0   0.1  2.3
2013                     1353.0  5130.0  11.0 29.2
2014                     2069.0  4477.0  16.8 25.4
2015                     3333.0  4136.0  27.0 23.5
2016                     5562.0  3439.0  45.1 19.5
Date of first line 1995   548.0   362.0   4.4  2.1
1996                      196.0   157.0   1.6  0.9
1997                      199.0   181.0   1.6  1.0
1998                      257.0   247.0   2.1  1.4
1999                      341.0   283.0   2.8  1.6
2000                      358.0   329.0   2.9  1.9
2001                      406.0   397.0   3.3  2.3
2002                      421.0   470.0   3.4  2.7
2003                      579.0   603.0   4.7  3.4
2004                      602.0   698.0   4.9  4.0
2005                      685.0   801.0   5.6  4.6
2006                      760.0   879.0   6.2  5.0
2007                      808.0  1004.0   6.6  5.7
2008                      856.0  1151.0   6.9  6.5
2009                      947.0  1218.0   7.7  6.9
```

```
2010                    946.0  1345.0   7.7  7.6
2011                    873.0  1515.0   7.1  8.6
2012                    704.0  1533.0   5.7  8.7
2013                    580.0  1720.0   4.7  9.8
2014                    510.0  1239.0   4.1  7.0
2015                    436.0   944.0   3.5  5.4
2016                    316.0   518.0   2.6  2.9
Frailty 0              8283.0 12644.0  67.2 71.9
1                      4045.0  4950.0  32.8 28.1
```

1.2.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- grep( "do[A-Z]", names( mset ) )
> wh <- wh[4:30]
> names( mset )[wh]
```

```
 [1] "doFL"      "doTIA"     "doAngina"  "doBleed"   "doCOPD"    "doPAD"     "doHF"
 [8] "doCancer"  "doDMcompl" "doNeuro"   "doDKD"     "doDiaEye"  "doHypo"    "doAtrFib"
[15] "doMI"      "doUnstAng" "doHmStr"   "doDiaFoot" "doOther"   "doPeriAng" "doIscStr"
[22] "doAmp"     "doCKD"     "doPCIsten" "doCABG"    "doKeto"    "doDial"
```

```
> comorb <- data.frame( pmax( mset[,wh] < mset[,"doIx"], 0, na.rm=TRUE ) )
> names( comorb ) <- gsub( "do", "prv.", names(comorb) )
> str( comorb )
```

```
'data.frame':        29922 obs. of  27 variables:
 $ prv.FL     : num  1 1 1 1 1 1 1 1 1 1 ...
 $ prv.TIA    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Angina : num  0 1 0 0 0 0 0 1 0 0 ...
 $ prv.Bleed  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.COPD   : num  0 0 0 1 0 0 0 0 0 0 ...
 $ prv.PAD    : num  0 0 0 0 0 0 1 0 0 0 ...
 $ prv.HF     : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Cancer : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.DMcompl: num  0 0 1 0 0 0 0 1 0 0 ...
 $ prv.Neuro  : num  1 0 0 1 0 0 0 1 0 0 ...
 $ prv.DKD    : num  0 0 0 1 0 0 0 0 0 0 ...
 $ prv.DiaEye : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Hypo   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.AtrFib : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.MI     : num  0 0 0 1 0 0 0 0 0 0 ...
 $ prv.UnstAng: num  0 0 0 1 0 0 0 0 0 0 ...
 $ prv.HmStr  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.DiaFoot: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Other  : num  0 0 0 0 0 0 1 0 0 0 ...
 $ prv.PeriAng: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.IscStr : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Amp    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.CKD    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PCIsten: num  0 0 0 1 0 0 0 0 0 0 ...
 $ prv.CABG   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Keto   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Dial   : num  0 0 0 0 0 0 0 0 0 0 ...
```

Later, in the modeling we will need the indicator of *any* previous CVD as well as *any* type of stroke and micro-vascular complications:

```
> comorb$pre.CVD <- with( comorb, pmax( prv.MI,
+                                       prv.UnstAng,
+                                       prv.Angina,
+                                       prv.HF,
+                                       prv.AtrFib,
+                                       prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA,
+                                       prv.PAD ) )
> comorb$pre.Str <- with( comorb, pmax( prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA ) )
> comorb$pre.FPA <- with( comorb, pmax( prv.DiaFoot,
+                                       prv.PeriAng ) )
> comorb$pre.Mic <- with( comorb, pmax( prv.DiaEye,
+                                       prv.DMcompl,
+                                       prv.Neuro,
+                                       prv.DKD,
+                                       prv.DiaFoot,
+                                       prv.PeriAng ) )
```

Note that we name the columns `pre.` to avoid including these in the propensity score estimation.

```
> ct.tab <- cbind(
+ t( sapply( comorb,
+            function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( comorb,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> # remove the dates of recurrent HF
> # wh <- grep( "HF[1-9]", rownames(ct.tab) )
> # ct.tab <- ct.tab[-wh,]
> ct.tab
            SGLT2    SU SGLT2   SU
prv.FL      12172 16391  98.7 93.2
prv.TIA       321   585   2.6  3.3
prv.Angina   1635  2219  13.3 12.6
prv.Bleed     522   894   4.2  5.1
prv.COPD      419   805   3.4  4.6
prv.PAD       599  1061   4.9  6.0
prv.HF        496   880   4.0  5.0
prv.Cancer    590  1284   4.8  7.3
prv.DMcompl  2291  1299  18.6  7.4
prv.Neuro     713   536   5.8  3.0
prv.DKD       461   420   3.7  2.4
prv.DiaEye   1501  1060  12.2  6.0
prv.Hypo      441   371   3.6  2.1
prv.AtrFib    740  1378   6.0  7.8
prv.MI       1003  1405   8.1  8.0
prv.UnstAng   470   640   3.8  3.6
prv.HmStr      96   163   0.8  0.9
prv.DiaFoot   121    98   1.0  0.6
prv.Other     554   791   4.5  4.5
prv.PeriAng   659   453   5.3  2.6
```

```
prv.IscStr    583  1028   4.7  5.8
prv.Amp        13    29   0.1  0.2
prv.CKD        69   434   0.6  2.5
prv.PCIsten   115   140   0.9  0.8
prv.CABG      326   451   2.6  2.6
prv.Keto       75    62   0.6  0.4
prv.Dial        0     8   0.0  0.0
pre.CVD      3681  5603  29.9 31.8
pre.Str       873  1535   7.1  8.7
pre.FPA       734   519   6.0  2.9
pre.Mic      4104  3035  33.3 17.3
```

1.2.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest, restricted to the period after 2011-12-01, one year prior to the first SGLT2 dispensation.

```
> wh <- grep( "dol", names(mset) )
> names( mset )[wh]
 [1] "dolACE"       "dolSta"       "dolBBl"       "dolARB"       "dolAlA"       "dolDHP"
 [7] "dolWtL"       "dolRPA"       "dolWrf"       "dolAsp"       "dolHCD"       "dolTHZ"
[13] "dolCcs"       "dolDXI"       "dolDgo"       "dolAPl"       "dolAmi"       "dolDTI"
[19] "dolNHP"       "dolFla"       "dolMetformin" "dolGLP1"      "dolMetxSGLT2" "dolMetxDPP4"
[25] "dolSGLT2"     "dollongIns"   "dolmixIns"    "dolDPP4"      "dolSU"        "dolintIns"
[31] "dolfastIns"   "dolTZD"       "dolAcarbose"  "dolTZDxDPP4"
> codisp <- data.frame( pmax( mset[,wh] > ( mset[,"doIx"] - 1 ), 0, na.rm=TRUE ) )
> names( codisp ) <- gsub( "dol", "had.", names(codisp) )
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )
[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"
> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )
[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
> ( names( codisp )[wh.cvd <- c(10,2,wh.hyp)] )
[1] "had.Asp" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"
> mt.tab <- cbind(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mt.tab
```

```
               SGLT2    SU SGLT2    SU
had.ACE         4676  5886  37.9  33.5
had.Sta         9176 10956  74.4  62.3
had.BBl         3333  4769  27.0  27.1
had.ARB         4299  4459  34.9  25.3
had.AlA          644   896   5.2   5.1
had.DHP         3704  4613  30.0  26.2
had.WtL           89    77   0.7   0.4
had.RPA          791  1146   6.4   6.5
had.Wrf          508  1102   4.1   6.3
had.Asp         4301  5362  34.9  30.5
had.HCD         1703  2850  13.8  16.2
had.THZ         1877  2630  15.2  14.9
had.Ccs          662  1364   5.4   7.8
had.DXI          196   247   1.6   1.4
had.Dgo          307   762   2.5   4.3
had.APl          122   285   1.0   1.6
had.Ami           30    71   0.2   0.4
had.DTI          153   263   1.2   1.5
had.NHP          212   256   1.7   1.5
had.Fla           10    19   0.1   0.1
had.Metformin   9881 14057  80.2  79.9
had.GLP1        4054  1332  32.9   7.6
had.MetxSGLT2    702     0   5.7   0.0
had.MetxDPP4    2702  2019  21.9  11.5
had.SGLT2      11626     0  94.3   0.0
had.longIns     2632   376  21.3   2.1
had.mixIns      1078   222   8.7   1.3
had.DPP4        2137  2264  17.3  12.9
had.SU             0 17594   0.0 100.0
had.intIns       935   332   7.6   1.9
had.fastIns     1052   229   8.5   1.3
had.TZD           28    27   0.2   0.2
had.Acarbose      15    35   0.1   0.2
had.TZDxDPP4       1     0   0.0   0.0
got.Ins         4147   952  33.6   5.4
got.Hyp         9593 12224  77.8  69.5
got.CVD        11229 14595  91.1  83.0
```

1.3 Propensity scoring

We now make a logistic regression of the indicator of SGLT2 assignment versus SU assignment. For convenience we append the just created data frames of the indicators we will use in the analysis:

```
> mset <- cbind( mset, comorb, codisp )
> names( mset )
 [1] "druggr"     "pnr"        "eksd"       "ATC"        "doDM"
 [6] "epiN"       "doIx"       "Ixdr"       "Ixatc"      "lastpr"
[11] "doTm"       "doFL"       "FLdr"       "FLatc"      "deCVDD"
[16] "coD"        "doTIA"      "doAngina"   "doBleed"    "doCOPD"
[21] "doPAD"      "doHF"       "doCancer"   "doDMcompl"  "doNeuro"
[26] "doDKD"      "doDiaEye"   "doHypo"     "doAtrFib"   "doMI"
[31] "doUnstAng"  "doHmStr"    "doDiaFoot"  "doOther"    "doPeriAng"
[36] "doIscStr"   "doAmp"      "doCKD"      "doPCIsten"  "doCABG"
```

```
 [41] "doKeto"        "doDial"        "doBari"        "sex"           "doBth"
 [46] "whBth"         "doDth"         "dSrc"          "dolACE"        "dolSta"
 [51] "dolBBl"        "dolARB"        "dolAlA"        "dolDHP"        "dolWtL"
 [56] "dolRPA"        "dolWrf"        "dolAsp"        "dolHCD"        "dolTHZ"
 [61] "dolCcs"        "dolDXI"        "dolDgo"        "dolAPl"        "dolAmi"
 [66] "dolDTI"        "dolNHP"        "dolFla"        "dolMetformin"  "dolGLP1"
 [71] "dolMetxSGLT2"  "dolMetxDPP4"   "dolSGLT2"      "dollongIns"    "dolmixIns"
 [76] "dolDPP4"       "dolSU"         "dolintIns"     "dolfastIns"    "dolTZD"
 [81] "dolAcarbose"   "dolTZDxDPP4"   "maxH"          "frail"         "recnum"
 [86] "C_ADIAG"       "compl"         "C_OPR"         "D_INDDTO"      "V_SENGDAGE"
 [91] "deHF"          "deMACE"        "deMI"          "deStr"         "deIscStr"
 [96] "deAF"          "deHH"          "deDKD"         "age"           "tff"
[101] "prv.FL"        "prv.TIA"       "prv.Angina"    "prv.Bleed"     "prv.COPD"
[106] "prv.PAD"       "prv.HF"        "prv.Cancer"    "prv.DMcompl"   "prv.Neuro"
[111] "prv.DKD"       "prv.DiaEye"    "prv.Hypo"      "prv.AtrFib"    "prv.MI"
[116] "prv.UnstAng"   "prv.HmStr"     "prv.DiaFoot"   "prv.Other"     "prv.PeriAng"
[121] "prv.IscStr"    "prv.Amp"       "prv.CKD"       "prv.PCIsten"   "prv.CABG"
[126] "prv.Keto"      "prv.Dial"      "pre.CVD"       "pre.Str"       "pre.FPA"
[131] "pre.Mic"       "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"
[136] "had.AlA"       "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"
[141] "had.Asp"       "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"
[146] "had.Dgo"       "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"
[151] "had.Fla"       "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"
[156] "had.SGLT2"     "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"
[161] "had.intIns"    "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"
[166] "got.Ins"       "got.Hyp"       "got.CVD"
```

With this in place it is quite easy to fit a propensity score model because we can easily fish out the relevant variables:

```
> table( mset$Ixdr )
SGLT2    SU
12328 17594
> ( prv <- grep( "prv", names(mset) ) )
 [1] 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122
[23] 123 124 125 126 127
> ( had <- grep( "had", names(mset) ) )
 [1] 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153
[23] 154 155 156 157 158 159 160 161 162 163 164 165
> rmd <- c( grep( "SGL", names( mset )[had] ),
+          grep( "SU" , names( mset )[had] ) )
> had <- had[-rmd]
> names( mset )[had]
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxDPP4"  "had.longIns"   "had.mixIns"
[26] "had.DPP4"      "had.intIns"    "had.fastIns"   "had.TZD"       "had.Acarbose"
[31] "had.TZDxDPP4"
> names( mset )[prv]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye"
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"
```

```
> system.time(
+ pr.0 <- glm( ( Ixdr == "SGLT2" ) ~
+              sex + age + frail + doIx + doFL +
+              as.matrix(mset[,prv]) +  as.matrix(mset[,had]),
+              family = binomial,
+              data = mset, maxit = 100 ) )
```

```
   user  system elapsed
   1.75    0.11    1.86
```

```
> print( summary( pr.0 ), digits = 3 )
```

```
Call:
glm(formula = (Ixdr == "SGLT2") ~ sex + age + frail + doIx +
    doFL + as.matrix(mset[, prv]) + as.matrix(mset[, had]), family = binomial,
    data = mset, maxit = 100)

Deviance Residuals:
   Min      1Q  Median      3Q     Max
-4.001  -0.751  -0.357   0.756   3.185

Coefficients:
                                     Estimate Std. Error z value Pr(>|z|)
(Intercept)                         -1.45e+03   2.78e+01  -52.23  < 2e-16 ***
sexF                                -4.46e-02   3.09e-02   -1.44  0.14887
age                                 -2.92e-02   1.44e-03  -20.29  < 2e-16 ***
frail                               -2.28e-03   3.46e-02   -0.07  0.94737
doIx                                 7.18e-01   1.40e-02   51.41  < 2e-16 ***
doFL                                 2.34e-03   3.58e-03    0.65  0.51351
as.matrix(mset[, prv])prv.FL         5.50e-01   9.91e-02    5.55  2.9e-08 ***
as.matrix(mset[, prv])prv.TIA       -6.98e-02   9.41e-02   -0.74  0.45811
as.matrix(mset[, prv])prv.Angina    -4.17e-02   5.31e-02   -0.79  0.43235
as.matrix(mset[, prv])prv.Bleed     -7.05e-02   7.21e-02   -0.98  0.32803
as.matrix(mset[, prv])prv.COPD      -9.39e-02   8.10e-02   -1.16  0.24689
as.matrix(mset[, prv])prv.PAD       -1.42e-01   7.05e-02   -2.02  0.04359 *
as.matrix(mset[, prv])prv.HF        -7.02e-02   8.47e-02   -0.83  0.40706
as.matrix(mset[, prv])prv.Cancer    -1.17e-01   6.56e-02   -1.78  0.07531 .
as.matrix(mset[, prv])prv.DMcompl    1.92e-01   5.12e-02    3.75  0.00017 ***
as.matrix(mset[, prv])prv.Neuro      1.52e-01   7.83e-02    1.94  0.05216 .
as.matrix(mset[, prv])prv.DKD       -2.17e-01   9.35e-02   -2.33  0.02002 *
as.matrix(mset[, prv])prv.DiaEye     6.93e-02   5.78e-02    1.20  0.23035
as.matrix(mset[, prv])prv.Hypo      -8.65e-02   9.90e-02   -0.87  0.38250
as.matrix(mset[, prv])prv.AtrFib     4.82e-02   8.66e-02    0.56  0.57788
as.matrix(mset[, prv])prv.MI         2.46e-02   6.56e-02    0.38  0.70754
as.matrix(mset[, prv])prv.UnstAng   -1.04e-01   8.80e-02   -1.19  0.23574
as.matrix(mset[, prv])prv.HmStr      3.29e-03   1.59e-01    0.02  0.98350
as.matrix(mset[, prv])prv.DiaFoot    2.00e-01   1.88e-01    1.07  0.28628
as.matrix(mset[, prv])prv.Other     -1.56e-01   8.13e-02   -1.92  0.05519 .
as.matrix(mset[, prv])prv.PeriAng    2.39e-01   8.58e-02    2.78  0.00537 **
as.matrix(mset[, prv])prv.IscStr    -1.43e-01   7.85e-02   -1.83  0.06762 .
as.matrix(mset[, prv])prv.Amp       -1.28e+00   4.88e-01   -2.62  0.00868 **
as.matrix(mset[, prv])prv.CKD       -1.33e+00   1.66e-01   -8.01  1.1e-15 ***
as.matrix(mset[, prv])prv.PCIsten    1.13e-01   1.71e-01    0.66  0.50765
as.matrix(mset[, prv])prv.CABG       6.18e-02   1.09e-01    0.57  0.56931
as.matrix(mset[, prv])prv.Keto       1.22e-03   2.32e-01    0.01  0.99582
as.matrix(mset[, prv])prv.Dial      -1.08e+01   9.06e+01   -0.12  0.90477
as.matrix(mset[, had])had.ACE        2.41e-01   3.54e-02    6.82  8.8e-12 ***
as.matrix(mset[, had])had.Sta        2.42e-01   3.41e-02    7.11  1.2e-12 ***
as.matrix(mset[, had])had.BBl        3.12e-03   3.99e-02    0.08  0.93778
```

```
as.matrix(mset[, had])had.ARB        4.27e-01   3.69e-02   11.57  < 2e-16 ***
as.matrix(mset[, had])had.AlA       -2.82e-03   7.41e-02   -0.04  0.96962
as.matrix(mset[, had])had.DHP        3.08e-02   3.55e-02    0.87  0.38689
as.matrix(mset[, had])had.WtL        6.42e-01   1.93e-01    3.32  0.00090 ***
as.matrix(mset[, had])had.RPA       -2.63e-02   6.99e-02   -0.38  0.70625
as.matrix(mset[, had])had.Wrf       -3.95e-02   9.00e-02   -0.44  0.66058
as.matrix(mset[, had])had.Asp        8.53e-02   3.71e-02    2.30  0.02130 *
as.matrix(mset[, had])had.HCD       -1.13e-01   4.99e-02   -2.26  0.02380 *
as.matrix(mset[, had])had.THZ        5.56e-02   4.28e-02    1.30  0.19406
as.matrix(mset[, had])had.Ccs       -3.34e-02   6.29e-02   -0.53  0.59499
as.matrix(mset[, had])had.DXI        1.85e-01   1.29e-01    1.44  0.14968
as.matrix(mset[, had])had.Dgo       -2.28e-01   1.09e-01   -2.09  0.03653 *
as.matrix(mset[, had])had.APl       -1.33e-01   1.49e-01   -0.89  0.37461
as.matrix(mset[, had])had.Ami       -4.68e-01   2.81e-01   -1.66  0.09606 .
as.matrix(mset[, had])had.DTI        3.80e-02   1.40e-01    0.27  0.78610
as.matrix(mset[, had])had.NHP        3.05e-01   1.23e-01    2.48  0.01306 *
as.matrix(mset[, had])had.Fla       -1.62e-01   4.61e-01   -0.35  0.72505
as.matrix(mset[, had])had.Metformin -4.48e-02   4.33e-02   -1.03  0.30123
as.matrix(mset[, had])had.GLP1       1.65e+00   4.37e-02   37.73  < 2e-16 ***
as.matrix(mset[, had])had.MetxDPP4   1.24e+00   4.38e-02   28.25  < 2e-16 ***
as.matrix(mset[, had])had.longIns    2.19e+00   7.03e-02   31.22  < 2e-16 ***
as.matrix(mset[, had])had.mixIns     1.97e+00   9.15e-02   21.53  < 2e-16 ***
as.matrix(mset[, had])had.DPP4       7.66e-01   4.02e-02   19.05  < 2e-16 ***
as.matrix(mset[, had])had.intIns     1.31e+00   8.40e-02   15.55  < 2e-16 ***
as.matrix(mset[, had])had.fastIns    4.95e-01   1.01e-01    4.90  9.7e-07 ***
as.matrix(mset[, had])had.TZD        5.01e-01   3.39e-01    1.48  0.13957
as.matrix(mset[, had])had.Acarbose   2.43e-03   3.82e-01    0.01  0.99491
as.matrix(mset[, had])had.TZDxDPP4   9.98e+00   3.25e+02    0.03  0.97549
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 40549  on 29921  degrees of freedom
Residual deviance: 28236  on 29858  degrees of freedom
AIC: 28364

Number of Fisher Scoring iterations: 11
```

With this fitted model we can now use the fitted values as propensity scores.

1.4 Propensity score matching

Based on this propensity score we take a matched sample of 1 per SGLT-2 user — note that we explicitly set a seed in order to get a fully reproducible code:

```
> set.seed( 1952 )
> system.time(
+ mt <- Match( Tr = (mset$Ixdr=="SGLT2"),
+               X = fitted( pr.0 ),
+               M = 1,
+         replace = FALSE,
+           exact = FALSE,
+            ties = FALSE,
+         caliper = 0.2 ) )
```

```
   user  system elapsed 
  17.58    0.00   17.58 
> str( mt )
List of 23
 $ est               : num [1, 1] 0
 $ se                : NULL
 $ est.noadj         : num 0
 $ se.standard       : num 0
 $ se.cond           : NULL
 $ mdata             :List of 4
  ..$ Y                          : num [1:13712] 0 0 0 0 0 0 0 0 0 0 ...
  ..$ Tr                         : num [1:13712] 1 1 1 1 1 1 1 1 1 1 ...
  ..$ X                          : num [1:2, 1:6856] 0.823 0.822 0.982 0.981 0.982 ...
  .. ..- attr(*, "dimnames")=List of 2
  .. .. ..$ : NULL
  .. .. ..$ : chr [1:6856] "5" "7" "16" "19" ...
  ..$ orig.weighted.treated.nobs: num 12328
 $ index.treated     : num [1:6856] 1 2 3 4 5 8 9 10 13 15 ...
 $ index.control     : num [1:6856] 13743 7222 29782 3360 7498 ...
 $ index.dropped     : int [1:5472] 1426 1620 1664 1667 1771 1824 1878 1929 1952 1984 ...
 $ weights           : num [1:6856] 1 1 1 1 1 1 1 1 1 1 ...
 $ orig.nobs         : int 29922
 $ orig.wnobs        : num 29922
 $ orig.treated.nobs: int 12328
 $ nobs              : int 29922
 $ wnobs             : num 6856
 $ caliper           : num 0.2
 $ ecaliper          : num 0.0591
 $ exact             : logi FALSE
 $ ndrops            : num 5472
 $ ndrops.matches    : num 5472
 $ MatchLoopC        : num [1:6856, 1:6] 1 2 3 4 5 8 9 10 13 15 ...
 $ version           : chr "fast"
 $ estimand          : chr "ATT"
 - attr(*, "class")= chr "Match"
```

The resulting matching (`index.`-variables) refers to rows in `mset`:

```
> addmargins( rbind(
+ table( mset$Ixdr[unique(mt$index.treated)] ),
+ table( mset$Ixdr[unique(mt$index.control)] ) ), 2 )
     SGLT2   SU  Sum
[1,]  6856    0 6856
[2,]     0 6856 6856
```

We just use the index numbers for the treated as factor levels for the match-factor (we shall not use the factor though):

```
> tnum <- mt$index.treated
> cnum <- mt$index.control
> # a numeric with the index number of SGLT-2 for persons matched up
> mf <- rep( NA, nrow(mset) )
> mf[tnum] <- tnum
> mf[cnum] <- tnum
> # create a factor of this and tabulate
> mset <- transform( mset, mfac = factor(mf),
+                          psco = fitted(pr.0) )
> ( mtab <- with( mset, table( Ixdr, !is.na(mfac), useNA="ifany" ) ) )
```

```
Ixdr    FALSE  TRUE
  SGLT2  5472  6856
  SU    10738  6856
```

```
> round( cbind( rbind( cbind( mtab,
+                              pctab( mtab ) ),
+                       NA,
+                       NA),
+                pctab( mtab, margin=1 ) )[-3,], 1 )
```

```
Ixdr      FALSE    TRUE     All       N
  SGLT2    44.4    55.6   100.0 12328.0
  SU       61.0    39.0   100.0 17594.0

Ixdr      FALSE    TRUE
  SGLT2    33.8    50.0
  SU       66.2    50.0
  All     100.0   100.0
  N     16210.0 13712.0
      FALSE TRUE FALSE TRUE All      N   FALSE  TRUE
SGLT2  5472 6856  44.4 55.6 100 12328    33.8    50
SU    10738 6856  61.0 39.0 100 17594    66.2    50
         NA   NA    NA   NA  NA     NA 16210.0 13712
```

We can see that not all persons can be matched with a caliper of 0.2; we can compare the propensity score among the matched and non-matched SGLT-2 patients:

```
> par( mar=c(3,3,1,1),mgp=c(3,1,0)/1.6,las=1,bty="n" )
> plot( mset$psco[mt$index.treated],
+       mset$psco[mt$index.control],
+       pch=16, cex=0.3 ,
+       xlim=0:1, xlab="SGLT-2i propensity score",
+       ylim=0:1, ylab="SU propensity score" )
```

For the use in further analyses we save a version for later use:

```
> oset <- mset
> pscore <- table( floor( oset$psco*100 ), oset$Ixdr )
```

Finally we make a dataset restricted to the matched persons:

```
> mset <- subset( oset, !is.na(mfac) )
> psmatch <- table( floor( mset$psco*100 ), mset$Ixdr )
> head( pscore )
```

```
   SGLT2  SU
  0     2  64
  1     2 218
  2     4 382
  3    14 519
  4    29 625
  5    31 678
```

```
> head( psmatch )
```

```
   SGLT2 SU
  0     2  2
  1     2  2
  2     4  4
  3    14 14
  4    29 28
  5    31 32
```

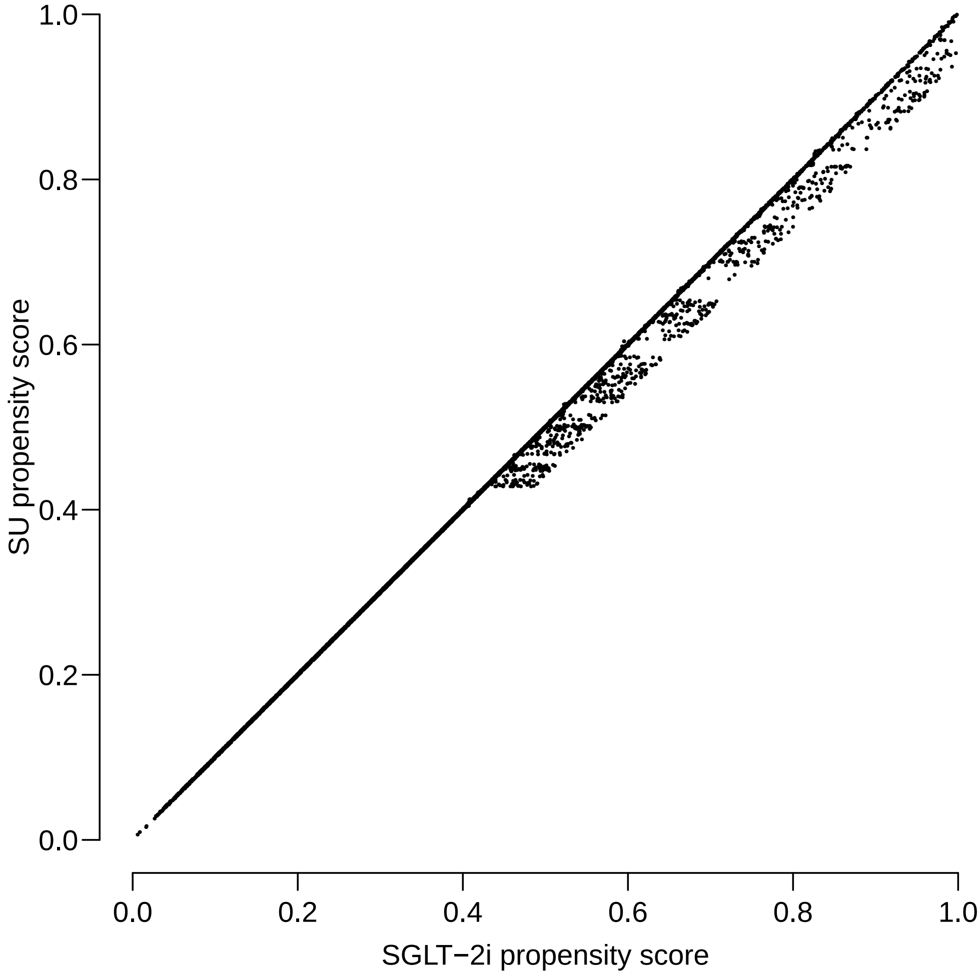

Figure 1.1: *Propensity scores from 1:1 matching; each matched set is represented by a dots.*
`./matchSGSU-cmp-ps`

```
> save( oset, mset, pscore, psmatch, file = "adatSGSU.Rda" )
> load( file = "adatSGSU.Rda" )
```

We also make histograms of the propensity scores, both for the original data and for the matched persons

```
> tt <- pscore
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
> head(tt)
                SGLT2        SU
0 -0.1622323 0.1622323  3.637604
1 -0.1622323 0.1622323 12.390588
2 -0.3244646 0.3244646 21.711947
3 -1.1356262 1.1356262 29.498693
4 -2.3523686 2.3523686 35.523474
5 -2.5146009 2.5146009 38.535864
> nam <- colnames( tt )[-1]
> clr <- c("transparent","red","blue")
```

```
> # we use the undocumented feature of boxplot that you can get stacked
> # bars starting in the negative by giving negative numbers to the first
> # column. But it will mysteriously ignore the first element of col...
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-65,65),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=0 )
```

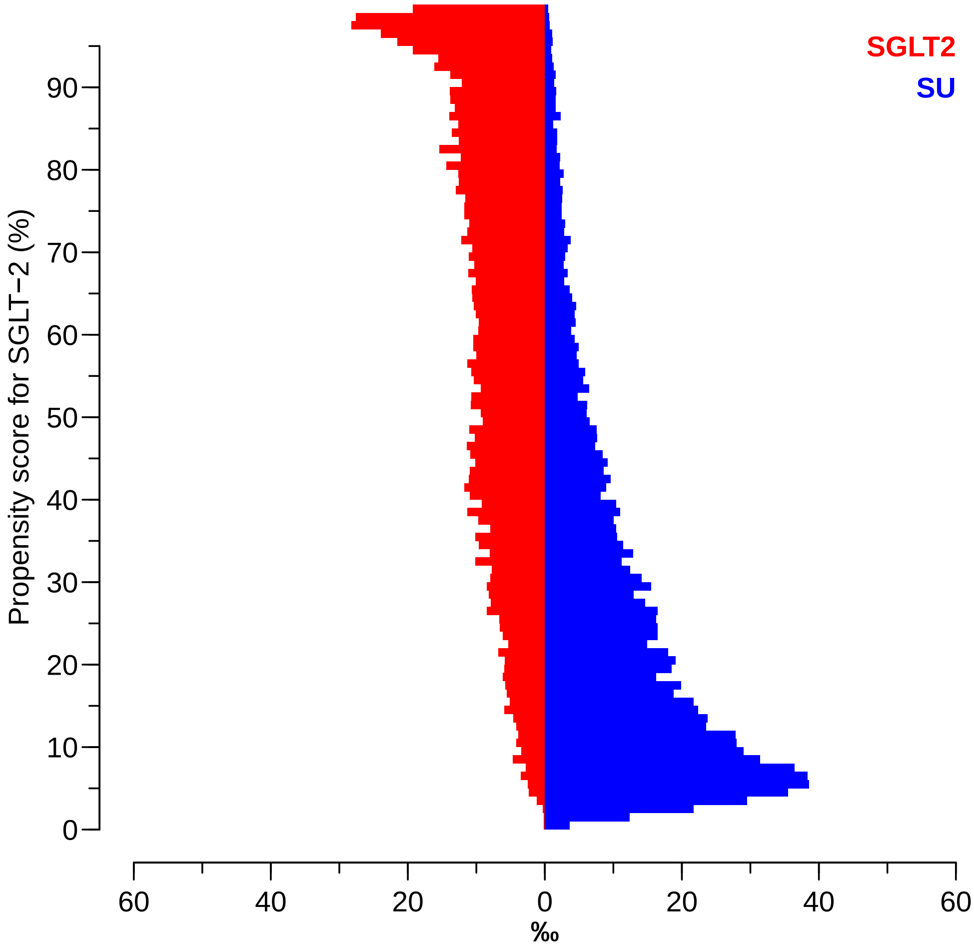

Figure 1.2: *Propensity scores for the SGLT-2 group (left, percent) and other groups (right, ‰) in the 1:3 propensity score matched study.* `./matchSGSU-pscoreo`

```
> tt <- psmatch
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
```

```
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-25,25),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=10 )
```

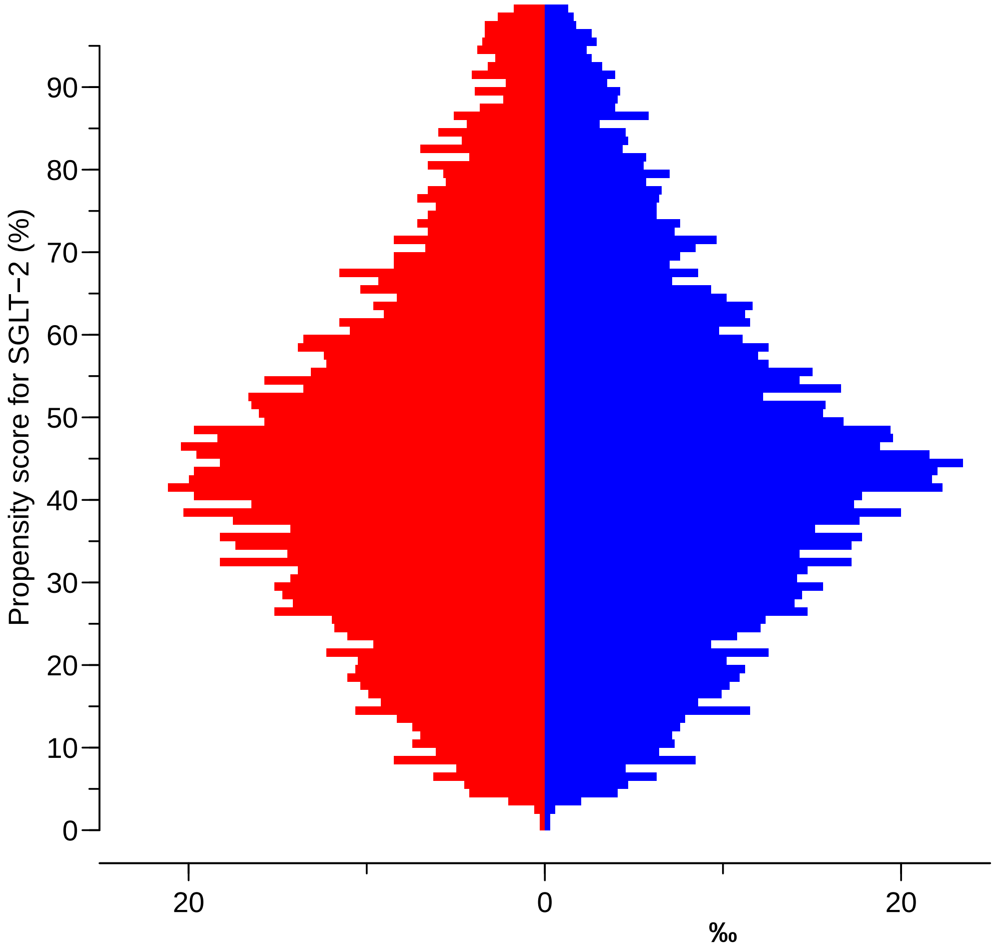

Figure 1.3: *Propensity scores for the SGLT-2 group resp. SU group in the 1:1 propensity score matched study.* `./matchSGSU-pscorem`

1.5 Baseline tables for propensity matched persons

We have the matched sets in the dataframe `mset`, so we can almost verbatim reuse the code doing the tables for the original sample, except for the names of the resulting tables: `dm.tab` (demographics for `matched` sample), `cm.tab` (comobidites for `matched` sample) and `mm.tab` (medication for `matched` sample).

1.5.1 Demographics

First the tabulations of the baseline demographics:

```
> t.sex <- with( mset, ptab( sex ) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0
```

```
                   SGLT2  SU SGLT2  SU
Index = First Line   154 128   2.2 1.9
```

```
> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                      tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0
```

```
                        [,1] [,2] [,3] [,4]
Index not FL: Mean / SD    7    7  4.8  5.1
```

```
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
+                                tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age
```

```
               [,1] [,2] [,3] [,4]
Age: Mean / SD 60.8 60.7 11.2 12.5
```

```
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )
```

```
       SGLT2   SU SGLT2   SU
2012.5     8   40   0.1  0.6
2013     458  430   6.7  6.3
2013.5   565  499   8.2  7.3
2014     665  666   9.7  9.7
2014.5   740  680  10.8  9.9
2015     965  986  14.1 14.4
2015.5   899 1004  13.1 14.6
2016    1376 1303  20.1 19.0
2016.5  1180 1248  17.2 18.2
```

```
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dm.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dm.tab
```

```
                         SGLT2     SU SGLT2   SU
Sex M                   4132.0 4111.0  60.3 60.0
F                       2724.0 2745.0  39.7 40.0
Index = First Line       154.0  128.0   2.2  1.9
Index not FL: Mean / SD    7.0    7.0   4.8  5.1
```

```
Age at index <40         230.0  360.0   3.4  5.3
40                       940.0  999.0  13.7 14.6
50                      1950.0 1771.0  28.4 25.8
60                      2285.0 2087.0  33.3 30.4
70                      1226.0 1293.0  17.9 18.9
80+                      225.0  346.0   3.3  5.0
Age: Mean / SD            60.8   60.7  11.2 12.5
Index date 2012            8.0   40.0   0.1  0.6
2013                    1023.0  929.0  14.9 13.6
2014                    1405.0 1346.0  20.5 19.6
2015                    1864.0 1990.0  27.2 29.0
2016                    2556.0 2551.0  37.3 37.2
Date of first line 1995  167.0  158.0   2.4  2.3
1996                      68.0   73.0   1.0  1.1
1997                      73.0   92.0   1.1  1.3
1998                      87.0  107.0   1.3  1.6
1999                     130.0  135.0   1.9  2.0
2000                     133.0  149.0   1.9  2.2
2001                     157.0  172.0   2.3  2.5
2002                     157.0  194.0   2.3  2.8
2003                     270.0  269.0   3.9  3.9
2004                     291.0  296.0   4.2  4.3
2005                     352.0  329.0   5.1  4.8
2006                     407.0  375.0   5.9  5.5
2007                     461.0  412.0   6.7  6.0
2008                     490.0  467.0   7.1  6.8
2009                     560.0  464.0   8.2  6.8
2010                     616.0  548.0   9.0  8.0
2011                     569.0  557.0   8.3  8.1
2012                     496.0  501.0   7.2  7.3
2013                     430.0  441.0   6.3  6.4
2014                     362.0  395.0   5.3  5.8
2015                     332.0  412.0   4.8  6.0
2016                     248.0  310.0   3.6  4.5
Frailty 0               4934.0 4977.0  72.0 72.6
1                       1922.0 1879.0  28.0 27.4
```

1.5.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- match( rownames(ct.tab), names( mset ) )
> names( mset )[wh]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye"
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"    "pre.CVD"     "pre.Str"     "pre.FPA"
[31] "pre.Mic"
```

```
> comorb <- mset[,wh]
> cm.tab <- cbind(
+ t( sapply( comorb,
+             function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
```

```
+ t( sapply( comorb,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> cm.tab
            SGLT2   SU SGLT2   SU
prv.FL       6702 6728  97.8 98.1
prv.TIA       184  175   2.7  2.6
prv.Angina    842  831  12.3 12.1
prv.Bleed     310  300   4.5  4.4
prv.COPD      252  263   3.7  3.8
prv.PAD       338  331   4.9  4.8
prv.HF        266  255   3.9  3.7
prv.Cancer    365  357   5.3  5.2
prv.DMcompl   760  722  11.1 10.5
prv.Neuro     270  254   3.9  3.7
prv.DKD       187  179   2.7  2.6
prv.DiaEye    543  532   7.9  7.8
prv.Hypo      161  163   2.3  2.4
prv.AtrFib    429  409   6.3  6.0
prv.MI        515  501   7.5  7.3
prv.UnstAng  228  245   3.3  3.6
prv.HmStr      56   50   0.8  0.7
prv.DiaFoot    40   39   0.6  0.6
prv.Other     283  286   4.1  4.2
prv.PeriAng   227  232   3.3  3.4
prv.IscStr    331  321   4.8  4.7
prv.Amp         6    7   0.1  0.1
prv.CKD        48   40   0.7  0.6
prv.PCIsten    52   49   0.8  0.7
prv.CABG      155  170   2.3  2.5
prv.Keto       30   33   0.4  0.5
prv.Dial        0    0   0.0  0.0
pre.CVD      2004 1907  29.2 27.8
pre.Str       499  482   7.3  7.0
pre.FPA       258  260   3.8  3.8
pre.Mic      1579 1500  23.0 21.9
```

1.5.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest — well, only in the period after 2011-12-01, one year prior to the first SGLT2 dispensation.

```
> wh <- grep( "had.", names( mset ) )
> names( mset )[wh]
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"
> codisp <- mset[,wh]
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )
[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"
> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )
```

```
[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> ( names( codisp )[wh.cvd <- c(8,2,wh.hyp)] )
```

```
[1] "had.RPA" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )
```

```
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"
```

```
> mm.tab <- cbind(
+ t( sapply( codisp,
+           function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+           function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mm.tab
```

```
              SGLT2   SU SGLT2    SU
had.ACE        2467 2435  36.0  35.5
had.Sta        4779 4796  69.7  70.0
had.BBl        1759 1747  25.7  25.5
had.ARB        2083 2106  30.4  30.7
had.AlA         328  321   4.8   4.7
had.DHP        1897 1883  27.7  27.5
had.WtL          43   46   0.6   0.7
had.RPA         411  402   6.0   5.9
had.Wrf         293  264   4.3   3.9
had.Asp        2134 2117  31.1  30.9
had.HCD         891  862  13.0  12.6
had.THZ         977 1017  14.3  14.8
had.Ccs         432  437   6.3   6.4
had.DXI         118  108   1.7   1.6
had.Dgo         194  179   2.8   2.6
had.APl          80   80   1.2   1.2
had.Ami          20   21   0.3   0.3
had.DTI          89   95   1.3   1.4
had.NHP         108  100   1.6   1.5
had.Fla           7    8   0.1   0.1
had.Metformin  5454 5484  79.6  80.0
had.GLP1       1194 1127  17.4  16.4
had.MetxSGLT2   418    0   6.1   0.0
had.MetxDPP4   1462 1464  21.3  21.4
had.SGLT2      6438    0  93.9   0.0
had.longIns     416  363   6.1   5.3
had.mixIns      227  192   3.3   2.8
had.DPP4       1306 1311  19.0  19.1
had.SU            0 6856   0.0 100.0
had.intIns      245  234   3.6   3.4
had.fastIns     182  164   2.7   2.4
had.TZD          16   14   0.2   0.2
```

```
had.Acarbose     10   10   0.1   0.1
had.TZDxDPP4      0    0   0.0   0.0
got.Ins         871  757  12.7  11.0
got.Hyp        5051 4976  73.7  72.6
got.CVD        6008 5899  87.6  86.0
```

1.6 Overview of pre- and post matching

The number of persons and episodes:

```
> addmargins( with( oset, table(table(pnr)) ) )
    1   Sum
29922 29922
```

```
> addmargins(
+ with( oset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4      0     1   Sum
  0       0 17594 17594
  1   12328     0 12328
  Sum 12328 17594 29922
```

```
> addmargins( with( mset, table(table(pnr)) ) )
    1   Sum
13712 13712
```

```
> addmargins(
+ with( mset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4      0     1   Sum
  0       0  6856  6856
  1    6856     0  6856
  Sum  6856  6856 13712
```

The best overview is created if we list the tables for the matched and un-matched next to each other. However we first check that that have the same sets of rows:

```
> identical( rownames(dt.tab), rownames(dm.tab) )
[1] TRUE
```

```
> identical( rownames(ct.tab), rownames(cm.tab) )
[1] TRUE
```

```
> identical( rownames(mt.tab), rownames(mm.tab) )
[1] TRUE
```

```
> cbind( dt.tab, dm.tab )
                         SGLT2      SU SGLT2   SU  SGLT2      SU SGLT2   SU
Sex M                   7525.0 10348.0  61.0 58.8 4132.0 4111.0  60.3 60.0
F                       4803.0  7246.0  39.0 41.2 2724.0 2745.0  39.7 40.0
Index = First Line       156.0  1203.0   1.3  6.8  154.0  128.0   2.2  1.9
Index not FL: Mean / SD    8.5     6.2   5.3  5.0    7.0    7.0   4.8  5.1
Age at index <40         509.0   637.0   4.1  3.6  230.0  360.0   3.4  5.3
40                      1782.0  1993.0  14.5 11.3  940.0  999.0  13.7 14.6
50                      3787.0  3912.0  30.7 22.2 1950.0 1771.0  28.4 25.8
```

```
60                      4007.0  5147.0  32.5 29.3 2285.0 2087.0  33.3 30.4
70                      1960.0  4092.0  15.9 23.3 1226.0 1293.0  17.9 18.9
80+                      283.0  1813.0   2.3 10.3  225.0  346.0   3.3  5.0
Age: Mean / SD            59.8    63.9  11.0 13.0   60.8   60.7  11.2 12.5
Index date 2012           11.0   412.0   0.1  2.3    8.0   40.0   0.1  0.6
2013                    1353.0  5130.0  11.0 29.2 1023.0  929.0  14.9 13.6
2014                    2069.0  4477.0  16.8 25.4 1405.0 1346.0  20.5 19.6
2015                    3333.0  4136.0  27.0 23.5 1864.0 1990.0  27.2 29.0
2016                    5562.0  3439.0  45.1 19.5 2556.0 2551.0  37.3 37.2
Date of first line 1995  548.0   362.0   4.4  2.1  167.0  158.0   2.4  2.3
1996                     196.0   157.0   1.6  0.9   68.0   73.0   1.0  1.1
1997                     199.0   181.0   1.6  1.0   73.0   92.0   1.1  1.3
1998                     257.0   247.0   2.1  1.4   87.0  107.0   1.3  1.6
1999                     341.0   283.0   2.8  1.6  130.0  135.0   1.9  2.0
2000                     358.0   329.0   2.9  1.9  133.0  149.0   1.9  2.2
2001                     406.0   397.0   3.3  2.3  157.0  172.0   2.3  2.5
2002                     421.0   470.0   3.4  2.7  157.0  194.0   2.3  2.8
2003                     579.0   603.0   4.7  3.4  270.0  269.0   3.9  3.9
2004                     602.0   698.0   4.9  4.0  291.0  296.0   4.2  4.3
2005                     685.0   801.0   5.6  4.6  352.0  329.0   5.1  4.8
2006                     760.0   879.0   6.2  5.0  407.0  375.0   5.9  5.5
2007                     808.0  1004.0   6.6  5.7  461.0  412.0   6.7  6.0
2008                     856.0  1151.0   6.9  6.5  490.0  467.0   7.1  6.8
2009                     947.0  1218.0   7.7  6.9  560.0  464.0   8.2  6.8
2010                     946.0  1345.0   7.7  7.6  616.0  548.0   9.0  8.0
2011                     873.0  1515.0   7.1  8.6  569.0  557.0   8.3  8.1
2012                     704.0  1533.0   5.7  8.7  496.0  501.0   7.2  7.3
2013                     580.0  1720.0   4.7  9.8  430.0  441.0   6.3  6.4
2014                     510.0  1239.0   4.1  7.0  362.0  395.0   5.3  5.8
2015                     436.0   944.0   3.5  5.4  332.0  412.0   4.8  6.0
2016                     316.0   518.0   2.6  2.9  248.0  310.0   3.6  4.5
Frailty 0               8283.0 12644.0  67.2 71.9 4934.0 4977.0  72.0 72.6
1                       4045.0  4950.0  32.8 28.1 1922.0 1879.0  28.0 27.4
```

```
> cbind( ct.tab, cm.tab )
            SGLT2    SU SGLT2   SU SGLT2   SU SGLT2   SU
prv.FL      12172 16391  98.7 93.2  6702 6728  97.8 98.1
prv.TIA       321   585   2.6  3.3   184  175   2.7  2.6
prv.Angina   1635  2219  13.3 12.6   842  831  12.3 12.1
prv.Bleed     522   894   4.2  5.1   310  300   4.5  4.4
prv.COPD      419   805   3.4  4.6   252  263   3.7  3.8
prv.PAD       599  1061   4.9  6.0   338  331   4.9  4.8
prv.HF        496   880   4.0  5.0   266  255   3.9  3.7
prv.Cancer    590  1284   4.8  7.3   365  357   5.3  5.2
prv.DMcompl  2291  1299  18.6  7.4   760  722  11.1 10.5
prv.Neuro     713   536   5.8  3.0   270  254   3.9  3.7
prv.DKD       461   420   3.7  2.4   187  179   2.7  2.6
prv.DiaEye   1501  1060  12.2  6.0   543  532   7.9  7.8
prv.Hypo      441   371   3.6  2.1   161  163   2.3  2.4
prv.AtrFib    740  1378   6.0  7.8   429  409   6.3  6.0
prv.MI       1003  1405   8.1  8.0   515  501   7.5  7.3
prv.UnstAng   470   640   3.8  3.6   228  245   3.3  3.6
prv.HmStr      96   163   0.8  0.9    56   50   0.8  0.7
prv.DiaFoot   121    98   1.0  0.6    40   39   0.6  0.6
prv.Other     554   791   4.5  4.5   283  286   4.1  4.2
prv.PeriAng   659   453   5.3  2.6   227  232   3.3  3.4
prv.IscStr    583  1028   4.7  5.8   331  321   4.8  4.7
prv.Amp        13    29   0.1  0.2     6    7   0.1  0.1
```

```
prv.CKD         69   434   0.6  2.5    48   40   0.7  0.6
prv.PCIsten    115   140   0.9  0.8    52   49   0.8  0.7
prv.CABG       326   451   2.6  2.6   155  170   2.3  2.5
prv.Keto        75    62   0.6  0.4    30   33   0.4  0.5
prv.Dial         0     8   0.0  0.0     0    0   0.0  0.0
pre.CVD       3681  5603  29.9 31.8  2004 1907  29.2 27.8
pre.Str        873  1535   7.1  8.7   499  482   7.3  7.0
pre.FPA        734   519   6.0  2.9   258  260   3.8  3.8
pre.Mic       4104  3035  33.3 17.3  1579 1500  23.0 21.9

> cbind( mt.tab, mm.tab )

              SGLT2    SU SGLT2    SU SGLT2   SU SGLT2    SU
had.ACE        4676  5886  37.9  33.5  2467 2435  36.0  35.5
had.Sta        9176 10956  74.4  62.3  4779 4796  69.7  70.0
had.BBl        3333  4769  27.0  27.1  1759 1747  25.7  25.5
had.ARB        4299  4459  34.9  25.3  2083 2106  30.4  30.7
had.AlA         644   896   5.2   5.1   328  321   4.8   4.7
had.DHP        3704  4613  30.0  26.2  1897 1883  27.7  27.5
had.WtL          89    77   0.7   0.4    43   46   0.6   0.7
had.RPA         791  1146   6.4   6.5   411  402   6.0   5.9
had.Wrf         508  1102   4.1   6.3   293  264   4.3   3.9
had.Asp        4301  5362  34.9  30.5  2134 2117  31.1  30.9
had.HCD        1703  2850  13.8  16.2   891  862  13.0  12.6
had.THZ        1877  2630  15.2  14.9   977 1017  14.3  14.8
had.Ccs         662  1364   5.4   7.8   432  437   6.3   6.4
had.DXI         196   247   1.6   1.4   118  108   1.7   1.6
had.Dgo         307   762   2.5   4.3   194  179   2.8   2.6
had.APl         122   285   1.0   1.6    80   80   1.2   1.2
had.Ami          30    71   0.2   0.4    20   21   0.3   0.3
had.DTI         153   263   1.2   1.5    89   95   1.3   1.4
had.NHP         212   256   1.7   1.5   108  100   1.6   1.5
had.Fla          10    19   0.1   0.1     7    8   0.1   0.1
had.Metformin  9881 14057  80.2  79.9  5454 5484  79.6  80.0
had.GLP1       4054  1332  32.9   7.6  1194 1127  17.4  16.4
had.MetxSGLT2   702     0   5.7   0.0   418    0   6.1   0.0
had.MetxDPP4   2702  2019  21.9  11.5  1462 1464  21.3  21.4
had.SGLT2     11626     0  94.3   0.0  6438    0  93.9   0.0
had.longIns    2632   376  21.3   2.1   416  363   6.1   5.3
had.mixIns     1078   222   8.7   1.3   227  192   3.3   2.8
had.DPP4       2137  2264  17.3  12.9  1306 1311  19.0  19.1
had.SU            0 17594   0.0 100.0     0 6856   0.0 100.0
had.intIns      935   332   7.6   1.9   245  234   3.6   3.4
had.fastIns    1052   229   8.5   1.3   182  164   2.7   2.4
had.TZD          28    27   0.2   0.2    16   14   0.2   0.2
had.Acarbose     15    35   0.1   0.2    10   10   0.1   0.1
had.TZDxDPP4      1     0   0.0   0.0     0    0   0.0   0.0
got.Ins        4147   952  33.6   5.4   871  757  12.7  11.0
got.Hyp        9593 12224  77.8  69.5  5051 4976  73.7  72.6
got.CVD       11229 14595  91.1  83.0  6008 5899  87.6  86.0

> save( dt.tab, dm.tab,
+       ct.tab, cm.tab,
+       mt.tab, mm.tab, file="btabSGSU.Rda" )
```

. . . now input from `../rep/anaSGSU.tex`

1.7 Survival analysis datasets: Lexis objects

In this section we take the original and the matched data and set up `Lexis`-objects for the survival analyses; we make separate objects for Death, heart failure (HF) and combined outcomes.

First get the relevant data:

```
> library( Epi )
> library( survival )
> print( sessionInfo(), l=F )
R version 3.5.0 (2018-04-23)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] survival_2.41-3 Epi_2.30

loaded via a namespace (and not attached):
 [1] cmprsk_2.2-7      zoo_1.8-1         MASS_7.3-49       compiler_3.5.0
 [5] Matrix_1.2-14     plyr_1.8.4        parallel_3.5.0    tools_3.5.0
 [9] etm_0.6-2         Rcpp_0.12.16      splines_3.5.0     grid_3.5.0
[13] numDeriv_2016.8-1 lattice_0.20-35
> clear()
> load( file = "adatSGSU.Rda" )
> lls()
  name    mode    class      dim              size(Kb)
1 mset    list    data.frame 13712 170        20,004.8
2 oset    list    data.frame 29922 170        43,184.4
3 pscore  numeric table      100 2                 8.1
4 psmatch numeric table      100 2                 8.1
```

We will follow persons from date of new use, `doIx`, till either date of event.

For later use we define both the time since index (`tfi`) and current date (period — `per`) and current age (`cua`) as timescales. The latter not to be confused with age at index date, `age`.

1.8 Types of index drugs

The datasets of all first users and all matched contian the variable `Ixatc`:

```
> tt <- cbind( table( oset$Ixatc ),
+              table( mset$Ixatc ) )
> tt <- data.frame( tt )
> str(tt)
'data.frame':        13 obs. of  2 variables:
 $ X1: int  960 290 753 1753 13490 313 11 378 7238 357 ...
 $ X2: int  380 119 290 685 5241 203 11 204 4481 204 ...
> tt$atc <- rownames(tt)
> str(tt)
```

```
'data.frame':        13 obs. of  3 variables:
 $ X1 : int  960 290 753 1753 13490 313 11 378 7238 357 ...
 $ X2 : int  380 119 290 685 5241 203 11 204 4481 204 ...
 $ atc: chr  "A10BB01" "A10BB03" "A10BB07" "A10BB09" ...
> head(tt)
           X1   X2     atc
A10BB01   960  380 A10BB01
A10BB03   290  119 A10BB03
A10BB07   753  290 A10BB07
A10BB09  1753  685 A10BB09
A10BB12 13490 5241 A10BB12
A10BD15   313  203 A10BD15
```

But we want a translation to text; this is in the file `atcnam.txt`:

```
> atc <- read.table( "atcnam.txt", header=TRUE )
> head(atc)
      atc                     drnam
1 A10BF01                  acarbose
2 A10BD07  metformin og sitagliptin
3 A10BD08 metformin og vildagliptin
4 A10BD09 pioglitazon og alogliptin
5 A10BD10  metformin og saxagliptin
6 A10BD11  metformin og linagliptin
> tt <- merge( tt, atc )
> tt
       atc    X1   X2                      drnam
1  A10BB01   960  380               glibenclamid
2  A10BB03   290  119                 tolbutamid
3  A10BB07   753  290                   glipizid
4  A10BB09  1753  685                  gliclazid
5  A10BB12 13490 5241                 glimepirid
6  A10BD15   313  203 metformin og dapagliflozin
7  A10BD15   313  203 metformin og dapagliflozin
8  A10BD16    11   11 metformin og canagliflozin
9  A10BD16    11   11 metformin og canagliflozin
10 A10BD20   378  204 metformin og empagliflozin
11 A10BD20   378  204 metformin og empagliflozin
12 A10BK01  7238 4481              dapagliflozin
13 A10BK02   357  204              canagliflozin
14 A10BK03  4031 1753              empagliflozin
15 A10BX02   347  141                 repaglinid
16 A10BX03     1  380                 nateglinid
> tt$drnam <- gsub( "metformin og ","", tt$drnam )
> tt$drnam <- gsub( "pioglitazon og ","", tt$drnam )
> aggregate( tt[,c("X1","X2")], tt[,"drnam",drop=FALSE], FUN=sum )
           drnam    X1   X2
1  canagliflozin   379  226
2  dapagliflozin  7864 4887
3  empagliflozin  4787 2161
4   glibenclamid   960  380
5      gliclazid  1753  685
6     glimepirid 13490 5241
7       glipizid   753  290
8     nateglinid     1  380
9     repaglinid   347  141
10    tolbutamid   290  119
```

1.9 Collecting analysis results and key data

We want to collect analysis results and background data for the analyses. The latter are classified by index drug and PY/events, the former by adjusted/non-adjusted analysis and HR/c.i./s.e. In addition both are classified by endpoint, data, and subset:

```
> lst <- list( endp = c("HF","ACD","ACD+HF","CVDD","MI","Str","IscStr",
+                       "CVDD+MI+Str","ACD+MI+Str","DKD"),
+              data = c("OnDr","Total"),
+               sub = c("AllPtt","preCVD","noCVD") )
> dat <- NArray( c( lst, list( ix = c("SGLT2","SU"),
+                             dat = c("N","PY","Event") ) ) )
> res <- NArray( c( lst, list( adj = c("Raw","Adj"),
+                              res = c("HR","lo","up","se") ) ) )
> length( dat ) ; str( dat )
[1] 360
 logi [1:10, 1:2, 1:3, 1:2, 1:3] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "SU"
  ..$ dat : chr [1:3] "N" "PY" "Event"
> length( res ) ; str( res )
[1] 480
 logi [1:10, 1:2, 1:3, 1:2, 1:4] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ adj : chr [1:2] "Raw" "Adj"
  ..$ res : chr [1:4] "HR" "lo" "up" "se"
```

1.10 Survival dataset: `Lexis` objects

Here is a definition of a function that produces a Lexis object with follow-up till `mset$doX` for the event `D`:

```
> mkLex <-
+ function( )
+    {
+ Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+        exit.status = factor( D, labels=c("OnDr","Event") ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
+ Lx <- cutLexis( Lx, cut = Lx$doTm,
+                 new.state = "OffDr",
+                       pre = "OnDr" )
+ Lx
+    }
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex( )
```

```
NOTE: entry.status has been set to "OnDr" for all.
> summary( lxHF )

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  8987  4583   139     13709     4722   15816.17     13709
  OffDr    0  4538    45      4583       45    5559.61      4583
  Sum   8987  9121   184     18292     4767   21375.78     13709
```

1.10.1 Follow-up data and events

First we devise a function to extract the person-years and events from the Lexis object:

```
> fill.dat <-
+ function( LexDat, outc )
+ {
+ whc <- c(" Persons:","Risk time:","Event")
+ cat( outc, ":\n" )
+ print( sm <- summary( LexDat, by="Ixdr" ) )
+ s2 <- summary( LexDat, by=c("Ixdr","pre.CVD") )
+ for( ix in c("SU","SGLT2") )
+    {
+ dat[outc,,"AllPtt",ix,] <<- sm[[ix]][[1]][c(1,3),whc]
+ dat[outc,,"noCVD" ,ix,] <<- s2[[paste(ix,0,sep=".")]][[1]][c(1,3),whc]
+ dat[outc,,"preCVD",ix,] <<- s2[[paste(ix,1,sep=".")]][[1]][c(1,3),whc]
+    }
+ invisible(NULL)
+ }
> fill.dat( lxHF, "HF" )
HF :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4634  2168    54      6856     2222    8139.88      6856
  OffDr    0  2144    24      2168       24    2721.79      2168
  Sum   4634  4312    78      9024     2246   10861.66      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4353  2415    85      6853     2500    7676.29      6853
  OffDr    0  2394    21      2415       21    2837.82      2415
  Sum   4353  4809   106      9268     2521   10514.11      6853
> round( ftable( dat[1:2,,,,], col.vars=c(4,5) ), 1 )
                  ix    SGLT2                      SU
                  dat         N      PY    Event         N      PY    Event
endp data  sub
HF   OnDr  AllPtt      6856.0  8139.9     54.0  6853.0  7676.3     85.0
           preCVD      2004.0  2295.0     43.0  1904.0  1982.7     63.0
           noCVD       4852.0  5844.8     11.0  4949.0  5693.6     22.0
```

```
     Total AllPtt      6856.0 10861.7    78.0  6853.0 10514.1   106.0
           preCVD      2004.0  3049.5    58.0  1904.0  2769.7    79.0
           noCVD       4852.0  7812.2    20.0  4949.0  7744.4    27.0
ACD  OnDr  AllPtt          NA      NA      NA      NA      NA      NA
           preCVD          NA      NA      NA      NA      NA      NA
           noCVD           NA      NA      NA      NA      NA      NA
     Total AllPtt          NA      NA      NA      NA      NA      NA
           preCVD          NA      NA      NA      NA      NA      NA
           noCVD           NA      NA      NA      NA      NA      NA
```

1.10.2 Analysis

Follow-up is now analysed by Cox-models adjusted and non-adjusted, total or on drug and separately for all persons and persons with and without prior CVD. These are named with an `m.` and combination of `r/a` (raw/adjusted), `t/d` (total/on drug) and `p/n/y` (patients/no CVD/yes CVD):

```
> m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
+               I(Ixdr=="SGLT2") + cluster(pnr),
+               data = lxHF )
> m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
+                             + prv.MI + prv.HF + prv.AtrFib + frail
+                             + had.BBl + had.NHP + had.AlA + had.ACE )
> m.dpr <- update( m.tpr, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.dpa <- update( m.tpa, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.tnr <- update( m.tpr, data = subset( lxHF, pre.CVD==1 ) )
> m.tna <- update( m.tpa, data = subset( lxHF, pre.CVD==1  ) )
> m.dnr <- update( m.dpr, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.dna <- update( m.dpa, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.tyr <- update( m.tpr, data = subset( lxHF, pre.CVD==0 ) )
> m.tya <- update( m.tpa, data = subset( lxHF, pre.CVD==0  ) )
> m.dyr <- update( m.dpr, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
> m.dya <- update( m.dpa, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
```

With these models fitted we can now extract the HRs etc. and put into the right slots of `res`:

```
> get4 <- function( m ) ci.lin( m, subset="SGLT2", Exp=TRUE )[,c(5:7,2)]
> res["HF","Total","AllPtt","Raw",] <- get4( m.tpr )
> res["HF","Total","AllPtt","Adj",] <- get4( m.tpa )
> res["HF","OnDr" ,"AllPtt","Raw",] <- get4( m.dpr )
> res["HF","OnDr" ,"AllPtt","Adj",] <- get4( m.dpa )
> res["HF","Total","preCVD","Raw",] <- get4( m.tnr )
> res["HF","Total","preCVD","Adj",] <- get4( m.tna )
> res["HF","OnDr" ,"preCVD","Raw",] <- get4( m.dnr )
> res["HF","OnDr" ,"preCVD","Adj",] <- get4( m.dna )
> res["HF","Total","noCVD" ,"Raw",] <- get4( m.tyr )
> res["HF","Total","noCVD" ,"Adj",] <- get4( m.tya )
> res["HF","OnDr" ,"noCVD" ,"Raw",] <- get4( m.dyr )
> res["HF","OnDr" ,"noCVD" ,"Adj",] <- get4( m.dya )
```

This can now be packed into a function that does this for a given type of event:

```
> fill.res <- function( LexDat, outc )
+      {
+ m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
```

```
+               I(Ixdr=="SGLT2") + cluster(pnr),
+               data = LexDat )
+ m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
+                              + prv.MI + prv.HF + prv.AtrFib + frail
+                              + had.BBl + had.NHP + had.AlA + had.ACE )
+ m.dpr <- update( m.tpr, data = subset( LexDat, lex.Cst=="OnDr" ) )
+ m.dpa <- update( m.tpa, data = subset( LexDat, lex.Cst=="OnDr" ) )
+
+ m.tnr <- update( m.tpr, data = subset( LexDat, pre.CVD==1 ) )
+ m.tna <- update( m.tpa, data = subset( LexDat, pre.CVD==1  ) )
+ m.dnr <- update( m.dpr, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
+ m.dna <- update( m.dpa, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
+
+ m.tyr <- update( m.tpr, data = subset( LexDat, pre.CVD==0 ) )
+ m.tya <- update( m.tpa, data = subset( LexDat, pre.CVD==0  ) )
+ m.dyr <- update( m.dpr, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+ m.dya <- update( m.dpa, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+
+ res[outc,"Total","AllPtt","Raw",] <<- get4( m.tpr )
+ res[outc,"Total","AllPtt","Adj",] <<- get4( m.tpa )
+ res[outc,"OnDr" ,"AllPtt","Raw",] <<- get4( m.dpr )
+ res[outc,"OnDr" ,"AllPtt","Adj",] <<- get4( m.dpa )
+
+ res[outc,"Total","preCVD","Raw",] <<- get4( m.tnr )
+ res[outc,"Total","preCVD","Adj",] <<- get4( m.tna )
+ res[outc,"OnDr" ,"preCVD","Raw",] <<- get4( m.dnr )
+ res[outc,"OnDr" ,"preCVD","Adj",] <<- get4( m.dna )
+
+ res[outc,"Total","noCVD" ,"Raw",] <<- get4( m.tyr )
+ res[outc,"Total","noCVD" ,"Adj",] <<- get4( m.tya )
+ res[outc,"OnDr" ,"noCVD" ,"Raw",] <<- get4( m.dyr )
+ res[outc,"OnDr" ,"noCVD" ,"Adj",] <<- get4( m.dya )
+ invisible( NULL )
+   }
```

So combining this with the function that constructs the Lexis object we get:

```
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxHF, "HF" )
> round( ftable( res[1:2,,,,], col.vars=c(2,5) ), 3 )
                data  OnDr                          Total
                res      HR    lo    up    se    HR    lo    up    se
endp sub    adj
HF   AllPtt Raw       0.608 0.432 0.854 0.174 0.714 0.533 0.956 0.149
            Adj       0.603 0.426 0.854 0.177 0.703 0.521 0.948 0.153
     preCVD Raw       0.606 0.411 0.892 0.198 0.671 0.478 0.943 0.173
            Adj       0.616 0.415 0.913 0.201 0.667 0.472 0.942 0.176
     noCVD  Raw       0.490 0.238 1.008 0.368 0.730 0.411 1.298 0.293
            Adj       0.515 0.247 1.074 0.375 0.751 0.421 1.337 0.295
ACD  AllPtt Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
     preCVD Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
     noCVD  Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
```

So we just repeat this for all types of outcome:

```
> mset$D   <- with( mset, !is.na(doDth) & doDth<2017 )
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
>    lxACD <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
```

```
> fill.res( lxACD, "ACD" )
> fill.dat( lxACD, "ACD" )

ACD :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4601  2185    70      6856     2255    8182.18      6856
  OffDr    0  2119    66      2185       66    2763.57      2185
  Sum   4601  4304   136      9041     2321   10945.74      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4247  2455   151      6853     2606    7750.92      6853
  OffDr    0  2374    81      2455       81    2907.51      2455
  Sum   4247  4829   232      9308     2687   10658.43      6853
```

```
> mset$D   <- with( mset, ( !is.na(deHF) | !is.na(doDth) ) &
+                         ( deHF<2017    | doDth<2017 ) )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>  lxACDHF <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
```

```
> fill.res( lxACDHF, "ACD+HF" )
> fill.dat( lxACDHF, "ACD+HF" )

ACD+HF :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4566  2168   122      6856     2290    8139.88      6856
  OffDr    0  2080    88      2168       88    2721.79      2168
  Sum   4566  4248   210      9024     2378   10861.66      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4212  2415   226      6853     2641    7676.29      6853
  OffDr    0  2318    97      2415       97    2837.82      2415
  Sum   4212  4733   323      9268     2738   10514.11      6853
```

```
> mset$D   <- with( mset, !is.na(deCVDD) & deCVDD<2017 )
> mset$doX <- with( mset, pmin( doDth, deCVDD, 2017, na.rm=TRUE ) )
>   lxCVDD <- mkLex()
```

```
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxCVDD, "CVDD" )
> fill.dat( lxCVDD, "CVDD" )
CVDD :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4659  2185    12      6856     2197    8182.18      6856
  OffDr    0  2177     8      2185        8    2763.57      2185
  Sum   4659  4362    20      9041     2205   10945.74      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4367  2455    31      6853     2486    7750.92      6853
  OffDr    0  2436    19      2455       19    2907.51      2455
  Sum   4367  4891    50      9308     2505   10658.43      6853
> mset$D   <- with( mset, !is.na(deMI) & deMI<2017 )
> mset$doX <- with( mset, pmin( doDth, deMI, 2017, na.rm=TRUE ) )
>     lxMI <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxMI, "MI" )
> fill.dat( lxMI, "MI" )
MI :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4640  2176    40      6856     2216    8151.09      6856
  OffDr    0  2167     9      2176        9    2749.55      2176
  Sum   4640  4343    49      9032     2225   10900.65      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4362  2430    61      6853     2491    7703.40      6853
  OffDr    0  2414    16      2430       16    2869.15      2430
  Sum   4362  4844    77      9283     2507   10572.55      6853
> mset$D   <- with( mset, !is.na(deStr) & deStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deStr, 2017, na.rm=TRUE ) )
>    lxStr <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxStr, "Str" )
> fill.dat( lxStr, "Str" )
Str :
$SGLT2
```

```
Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4640  2163    53      6856     2216    8137.34      6856
  OffDr    0  2146    17      2163       17    2732.69      2163
  Sum   4640  4309    70      9019     2233   10870.03      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4352  2431    70      6853     2501    7696.22      6853
  OffDr    0  2406    25      2431       25    2857.20      2431
  Sum   4352  4837    95      9284     2526   10553.42      6853
```

```
> mset$D   <- with( mset, !is.na(deIscStr) & deIscStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deIscStr, 2017, na.rm=TRUE ) )
>   lxIStr <- mkLex()
```

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

```
> fill.res( lxIStr, "IscStr" )
> fill.dat( lxIStr, "IscStr" )
```

```
IscStr :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4640  2166    50      6856     2216    8138.60      6856
  OffDr    0  2152    14      2166       14    2736.75      2166
  Sum   4640  4318    64      9022     2230   10875.36      6856

$SU

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4357  2432    64      6853     2496    7699.68      6853
  OffDr    0  2416    16      2432       16    2867.21      2432
  Sum   4357  4848    80      9285     2512   10566.89      6853
```

```
> mset$D   <- with( mset, ( ( !is.na(deCVDD) & deCVDD < 2017 ) |
+                           ( !is.na(deMI)   & deMI   < 2017 ) |
+                           ( !is.na(deStr)  & deStr  < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deCVDD, deMI, deStr, 2017, na.rm=TRUE ) )
>  lxCVDDx <- mkLex()
```

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

```
> fill.res( lxCVDDx, "CVDD+MI+Str" )
> fill.dat( lxCVDDx, "CVDD+MI+Str" )
```

```
CVDD+MI+Str :
$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4599  2154   103      6856     2257    8106.84      6856
```

```
  OffDr     0  2123    31       2154       31    2718.67       2154
  Sum    4599  4277   134       9010     2288   10825.51       6856

$SU

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   4296  2406   151       6853     2557    7650.81       6853
  OffDr     0  2353    53       2406       53    2818.85       2406
  Sum    4296  4759   204       9259     2610   10469.65       6853
```

```
> mset$D   <- with( mset, ( ( !is.na(doDth) & doDth < 2017 ) |
+                           ( !is.na(deMI)  & deMI  < 2017 ) |
+                           ( !is.na(deStr) & deStr < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deMI, deStr, 2017, na.rm=TRUE ) )
>   lxACDx <- mkLex()
```

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

```
> fill.res( lxACDx, "ACD+MI+Str" )
> fill.dat( lxACDx, "ACD+MI+Str" )
```

```
ACD+MI+Str :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   4544  2154   158       6856     2312    8106.84       6856
  OffDr     0  2072    82       2154       82    2718.67       2154
  Sum    4544  4226   240       9010     2394   10825.51       6856

$SU

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   4180  2406   267       6853     2673    7650.81       6853
  OffDr     0  2294   112       2406      112    2818.85       2406
  Sum    4180  4700   379       9259     2785   10469.65       6853
```

```
> mset$D   <- with( mset, !is.na(deDKD) & deDKD<2017 )
> mset$doX <- with( mset, pmin( doDth, deDKD, 2017, na.rm=TRUE ) )
>    lxKid <- mkLex()
```

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

```
> fill.res( lxKid, "DKD" )
> fill.dat( lxKid, "DKD" )
```

```
DKD :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   4647  2161    48       6856     2209    8141.67       6856
  OffDr     0  2140    21       2161       21    2715.16       2161
  Sum    4647  4301    69       9017     2230   10856.83       6856

$SU
```

```
Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  4355  2416    82       6853     2498    7682.32      6853
  OffDr    0  2382    34       2416       34    2844.94      2416
  Sum   4355  4798   116       9269     2532   10527.26      6853
```

So we can summarize results:

```
> round( ftable( dat, col.vars=c(2,4,5) ), 0 )
                   data  OnDr                               Total
                   ix   SGLT2                SU             SGLT2                SU
                   dat      N    PY Event     N    PY Event     N    PY Event     N    PY Ever
endp        sub
HF          AllPtt       6856  8140    54  6853  7676    85  6856 10862    78  6853 10514   10
            preCVD       2004  2295    43  1904  1983    63  2004  3049    58  1904  2770   7
            noCVD        4852  5845    11  4949  5694    22  4852  7812    20  4949  7744   2
ACD         AllPtt       6856  8182    70  6853  7751   151  6856 10946   136  6853 10658   23
            preCVD       2004  2328    35  1904  2038    86  2004  3115    73  1904  2879   12
            noCVD        4852  5854    35  4949  5713    65  4852  7831    63  4949  7780   10
ACD+HF      AllPtt       6856  8140   122  6853  7676   226  6856 10862   210  6853 10514   32
            preCVD       2004  2295    76  1904  1983   140  2004  3049   127  1904  2770   19
            noCVD        4852  5845    46  4949  5694    86  4852  7812    83  4949  7744   13
CVDD        AllPtt       6856  8182    12  6853  7751    31  6856 10946    20  6853 10658   5
            preCVD       2004  2328     8  1904  2038    25  2004  3115    13  1904  2879   3
            noCVD        4852  5854     4  4949  5713     6  4852  7831     7  4949  7780   1
MI          AllPtt       6856  8151    40  6853  7703    61  6856 10901    49  6853 10573   7
            preCVD       2004  2312    20  1904  2007    34  2004  3090    26  1904  2827   4
            noCVD        4852  5839    20  4949  5696    27  4852  7811    23  4949  7745   3
Str         AllPtt       6856  8137    53  6853  7696    70  6856 10870    70  6853 10553   9
            preCVD       2004  2312    27  1904  2010    35  2004  3082    34  1904  2832   4
            noCVD        4852  5825    26  4949  5686    35  4852  7788    36  4949  7722   4
IscStr      AllPtt       6856  8139    50  6853  7700    64  6856 10875    64  6853 10567   8
            preCVD       2004  2313    24  1904  2011    33  2004  3088    29  1904  2835   3
            noCVD        4852  5825    26  4949  5689    31  4852  7788    35  4949  7732   4
CVDD+MI+Str AllPtt       6856  8107   103  6853  7651   151  6856 10826   134  6853 10470   20
            preCVD       2004  2295    54  1904  1981    87  2004  3058    70  1904  2782   11
            noCVD        4852  5812    49  4949  5670    64  4852  7768    64  4949  7688   9
ACD+MI+Str  AllPtt       6856  8107   158  6853  7651   267  6856 10826   240  6853 10470   37
            preCVD       2004  2295    79  1904  1981   146  2004  3058   124  1904  2782   19
            noCVD        4852  5812    79  4949  5670   121  4852  7768   116  4949  7688   18
DKD         AllPtt       6856  8142    48  6853  7682    82  6856 10857    69  6853 10527   11
            preCVD       2004  2314    19  1904  2017    29  2004  3079    27  1904  2831   4
            noCVD        4852  5827    29  4949  5666    53  4852  7778    42  4949  7696   6
```

```
> round( ftable( res, col.vars=c(2,5) ), 3 )
                       data  OnDr                   Total
                       res     HR    lo    up    se    HR    lo    up    se
endp        sub    adj
HF          AllPtt Raw      0.608 0.432 0.854 0.174 0.714 0.533 0.956 0.149
                   Adj      0.603 0.426 0.854 0.177 0.703 0.521 0.948 0.153
            preCVD Raw      0.606 0.411 0.892 0.198 0.671 0.478 0.943 0.173
                   Adj      0.616 0.415 0.913 0.201 0.667 0.472 0.942 0.176
            noCVD  Raw      0.490 0.238 1.008 0.368 0.730 0.411 1.298 0.293
                   Adj      0.515 0.247 1.074 0.375 0.751 0.421 1.337 0.295
ACD         AllPtt Raw      0.442 0.333 0.587 0.144 0.570 0.462 0.705 0.108
                   Adj      0.506 0.381 0.674 0.146 0.614 0.497 0.759 0.108
```

```
            preCVD Raw      0.359 0.243 0.532 0.200 0.541 0.405 0.721 0.147
                   Adj      0.418 0.282 0.620 0.201 0.601 0.450 0.803 0.148
            noCVD  Raw      0.530 0.352 0.798 0.209 0.584 0.428 0.797 0.159
                   Adj      0.603 0.398 0.913 0.212 0.623 0.456 0.852 0.160
ACD+HF      AllPtt Raw      0.515 0.414 0.642 0.112 0.629 0.529 0.749 0.089
                   Adj      0.562 0.450 0.702 0.114 0.659 0.553 0.785 0.090
            preCVD Raw      0.480 0.363 0.634 0.142 0.600 0.480 0.750 0.114
                   Adj      0.526 0.397 0.698 0.144 0.642 0.512 0.806 0.116
            noCVD  Raw      0.525 0.367 0.750 0.182 0.631 0.480 0.831 0.140
                   Adj      0.585 0.407 0.841 0.185 0.663 0.503 0.874 0.141
CVDD        AllPtt Raw      0.373 0.192 0.722 0.338 0.392 0.234 0.658 0.264
                   Adj      0.424 0.214 0.841 0.349 0.427 0.253 0.721 0.267
            preCVD Raw      0.287 0.130 0.631 0.402 0.312 0.167 0.583 0.319
                   Adj      0.318 0.143 0.708 0.408 0.334 0.177 0.629 0.324
            noCVD  Raw      0.665 0.189 2.337 0.642 0.643 0.250 1.650 0.481
                   Adj      0.835 0.215 3.238 0.692 0.692 0.270 1.776 0.481
MI          AllPtt Raw      0.629 0.421 0.938 0.204 0.622 0.434 0.890 0.183
                   Adj      0.628 0.419 0.941 0.206 0.619 0.432 0.887 0.184
            preCVD Raw      0.521 0.299 0.906 0.283 0.582 0.356 0.950 0.251
                   Adj      0.552 0.313 0.974 0.290 0.606 0.369 0.995 0.253
            noCVD  Raw      0.735 0.411 1.317 0.297 0.640 0.378 1.083 0.269
                   Adj      0.735 0.410 1.316 0.297 0.640 0.378 1.082 0.268
Str         AllPtt Raw      0.726 0.507 1.038 0.183 0.718 0.527 0.978 0.157
                   Adj      0.750 0.524 1.074 0.183 0.727 0.533 0.990 0.158
            preCVD Raw      0.690 0.417 1.141 0.256 0.684 0.439 1.065 0.226
                   Adj      0.726 0.437 1.206 0.259 0.698 0.446 1.090 0.228
            noCVD  Raw      0.729 0.438 1.214 0.260 0.730 0.475 1.122 0.219
                   Adj      0.730 0.438 1.216 0.260 0.728 0.473 1.120 0.220
IscStr      AllPtt Raw      0.747 0.516 1.083 0.189 0.781 0.563 1.085 0.167
                   Adj      0.773 0.534 1.120 0.189 0.788 0.568 1.094 0.167
            preCVD Raw      0.648 0.383 1.097 0.269 0.689 0.427 1.113 0.245
                   Adj      0.674 0.398 1.142 0.269 0.695 0.430 1.122 0.244
            noCVD  Raw      0.822 0.487 1.388 0.267 0.849 0.541 1.333 0.230
                   Adj      0.826 0.489 1.397 0.268 0.846 0.538 1.329 0.231
CVDD+MI+Str AllPtt Raw      0.653 0.508 0.839 0.128 0.639 0.514 0.795 0.111
                   Adj      0.674 0.523 0.868 0.129 0.648 0.521 0.806 0.111
            preCVD Raw      0.549 0.391 0.770 0.173 0.568 0.422 0.765 0.152
                   Adj      0.591 0.419 0.834 0.176 0.593 0.440 0.800 0.153
            noCVD  Raw      0.757 0.521 1.100 0.191 0.701 0.509 0.966 0.163
                   Adj      0.764 0.525 1.111 0.191 0.701 0.509 0.966 0.163
ACD+MI+Str  AllPtt Raw      0.564 0.464 0.687 0.100 0.614 0.522 0.722 0.082
                   Adj      0.607 0.498 0.740 0.101 0.639 0.543 0.751 0.083
            preCVD Raw      0.475 0.361 0.625 0.140 0.584 0.466 0.731 0.115
                   Adj      0.534 0.405 0.705 0.141 0.633 0.505 0.794 0.115
            noCVD  Raw      0.643 0.484 0.854 0.145 0.622 0.493 0.784 0.119
                   Adj      0.672 0.506 0.893 0.145 0.633 0.502 0.799 0.119
DKD         AllPtt Raw      0.555 0.388 0.794 0.183 0.576 0.427 0.776 0.152
                   Adj      0.567 0.396 0.811 0.183 0.585 0.434 0.788 0.152
            preCVD Raw      0.580 0.323 1.040 0.298 0.527 0.328 0.846 0.242
                   Adj      0.651 0.353 1.200 0.312 0.557 0.339 0.913 0.253
            noCVD  Raw      0.532 0.338 0.838 0.232 0.601 0.409 0.882 0.196
                   Adj      0.537 0.341 0.845 0.231 0.611 0.417 0.896 0.195
```

1.11 Exposure tables by drug

We can then produce an overview of the number of persons, risk time and events by index medication; to this end we define functions that uses the `by` argument of the `summary.Lexis` to classify events and follow-up by index drug in various groupings:

```
> tabFU <- ZArray( list( Ix = c("SU","SGLT2","Dapa","Empa","Cana"),
+                       wh = c("nPers","FU","meanfu","sdFU","maxFU") ) )
> getFU <-
+ function( lx ) c( length( unique( lx$lex.id ) ),
+                      sum( lx$lex.dur ),
+                     mean( lx$lex.dur ),
+                       sd( lx$lex.dur ),
+                      max( lx$lex.dur ) )
> mset$D   <- 0
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
> Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+        exit.status = factor( D, levels=0:1, labels=c("OnDr","Event") ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
NOTE: entry.status has been set to "OnDr" for all.
```

```
> summary( Lx, by="Ixdr" , simplify=FALSE )
$SGLT2

Transitions:
     To
From    OnDr Event  Records:  Events: Risk time:  Persons:
  OnDr  6856     0      6856        0   10945.74      6856
  Event    0     0         0        0         NA        NA
  Sum   6856     0      6856        0   10945.74      6856

$SU

Transitions:
     To
From    OnDr Event  Records:  Events: Risk time:  Persons:
  OnDr  6853     0      6853        0   10658.43      6853
  Event    0     0         0        0         NA        NA
  Sum   6853     0      6853        0   10658.43      6853
```

```
> tabFU["SU"   ,] <- getFU( subset( Lx, Ixdr=="SU") )
> tabFU["SGLT2",] <- getFU( subset( Lx, Ixdr=="SGLT2") )
> tabFU["Dapa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD15","A10BK01") ) )
> tabFU["Cana" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD16","A10BK02") ) )
> tabFU["Empa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD20","A10BK03") ) )
> round( tabFU, 2 )
```

```
       wh
Ix       nPers       FU meanfu sdFU maxFU
  SU      6853 10658.43   1.56 1.09  4.08
  SGLT2   6856 10945.74   1.60 1.09  4.05
  Dapa    4684  9145.68   1.95 1.09  4.05
  Empa    1957  1495.64   0.76 0.54  2.33
  Cana     215   304.42   1.42 0.65  2.54
```

1.12 Saving it all

Fially we save all results:

```
> save( res, dat, tabFU, file = "resSGSU.Rda" )
```

1.13 Reformatting

The results are here reformatted to `Excel`-format, `xlsx`, by the `xlsx` package of R, so we load that concomitantly with the data.

```
> library( Epi )
> library( xlsx )
> clear()
> load( "btabSGSU.Rda" )
> load( "resSGSU.Rda" )
> lls()
  name   mode    class  dim              size(Kb)
1 cm.tab numeric matrix 31 4                  3.4
2 ct.tab numeric matrix 31 4                  3.4
3 dat    numeric array  10 2 3 2 3            5.5
4 dm.tab numeric matrix 40 4                  3.9
5 dt.tab numeric matrix 40 4                  3.9
6 mm.tab numeric matrix 37 4                  3.8
7 mt.tab numeric matrix 37 4                  3.8
8 res    numeric array  10 2 3 2 4            6.4
9 tabFU  numeric matrix 5 5                   1.7
```

With this in place we can now construct the tables wanted for the sheet in the desired order.

1.13.1 Baseline tables

In order to check that we get the rows correct we read the row-names from the supplied spreadsheet, in order to put these in as a column in the new sheet for control:

```
> cat("Sample size
+ Age, years
+ Women
+ CV-history
+ Myocardial infarction
+ Unstable angina
+ Heart failure
+ Atrial fibrillation
+ Stroke
+ PAD
+ Microvascular disease
+ CKD
+ Frailty (yes)
+ Metformin
+ DPP4
+ TZD
+ GLP1
+ Insulin
+ Anti hypertensive therapy
```

```
                                                  ...now input from ../rep/2xlSGSU.tex
+ LOOP diuretics
+ Low ceiling diuretics
+ ACE Inhibitors
+ ARBs
+ Statin therapy
+ Beta blockers
+ Aldosterone antagonists
+ Index year
+ 2012
+ 2013
+ 2014
+ 2015
+ 2016
+ 2017
+ ", file='ol.txt' )
> ol <- read.table('ol.txt',header=FALSE,sep='\t',as.is=TRUE)
```

Baseline pre-matching

We can now construct the pre-matching table

```
> bt <- rbind( "Sample size"= dt.tab[1,2:1]+dt.tab[2,2:1],
+              "Age" = NA,
+              dt.tab["F",2:1,drop=FALSE],
+              ct.tab["pre.CVD",2:1,drop=FALSE],
+              ct.tab["prv.MI",2:1,drop=FALSE],
+              ct.tab["prv.UnstAng",2:1,drop=FALSE],
+              ct.tab["prv.HF",2:1,drop=FALSE],
+              ct.tab["prv.AtrFib",2:1,drop=FALSE],
+              ct.tab["pre.Str",2:1,drop=FALSE],
+              ct.tab["prv.PAD",2:1,drop=FALSE],
+              ct.tab["pre.Mic",2:1,drop=FALSE],
+              ct.tab["prv.CKD",2:1,drop=FALSE],
+              "Frail"=dt.tab["1",2:1],
+              mt.tab["had.Metformin",2:1,drop=FALSE],
+              mt.tab["had.DPP4",2:1,drop=FALSE],
+              mt.tab["had.TZD",2:1,drop=FALSE],
+              mt.tab["had.GLP1",2:1,drop=FALSE],
+              mt.tab["got.Ins",2:1,drop=FALSE],
+              mt.tab["got.Hyp",2:1,drop=FALSE],
+              mt.tab["had.HCD",2:1,drop=FALSE],
+              mt.tab["had.THZ",2:1,drop=FALSE],
+              mt.tab["had.ACE",2:1,drop=FALSE],
+              mt.tab["had.ARB",2:1,drop=FALSE],
+              mt.tab["had.Sta",2:1,drop=FALSE],
+              mt.tab["had.BBl",2:1,drop=FALSE],
+              mt.tab["had.AlA",2:1,drop=FALSE],
+              "Index year"=NA,
+              dt.tab["Index date 2012",2:1,drop=FALSE],
+              dt.tab["2013",2:1,drop=FALSE],
+              dt.tab["2014",2:1,drop=FALSE],
+              dt.tab["2015",2:1,drop=FALSE],
+              dt.tab["2016",2:1,drop=FALSE],
+              '2017'=NA)
> str(ol)
```

```
'data.frame':        33 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
```

```
> bt <- cbind(bt[,1],NA,NA,bt[,2],NA,NA)
> bt["Age",c(2,3,5,6)] <- dt.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bt ) <- c("SGLT-2","mean","sd","SU","mean","sd")
>  cbind( ol, bt )
```

```
                                        V1 SGLT-2 mean sd    SU mean sd
Sample size                    Sample size  17594   NA NA 12328   NA NA
Age                             Age, years     NA 59.8 11    NA 63.9 13
F                                    Women   7246   NA NA  4803   NA NA
pre.CVD                         CV-history   5603   NA NA  3681   NA NA
prv.MI               Myocardial infarction   1405   NA NA  1003   NA NA
prv.UnstAng                Unstable angina    640   NA NA   470   NA NA
prv.HF                       Heart failure    880   NA NA   496   NA NA
prv.AtrFib             Atrial fibrillation   1378   NA NA   740   NA NA
pre.Str                             Stroke   1535   NA NA   873   NA NA
prv.PAD                               PAD    1061   NA NA   599   NA NA
pre.Mic              Microvascular disease   3035   NA NA  4104   NA NA
prv.CKD                                CKD    434   NA NA    69   NA NA
Frail                        Frailty (yes)   4950   NA NA  4045   NA NA
had.Metformin                    Metformin  14057   NA NA  9881   NA NA
had.DPP4                             DPP4    2264   NA NA  2137   NA NA
had.TZD                               TZD      27   NA NA    28   NA NA
had.GLP1                             GLP1    1332   NA NA  4054   NA NA
got.Ins                           Insulin     952   NA NA  4147   NA NA
got.Hyp         Anti hypertensive therapy   12224   NA NA  9593   NA NA
had.HCD                    LOOP diuretics    2850   NA NA  1703   NA NA
had.THZ              Low ceiling diuretics   2630   NA NA  1877   NA NA
had.ACE                     ACE Inhibitors   5886   NA NA  4676   NA NA
had.ARB                               ARBs   4459   NA NA  4299   NA NA
had.Sta                     Statin therapy  10956   NA NA  9176   NA NA
had.BBl                      Beta blockers   4769   NA NA  3333   NA NA
had.AlA            Aldosterone antagonists    896   NA NA   644   NA NA
Index year                      Index year     NA   NA NA    NA   NA NA
Index date 2012                       2012    412   NA NA    11   NA NA
2013                                  2013   5130   NA NA  1353   NA NA
2014                                  2014   4477   NA NA  2069   NA NA
2015                                  2015   4136   NA NA  3333   NA NA
2016                                  2016   3439   NA NA  5562   NA NA
2017                                  2017     NA   NA NA    NA   NA NA
```

```
> write.xlsx( cbind( 'Org. labs'=ol, bt ),
+             "SGSU.xlsx",
+ sheetName = "Baseline pre-matching",
+    append = FALSE,
+    showNA = FALSE )
```

Baseline after matching

The data for post matching have exactly the same structure; the tables are just called ’`m.tab`’ instead of ’`t.tab`’:

```
> bm <- rbind( "Sample size"= dm.tab[1,2:1]+dm.tab[2,2:1],
+               "Age" = NA,
+               dm.tab["F",2:1,drop=FALSE],
+               cm.tab["pre.CVD",2:1,drop=FALSE],
+               cm.tab["prv.MI",2:1,drop=FALSE],
+               cm.tab["prv.UnstAng",2:1,drop=FALSE],
+               cm.tab["prv.HF",2:1,drop=FALSE],
+               cm.tab["prv.AtrFib",2:1,drop=FALSE],
+               cm.tab["pre.Str",2:1,drop=FALSE],
+               cm.tab["prv.PAD",2:1,drop=FALSE],
+               cm.tab["pre.Mic",2:1,drop=FALSE],
+               cm.tab["prv.CKD",2:1,drop=FALSE],
+               "Frail"=dm.tab["1",2:1],
+               mm.tab["had.Metformin",2:1,drop=FALSE],
+               mm.tab["had.DPP4",2:1,drop=FALSE],
+               mm.tab["had.TZD",2:1,drop=FALSE],
+               mm.tab["had.GLP1",2:1,drop=FALSE],
+               mm.tab["got.Ins",2:1,drop=FALSE],
+               mm.tab["got.Hyp",2:1,drop=FALSE],
+               mm.tab["had.HCD",2:1,drop=FALSE],
+               mm.tab["had.THZ",2:1,drop=FALSE],
+               mm.tab["had.ACE",2:1,drop=FALSE],
+               mm.tab["had.ARB",2:1,drop=FALSE],
+               mm.tab["had.Sta",2:1,drop=FALSE],
+               mm.tab["had.BBl",2:1,drop=FALSE],
+               mm.tab["had.AlA",2:1,drop=FALSE],
+               "Index year"=NA,
+               dm.tab["Index date 2012",2:1,drop=FALSE],
+               dm.tab["2013",2:1,drop=FALSE],
+               dm.tab["2014",2:1,drop=FALSE],
+               dm.tab["2015",2:1,drop=FALSE],
+               dm.tab["2016",2:1,drop=FALSE],
+               '2017'=NA)
> str(ol)
'data.frame':        33 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
> bm <- cbind(bm[,1],NA,NA,bm[,2],NA,NA)
> bm["Age",c(2,3,5,6)] <- dm.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bm ) <- c("SGLT-2","mean","sd","SU","mean","sd")
> cbind( ol, bm )
                                        V1 SGLT-2 mean   sd   SU mean   sd
Sample size                    Sample size   6856   NA   NA 6856   NA   NA
Age                             Age, years     NA 60.8 11.2   NA 60.7 12.5
F                                    Women   2745   NA   NA 2724   NA   NA
pre.CVD                         CV-history   1907   NA   NA 2004   NA   NA
prv.MI               Myocardial infarction    501   NA   NA  515   NA   NA
prv.UnstAng                Unstable angina    245   NA   NA  228   NA   NA
prv.HF                       Heart failure    255   NA   NA  266   NA   NA
prv.AtrFib             Atrial fibrillation    409   NA   NA  429   NA   NA
pre.Str                             Stroke    482   NA   NA  499   NA   NA
prv.PAD                               PAD     331   NA   NA  338   NA   NA
pre.Mic              Microvascular disease   1500   NA   NA 1579   NA   NA
prv.CKD                                CKD     40   NA   NA   48   NA   NA
Frail                        Frailty (yes)   1879   NA   NA 1922   NA   NA
had.Metformin                    Metformin   5484   NA   NA 5454   NA   NA
had.DPP4                              DPP4   1311   NA   NA 1306   NA   NA
had.TZD                               TZD      14   NA   NA   16   NA   NA
```

```
had.GLP1                                GLP1    1127   NA    NA 1194    NA    NA
got.Ins                              Insulin     757   NA    NA  871    NA    NA
got.Hyp         Anti hypertensive therapy   4976   NA    NA 5051    NA    NA
had.HCD                       LOOP diuretics     862   NA    NA  891    NA    NA
had.THZ                  Low ceiling diuretics   1017   NA    NA  977    NA    NA
had.ACE                      ACE Inhibitors   2435   NA    NA 2467    NA    NA
had.ARB                                ARBs   2106   NA    NA 2083    NA    NA
had.Sta                     Statin therapy   4796   NA    NA 4779    NA    NA
had.BBl                      Beta blockers   1747   NA    NA 1759    NA    NA
had.AlA             Aldosterone antagonists     321   NA    NA  328    NA    NA
Index year                        Index year      NA   NA    NA   NA    NA    NA
Index date 2012                         2012      40   NA    NA    8    NA    NA
2013                                    2013     929   NA    NA 1023    NA    NA
2014                                    2014    1346   NA    NA 1405    NA    NA
2015                                    2015    1990   NA    NA 1864    NA    NA
2016                                    2016    2551   NA    NA 2556    NA    NA
2017                                    2017      NA   NA    NA   NA    NA    NA
```

```
> write.xlsx( cbind( 'Org. labs'=ol, bm ),
+             "SGSU.xlsx",
+ sheetName = "Baseline after matching",
+    append = TRUE,
+    showNA = FALSE )
```

1.13.2 Treatment distribution

```
> ( FUtab <- tabFU[c(2:5,rep(NA,4),1),] )
       wh
Ix       nPers         FU    meanfu      sdFU    maxFU
  SGLT2   6856 10945.7413 1.5965200 1.0895279 4.051335
  Dapa    4684  9145.6769 1.9525356 1.0852049 4.051335
  Empa    1957  1495.6441 0.7642535 0.5430833 2.331964
  Cana     215   304.4203 1.4159082 0.6456059 2.540041
  <NA>      NA         NA        NA        NA       NA
  <NA>      NA         NA        NA        NA       NA
  <NA>      NA         NA        NA        NA       NA
  <NA>      NA         NA        NA        NA       NA
  SU      6853 10658.4278 1.5552937 1.0900305 4.078713
```

```
> colnames(FUtab) <- c(
+ 'Number of patients',
+ 'Total follow-up time',
+ 'Mean follow-up time',
+ 'Sd follow-up time',
+ 'maximum follow-up time')
> rownames( FUtab ) <- c(
+ 'SGLT-2',
+ '   Dapagliflozin',
+ '   Empagliflozin',
+ '   Canagliflozin',
+ '   Ipragliflozin',
+ '   Luseogliflozin',
+ '   Tofugliflozin',
+ '-',
+ 'SU')
> FUtab
```

```
                   wh
Ix                   Number of patients Total follow-up time Mean follow-up time Sd follow-up t
  SGLT-2                          6856           10945.7413           1.5965200         1.0895
     Dapagliflozin                4684            9145.6769           1.9525356         1.0852
     Empagliflozin                1957            1495.6441           0.7642535         0.5430
     Canagliflozin                 215             304.4203           1.4159082         0.6456
     Ipragliflozin                  NA                   NA                  NA
     Luseogliflozin                 NA                   NA                  NA
     Tofugliflozin                  NA                   NA                  NA
  -                                 NA                   NA                  NA
  SU                              6853           10658.4278           1.5552937         1.0900
                   wh
Ix                   maximum follow-up time
  SGLT-2                           4.051335
     Dapagliflozin                 4.051335
     Empagliflozin                 2.331964
     Canagliflozin                 2.540041
     Ipragliflozin                       NA
     Luseogliflozin                      NA
     Tofugliflozin                       NA
  -                                      NA
  SU                               4.078713
```

```
> write.xlsx( FUtab,
+             "SGSU.xlsx",
+ sheetName = "Treatment distribution",
+    append = TRUE,
+    showNA = FALSE )
```

1.13.3 Events

```
> cat(
+ 'Number of patients
+ Total follow-up time - on treatment
+ Number of patients with event - on treatment
+ Total follow-up time - ITT
+ Number of patients with event - ITT
+ ', file='oc' )
> ( oc <- read.table('oc',header=FALSE,sep='\t',as.is=TRUE)[,1] )
[1] "Number of patients"                            "Total follow-up time - on treatment"
[3] "Number of patients with event - on treatment" "Total follow-up time - ITT"
[5] "Number of patients with event - ITT"
```

```
> cat(
+ 'HHF
+ All-cause death
+ All-cause death or HHF
+ Cardiavascular death
+ Myocardial infarction
+ Stroke
+ Ischemic stroke
+ MACE (cardivascular death, MI or stroke)
+ modified MACE (All-cause death, MI or stroke)
+ Kidney disease
+ ', file='ol' )
> ( ol <- read.table('ol',header=FALSE,sep='\t',as.is=TRUE)[,1] )
```

```
 [1] "HHF"                                            "All-cause death"
 [3] "All-cause death or HHF"                         "Cardiavascular death"
 [5] "Myocardial infarction"                          "Stroke"
 [7] "Ischemic stroke"                                "MACE (cardivascular death, MI or stroke)
 [9] "modified MACE (All-cause death, MI or stroke)" "Kidney disease"
```

The data for this is in the `dat` object:

```
> str( dat )
 num [1:10, 1:2, 1:3, 1:2, 1:3] 6856 6856 6856 6856 6856 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "SU"
  ..$ dat : chr [1:3] "N" "PY" "Event"
```

```
> cbind( ol, dimnames(dat)[[1]] )
      ol
 [1,] "HHF"                                            "HF"
 [2,] "All-cause death"                                "ACD"
 [3,] "All-cause death or HHF"                         "ACD+HF"
 [4,] "Cardiavascular death"                           "CVDD"
 [5,] "Myocardial infarction"                          "MI"
 [6,] "Stroke"                                         "Str"
 [7,] "Ischemic stroke"                                "IscStr"
 [8,] "MACE (cardivascular death, MI or stroke)"       "CVDD+MI+Str"
 [9,] "modified MACE (All-cause death, MI or stroke)" "ACD+MI+Str"
[10,] "Kidney disease"                                 "DKD"
```

```
> ft <- ftable( dat[,,1,1:2,,drop=FALSE], col.vars=c(4,2,5) )
> round( ft, 1 )
                    ix     SGLT2                                               SU
                    data    OnDr                   Total                      OnDr
                    dat        N      PY   Event        N      PY   Event        N      PY   Ever
endp        sub
HF          AllPtt        6856.0  8139.9    54.0   6856.0 10861.7    78.0   6853.0  7676.3    85.
ACD         AllPtt        6856.0  8182.2    70.0   6856.0 10945.7   136.0   6853.0  7750.9   151.
ACD+HF      AllPtt        6856.0  8139.9   122.0   6856.0 10861.7   210.0   6853.0  7676.3   226.
CVDD        AllPtt        6856.0  8182.2    12.0   6856.0 10945.7    20.0   6853.0  7750.9    31.
MI          AllPtt        6856.0  8151.1    40.0   6856.0 10900.6    49.0   6853.0  7703.4    61.
Str         AllPtt        6856.0  8137.3    53.0   6856.0 10870.0    70.0   6853.0  7696.2    70.
IscStr      AllPtt        6856.0  8138.6    50.0   6856.0 10875.4    64.0   6853.0  7699.7    64.
CVDD+MI+Str AllPtt        6856.0  8106.8   103.0   6856.0 10825.5   134.0   6853.0  7650.8   151.
ACD+MI+Str  AllPtt        6856.0  8106.8   158.0   6856.0 10825.5   240.0   6853.0  7650.8   267.
DKD         AllPtt        6856.0  8141.7    48.0   6856.0 10856.8    69.0   6853.0  7682.3    82.
```

This is the table needed (except for the column on persons, which should not be repeated):

```
> py <- data.frame( as.matrix(ft) )[-c(4,10)]
> py
                   SGLT2_OnDr_N SGLT2_OnDr_PY SGLT2_OnDr_Event SGLT2_Total_PY SGLT2_Total_Ever
HF_AllPtt                  6856      8139.875               54       10861.66                7
ACD_AllPtt                 6856      8182.176               70       10945.74               13
ACD+HF_AllPtt              6856      8139.875              122       10861.66               21
CVDD_AllPtt                6856      8182.176               12       10945.74                2
MI_AllPtt                  6856      8151.094               40       10900.65                4
Str_AllPtt                 6856      8137.341               53       10870.03                7
```

```
IscStr_AllPtt              6856      8138.600               50       10875.36                6
CVDD+MI+Str_AllPtt         6856      8106.839              103       10825.51               13
ACD+MI+Str_AllPtt          6856      8106.839              158       10825.51               24
DKD_AllPtt                 6856      8141.666               48       10856.83                6
                   SU_OnDr_N SU_OnDr_PY SU_OnDr_Event SU_Total_PY SU_Total_Event
HF_AllPtt               6853   7676.290            85    10514.11            106
ACD_AllPtt              6853   7750.916           151    10658.43            232
ACD+HF_AllPtt           6853   7676.290           226    10514.11            323
CVDD_AllPtt             6853   7750.916            31    10658.43             50
MI_AllPtt               6853   7703.396            61    10572.55             77
Str_AllPtt              6853   7696.223            70    10553.42             95
IscStr_AllPtt           6853   7699.676            64    10566.89             80
CVDD+MI+Str_AllPtt      6853   7650.806           151    10469.65            204
ACD+MI+Str_AllPtt       6853   7650.806           267    10469.65            379
DKD_AllPtt              6853   7682.322            82    10527.26            116
```

```
> colnames( py )
```

```
 [1] "SGLT2_OnDr_N"      "SGLT2_OnDr_PY"     "SGLT2_OnDr_Event"  "SGLT2_Total_PY"
 [5] "SGLT2_Total_Event" "SU_OnDr_N"         "SU_OnDr_PY"        "SU_OnDr_Event"
 [9] "SU_Total_PY"       "SU_Total_Event"
```

```
> colnames(py) <- c(oc,oc[-1])
> rownames(py) <- ol
```

With this in order we can now write it to the excel sheet:

```
> write.xlsx( py,
+              "SGSU.xlsx",
+ sheetName = "Events",
+    append = TRUE,
+    showNA = FALSE )
```

1.13.4 Hazard ratios

```
> ft <- ftable((dat[c(1:3,9,5,6),1:2,1,"SGLT2",,drop=FALSE]+
+               dat[c(1:3,9,5,6),1:2,1,"SU" ,,drop=FALSE])[,,,c(1,1),],row.vars=c(1,2,3))
> YD <- data.frame(as.matrix(ft))
> HR <- data.frame(as.matrix(ftable(res[c(1:3,9,5,6),1:2,1,1:2,c(1,4)],row.vars=c(1,2,3))))
> Endpoint <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[1] )
> Adjusted <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[3] )
> Analysis <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[2] )
> ( HR <- cbind(Endpoint,Adjusted,Analysis,HR,YD)[,c(1:3,6:8,4:5)] )
```

```
                       Endpoint Adjusted Analysis     N       PY Event        HR         se
HF_OnDr_Raw                  HF      Raw     OnDr 13709 15816.17   139 0.6077071 0.17365434
HF_OnDr_Adj                  HF      Adj     OnDr 13709 15816.17   139 0.6031188 0.17739474
HF_Total_Raw                 HF      Raw    Total 13709 21375.78   184 0.7140715 0.14897696
HF_Total_Adj                 HF      Adj    Total 13709 21375.78   184 0.7027171 0.15289665
ACD_OnDr_Raw                ACD      Raw     OnDr 13709 15933.09   221 0.4422793 0.14420681
ACD_OnDr_Adj                ACD      Adj     OnDr 13709 15933.09   221 0.5064158 0.14558176
ACD_Total_Raw               ACD      Raw    Total 13709 21604.17   368 0.5702962 0.10783769
ACD_Total_Adj               ACD      Adj    Total 13709 21604.17   368 0.6140819 0.10825180
ACD+HF_OnDr_Raw          ACD+HF      Raw     OnDr 13709 15816.17   348 0.5154844 0.11198305
ACD+HF_OnDr_Adj          ACD+HF      Adj     OnDr 13709 15816.17   348 0.5619028 0.11374067
ACD+HF_Total_Raw         ACD+HF      Raw    Total 13709 21375.78   533 0.6293378 0.08850966
ACD+HF_Total_Adj         ACD+HF      Adj    Total 13709 21375.78   533 0.6590630 0.08951955
ACD+MI+Str_OnDr_Raw  ACD+MI+Str      Raw     OnDr 13709 15757.65   425 0.5644601 0.10046010
```

```
ACD+MI+Str_OnDr_Adj  ACD+MI+Str      Adj     OnDr 13709 15757.65   425 0.6072930 0.10086093
ACD+MI+Str_Total_Raw ACD+MI+Str      Raw    Total 13709 21295.16   619 0.6138429 0.08247205
ACD+MI+Str_Total_Adj ACD+MI+Str      Adj    Total 13709 21295.16   619 0.6387273 0.08263003
MI_OnDr_Raw                  MI      Raw     OnDr 13709 15854.49   101 0.6287445 0.20433098
MI_OnDr_Adj                  MI      Adj     OnDr 13709 15854.49   101 0.6278277 0.20632178
MI_Total_Raw                 MI      Raw    Total 13709 21473.19   126 0.6216086 0.18332122
MI_Total_Adj                 MI      Adj    Total 13709 21473.19   126 0.6186374 0.18365548
Str_OnDr_Raw                Str      Raw     OnDr 13709 15833.56   123 0.7255626 0.18254770
Str_OnDr_Adj                Str      Adj     OnDr 13709 15833.56   123 0.7498096 0.18327263
Str_Total_Raw               Str      Raw    Total 13709 21423.45   165 0.7180294 0.15741846
Str_Total_Adj               Str      Adj    Total 13709 21423.45   165 0.7265511 0.15777364
```

```
> write.xlsx( HR,
+              "SGSU.xlsx",
+ sheetName = "Hazard ratios",
+    append = TRUE,
+    showNA = FALSE )
```

1.13.5 Subgroup OT

This is same as above, except the we restrict to “OnDr”, and subclassify by previous CVD:

```
> str(dat)
 num [1:10, 1:2, 1:3, 1:2, 1:3] 6856 6856 6856 6856 6856 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "SU"
  ..$ dat : chr [1:3] "N" "PY" "Event"
```

```
> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"OnDr",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"OnDr",,"SU"   ,],row.vars=c(1,2))))
> str( YD )
```

```
'data.frame':        18 obs. of  3 variables:
 $ N    : num  13709 3908 9801 13709 3908 ...
 $ PY   : num  15816 4278 11538 15933 4366 ...
 $ Event: num  139 106 33 221 121 100 348 216 132 425 ...
```

```
> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"OnDr",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+              "SGSU.xlsx",
+ sheetName = "Subgroups OT",
+    append = TRUE,
+    showNA = FALSE )
```

`../rep/2xlSGSU.tex`

1.13.6 Subgroup ITT

This is same as above, except the we restrict to “Total”, and subclassify by previous CVD:

```
> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"Total",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"Total",,"SU"    ,],row.vars=c(1,2))))
> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"Total",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+             "SGSU.xlsx",
+ sheetName = "Subgroups ITT",
+    append = TRUE,
+    showNA = FALSE )
```

Chapter 2

Analysis of SGLT-2i vs. DPP4

2.1 Dataset for analysis od SGLT-2i vs DPP-4

First load the relevant package:

```
> options( width=95 )
> library( Epi )
> library( splines )
> library( haven )
> library( Matching )
> clear()
> print( sessionInfo(), l=F )
R version 3.4.1 (2017-06-30)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] Matching_4.9-2 MASS_7.3-47    haven_1.1.0    Epi_2.26

loaded via a namespace (and not attached):
 [1] Rcpp_0.12.12      lattice_0.20-35   zoo_1.8-0         grid_3.4.1        plyr_1.8.4
 [6] magrittr_1.5      etm_0.6-2         rlang_0.1.2       Matrix_1.2-11     forcats_0.2.0
[11] tools_3.4.1       cmprsk_2.2-7      numDeriv_2016.8-1 survival_2.41-3   parallel_3.4.1
[16] compiler_3.4.1    tibble_1.3.4
```

Then we can read the data:

```
> system.time(
+ mset <- read_sas( "../data/episodes.sas7bdat" ) )
   user  system elapsed
   8.39    0.26   24.04
```

```
> dim( mset )
```

```
[1] 244715     98
```

```
> names( mset )
```

```
                                               ...now input from ../rep/matchSGDP.tex
 [1] "druggr"       "pnr"          "eksd"         "ATC"          "doDM"         "epiN"
 [7] "doIx"         "Ixdr"         "Ixatc"        "lastpr"       "doTm"         "doFL"
[13] "FLdr"         "FLatc"        "deCVDD"       "coD"          "doTIA"        "doAngina"
[19] "doBleed"      "doCOPD"       "doPAD"        "doHF"         "doCancer"     "doDMcompl"
[25] "doNeuro"      "doDKD"        "doDiaEye"     "doHypo"       "doAtrFib"     "doMI"
[31] "doUnstAng"    "doHmStr"      "doDiaFoot"    "doOther"      "doPeriAng"    "doIscStr"
[37] "doAmp"        "doCKD"        "doPCIsten"    "doCABG"       "doKeto"       "doDial"
[43] "doBari"       "sex"          "doBth"        "whBth"        "doDth"        "dSrc"
[49] "dolACE"       "dolSta"       "dolBBl"       "dolARB"       "dolAlA"       "dolDHP"
[55] "dolWtL"       "dolRPA"       "dolWrf"       "dolAsp"       "dolHCD"       "dolTHZ"
[61] "dolCcs"       "dolDXI"       "dolDgo"       "dolAPl"       "dolAmi"       "dolDTI"
[67] "dolNHP"       "dolFla"       "dolMetformin" "dolGLP1"      "dolMetxSGLT2" "dolMetxDPP4"
[73] "dolSGLT2"     "dollongIns"   "dolmixIns"    "dolDPP4"      "dolSU"        "dolintIns"
[79] "dolfastIns"   "dolTZD"       "dolAcarbose"  "dolTZDxDPP4"  "maxH"         "frail"
[85] "recnum"       "C_ADIAG"      "compl"        "C_OPR"        "D_INDDTO"     "V_SENGDAGE"
[91] "deHF"         "deMACE"       "deMI"         "deStr"        "deIscStr"     "deAF"
[97] "deHH"         "deDKD"
```

We subset to SGLT-2i / DPP-4 and on the fly convert all dates to fractions of years to facilitate programming:

```
> mset <- cal.yr( subset( as.data.frame( mset ), Ixdr %in% c("SGLT2","DPP4") ) )
```

We then select the first of these episodes from each person, and exclude those with the other in the baseline. Note that persons where both drugs are initiated the same day, will be excluded entirely, because drugs initiated on the index day are coded as baseline drug with the same date.

```
> nrow( mset )
[1] 56984
```

```
> mset <- mset[order(mset$pnr,mset$doIx),]
> mset <- mset[!duplicated(mset$pnr),]
> mset <- subset( mset, ( Ixdr=="SGLT2" & is.na(dolDPP4 ) ) |
+                       ( Ixdr=="DPP4"  & is.na(dolSGLT2) ) )
> with( mset, table(table(pnr)) )
```

```
    1
48140
```

Thus we see that we have precisely one episode per person after these exclusions.

To make `FLdr` and `Ixdr` into factors we need some sensible levels:

```
> ( drlab <- read.table( "drlab.txt", header=TRUE, as.is=TRUE ) )
        gr  lab      longlab
1       11  Met    Metformin
2       12   SU Sulfonylurea
3       13  TZD          TZD
4       14  DPP        DPP-4
5       15  GLP        GLP-1
6       16  SGL        SGLT2
7  fastIns fIns      fastIns
8   intIns iIns       intIns
9   mixIns mIns       mixIns
10 longIns lIns      longIns
11      18  Aca     Acarbose
12      19  Meg  Meglitinide
```

```
13     212  M+U       Met+SU
14     213  M+T      Met+TZD
15     214  M+D     Met+DPP4
16     216  M+S    Met+SGLT2
17     218  M+A Met+Acarbose
18     223  U+T       SU+TZD
19     234  D+T     TZD+DPP4
20     246  D+S   DPP4+SGLT2
```

Then we can define the first line and the index drug variables as factors:

```
> mset <- transform( mset, FLdr = factor( FLdr,
+                                         levels = drlab$gr,
+                                         labels = drlab$lab ),
+                           Ixdr = factor( Ixdr ) )
```

We tabulate the index drug versus the first-line drug separately for those where the index date and first-line dates are the same:

```
> print( ftable( with( mset, addmargins(
+                 table( "doIx=doFL"=abs(doIx-doFL)<0.1, FLdr, Ixdr ), 1:2 ) ),
+                 col.vars=c(3,1) ),
+        zero = "." )
     Ixdr       DPP4              SGLT2
     doIx=doFL FALSE  TRUE   Sum FALSE  TRUE   Sum
FLdr
Met            25926  1074 27000  7973   123  8096
SU              7763    30  7793  2588     1  2589
TZD                5     .     5     2     .     2
DPP               34   676   710     9     .     9
GLP               25     3    28    21     1    22
SGL                .     .     .     .    90    90
fIns             259     4   263   165     .   165
iIns             246     3   249   125     .   125
mIns             229     1   230    92     1    93
lIns              43     5    48    16     .    16
Aca               33     1    34    12     .    12
Meg                .     .     .     .     .     .
M+U                .     .     .     .     .     .
M+T               24     .    24    12     .    12
M+D               43   422   465    37     .    37
M+S                .     .     .     .    23    23
M+A                .     .     .     .     .     .
U+T                .     .     .     .     .     .
D+T                .     .     .     .     .     .
D+S                .     .     .     .     .     .
Sum            34630  2219 36849 11052   239 11291
```

We see that among those where the two dates are equal, there are still some where the first line and Index drug are not the same. This is because each initiating drug generates its own episode.

2.2 Baseline tables for all new-starters

We produce an overview of the the exposure status, but first we need a few derived variables, including the indicator of *any* previous CVD:

```
> mset <- transform( mset, age = doIx - doBth,
+                           tff = doIx - doFL,
+                           sex = factor( sex, labels=c("M","F") ),
+                         frail = pmax( frail, 0, na.rm=TRUE ),
+                          maxH = pmax( 0, maxH, na.rm=TRUE ) )
> with( mset, addmargins( table( Ixatc, Ixdr ), 1 ) )
         Ixdr
Ixatc      DPP4 SGLT2
  A10BD07  7110     0
  A10BD08  6427     0
  A10BD09     5     0
  A10BD10    15     0
  A10BD11    99     0
  A10BD13   316     0
  A10BD15     0   309
  A10BD16     0    11
  A10BD20     0   372
  A10BH01 13719     0
  A10BH02  2752     0
  A10BH03   826     0
  A10BH04   651     0
  A10BH05  4929     0
  A10BK01     0  6665
  A10BK02     0   321
  A10BK03     0  3613
  Sum     36849 11291
```

We now produce the baseline baseline tables for the entire set of new users, the result is in three tables, `dt.tab` (demographics for total sample), `ct.tab` (comobidites for total sample) and `mt.tab` (medication for total sample).

```
> ptab <- function( var ) cbind( tt <- table( var, mset$Ixdr ),
+                                round( prop.table( tt, 2 ) * 100, 1 ) )
```

2.2.1 Demographics

First the tabulations of the baseline demographics:

```
> t.sex <- with( mset, ptab(sex) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0
                   DPP4 SGLT2 DPP4 SGLT2
Index = First Line 1383   152  3.8   1.3

> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                      tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0

                        [,1] [,2] [,3] [,4]
Index not FL: Mean / SD  6.9  9.2  5.2  5.4
```

```
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
+                                tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age
```

```
               [,1] [,2] [,3] [,4]
Age: Mean / SD 64.6 60.1 12.6 10.9
```

```
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )
```

```
       DPP4 SGLT2 DPP4 SGLT2
2012.5  673    18  1.8   0.2
2013   4468   665 12.1   5.9
2013.5 4216   829 11.4   7.3
2014   4864   983 13.2   8.7
2014.5 4033  1108 10.9   9.8
2015   5043  1438 13.7  12.7
2015.5 4349  1493 11.8  13.2
2016   5031  2467 13.7  21.8
2016.5 4172  2290 11.3  20.3
```

```
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dt.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dt.tab
```

```
                           DPP4  SGLT2 DPP4 SGLT2
Sex M                   22246.0 6904.0 60.4  61.1
F                       14603.0 4387.0 39.6  38.9
Index = First Line       1383.0  152.0  3.8   1.3
Index not FL: Mean / SD     6.9    9.2  5.2   5.4
Age at index <40         1147.0  431.0  3.1   3.8
40                       3772.0 1555.0 10.2  13.8
50                       7959.0 3405.0 21.6  30.2
60                      10916.0 3760.0 29.6  33.3
70                       9037.0 1892.0 24.5  16.8
80+                      4018.0  248.0 10.9   2.2
Age: Mean / SD             64.6   60.1 12.6  10.9
Index date 2012           673.0   18.0  1.8   0.2
2013                     8684.0 1494.0 23.6  13.2
2014                     8897.0 2091.0 24.1  18.5
2015                     9392.0 2931.0 25.5  26.0
2016                     9203.0 4757.0 25.0  42.1
Date of first line 1995  1200.0  560.0  3.3   5.0
1996                      457.0  202.0  1.2   1.8
1997                      491.0  226.0  1.3   2.0
1998                      633.0  288.0  1.7   2.6
1999                      716.0  384.0  1.9   3.4
2000                      812.0  411.0  2.2   3.6
2001                      952.0  449.0  2.6   4.0
```

```
2002                     1129.0  499.0  3.1   4.4
2003                     1447.0  612.0  3.9   5.4
2004                     1512.0  634.0  4.1   5.6
2005                     1717.0  688.0  4.7   6.1
2006                     1862.0  731.0  5.1   6.5
2007                     2082.0  760.0  5.7   6.7
2008                     2509.0  780.0  6.8   6.9
2009                     2551.0  816.0  6.9   7.2
2010                     2942.0  760.0  8.0   6.7
2011                     3090.0  660.0  8.4   5.8
2012                     2897.0  461.0  7.9   4.1
2013                     2698.0  384.0  7.3   3.4
2014                     2181.0  357.0  5.9   3.2
2015                     1922.0  344.0  5.2   3.0
2016                     1049.0  285.0  2.8   2.5
Frailty 0               25973.0 7459.0 70.5  66.1
1                       10876.0 3832.0 29.5  33.9
```

2.2.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- grep( "do[A-Z]", names( mset ) )
> wh <- wh[4:30]
> names( mset )[wh]
 [1] "doFL"      "doTIA"     "doAngina"  "doBleed"   "doCOPD"    "doPAD"     "doHF"
 [8] "doCancer"  "doDMcompl" "doNeuro"   "doDKD"     "doDiaEye"  "doHypo"    "doAtrFib"
[15] "doMI"      "doUnstAng" "doHmStr"   "doDiaFoot" "doOther"   "doPeriAng" "doIscStr"
[22] "doAmp"     "doCKD"     "doPCIsten" "doCABG"    "doKeto"    "doDial"
```

```
> comorb <- data.frame( pmax( mset[,wh] < mset[,"doIx"], 0, na.rm=TRUE ) )
> names( comorb ) <- gsub( "do", "prv.", names(comorb) )
> str( comorb )
```

```
'data.frame':        48140 obs. of  27 variables:
 $ prv.FL     : num  1 1 1 1 1 1 1 1 0 1 ...
 $ prv.TIA    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Angina : num  0 0 0 1 1 0 0 0 0 0 ...
 $ prv.Bleed  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.COPD   : num  0 0 0 0 0 0 1 0 0 0 ...
 $ prv.PAD    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.HF     : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Cancer : num  1 0 0 0 0 0 0 0 0 0 ...
 $ prv.DMcompl: num  1 0 0 0 0 1 0 0 0 0 ...
 $ prv.Neuro  : num  0 1 0 0 0 0 1 0 0 0 ...
 $ prv.DKD    : num  0 0 0 0 0 0 1 0 0 0 ...
 $ prv.DiaEye : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Hypo   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.AtrFib : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.MI     : num  0 0 0 0 1 0 1 0 0 0 ...
 $ prv.UnstAng: num  0 0 0 0 1 0 1 0 0 0 ...
 $ prv.HmStr  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.DiaFoot: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Other  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PeriAng: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.IscStr : num  0 0 0 0 0 0 0 0 0 0 ...
```

```
 $ prv.Amp    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.CKD    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PCIsten: num  0 0 0 0 0 0 1 0 0 0 ...
 $ prv.CABG   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Keto   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Dial   : num  0 0 0 0 0 0 0 0 0 0 ...
```

Later, in the modeling we will need the indicator of *any* previous CVD as well as *any* type of stroke and micro-vascular complications:

```
> comorb$pre.CVD <- with( comorb, pmax( prv.MI,
+                                       prv.UnstAng,
+                                       prv.Angina,
+                                       prv.HF,
+                                       prv.AtrFib,
+                                       prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA,
+                                       prv.PAD ) )
> comorb$pre.Str <- with( comorb, pmax( prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA ) )
> comorb$pre.FPA <- with( comorb, pmax( prv.DiaFoot,
+                                       prv.PeriAng ) )
> comorb$pre.Mic <- with( comorb, pmax( prv.DiaEye,
+                                       prv.DMcompl,
+                                       prv.Neuro,
+                                       prv.DKD,
+                                       prv.DiaFoot,
+                                       prv.PeriAng ) )
```

Note that we name the columns `pre.` to avoid including these in the propensity score estimation.

```
> ct.tab <- cbind(
+ t( sapply( comorb,
+           function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( comorb,
+           function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> # remove the dates of recurrent HF
> # wh <- grep( "HF[1-9]", rownames(ct.tab) )
> # ct.tab <- ct.tab[-wh,]
> ct.tab
             DPP4 SGLT2 DPP4 SGLT2
prv.FL      35466 11139 96.2  98.7
prv.TIA      1254   301  3.4   2.7
prv.Angina   4864  1574 13.2  13.9
prv.Bleed    1827   493  5.0   4.4
prv.COPD     1841   386  5.0   3.4
prv.PAD      2311   562  6.3   5.0
prv.HF       2080   475  5.6   4.2
prv.Cancer   2648   558  7.2   4.9
prv.DMcompl  3563  2307  9.7  20.4
prv.Neuro    1278   724  3.5   6.4
prv.DKD      1383   445  3.8   3.9
prv.DiaEye   2798  1569  7.6  13.9
```

```
prv.Hypo     1040   425  2.8   3.8
prv.AtrFib   3134   677  8.5   6.0
prv.MI       3253   956  8.8   8.5
prv.UnstAng  1403   440  3.8   3.9
prv.HmStr     411    85  1.1   0.8
prv.DiaFoot   285   112  0.8   1.0
prv.Other    1855   533  5.0   4.7
prv.PeriAng  1266   637  3.4   5.6
prv.IscStr   2443   535  6.6   4.7
prv.Amp        58    13  0.2   0.1
prv.CKD      1131    56  3.1   0.5
prv.PCIsten   383   105  1.0   0.9
prv.CABG     1128   314  3.1   2.8
prv.Keto      155    67  0.4   0.6
prv.Dial        9     1  0.0   0.0
pre.CVD     12424  3445 33.7  30.5
pre.Str      3551   802  9.6   7.1
pre.FPA      1470   703  4.0   6.2
pre.Mic      7800  4132 21.2  36.6
```

2.2.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest, restricted to the period after 2011-12-01, one year prior to the first SGLT2 dispensation.

```
> wh <- grep( "dol", names(mset) )
> names( mset )[wh]
 [1] "dolACE"       "dolSta"       "dolBBl"       "dolARB"       "dolAlA"       "dolDHP"
 [7] "dolWtL"       "dolRPA"       "dolWrf"       "dolAsp"       "dolHCD"       "dolTHZ"
[13] "dolCcs"       "dolDXI"       "dolDgo"       "dolAPl"       "dolAmi"       "dolDTI"
[19] "dolNHP"       "dolFla"       "dolMetformin" "dolGLP1"      "dolMetxSGLT2" "dolMetxDPP4"
[25] "dolSGLT2"     "dollongIns"   "dolmixIns"    "dolDPP4"      "dolSU"        "dolintIns"
[31] "dolfastIns"   "dolTZD"       "dolAcarbose"  "dolTZDxDPP4"
```

```
> codisp <- data.frame( pmax( mset[,wh] > ( mset[,"doIx"] - 1 ), 0, na.rm=TRUE ) )
> names( codisp ) <- gsub( "dol", "had.", names(codisp) )
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )
```

```
[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"
```

```
> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )
```

```
[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> ( names( codisp )[wh.cvd <- c(10,2,wh.hyp)] )
```

```
[1] "had.Asp" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )
```

```
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"
```

```
> mt.tab <- cbind(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mt.tab
```

```
               DPP4 SGLT2 DPP4 SGLT2
had.ACE       13775  4463 37.4  39.5
had.Sta       25543  8459 69.3  74.9
had.BBl       10977  3124 29.8  27.7
had.ARB       10731  3954 29.1  35.0
had.AlA        2169   607  5.9   5.4
had.DHP       11043  3529 30.0  31.3
had.WtL         109    91  0.3   0.8
had.RPA        2664   716  7.2   6.3
had.Wrf        2498   460  6.8   4.1
had.Asp       12479  4159 33.9  36.8
had.HCD        6956  1577 18.9  14.0
had.THZ        5651  1735 15.3  15.4
had.Ccs        2803   569  7.6   5.0
had.DXI         754   174  2.0   1.5
had.Dgo        1723   277  4.7   2.5
had.APl         645   121  1.8   1.1
had.Ami         240    27  0.7   0.2
had.DTI         592   139  1.6   1.2
had.NHP         620   197  1.7   1.7
had.Fla          48     9  0.1   0.1
had.Metformin 32241  9074 87.5  80.4
had.GLP1       1567  4516  4.3  40.0
had.MetxSGLT2     0   693  0.0   6.1
had.MetxDPP4  14134  1601 38.4  14.2
had.SGLT2         0 10599  0.0  93.9
had.longIns    1934  2438  5.2  21.6
had.mixIns     1109   994  3.0   8.8
had.DPP4      22733     0 61.7   0.0
had.SU         9683  2622 26.3  23.2
had.intIns     1207   890  3.3   7.9
had.fastIns    1002   979  2.7   8.7
had.TZD          54    44  0.1   0.4
had.Acarbose     53    19  0.1   0.2
had.TZDxDPP4      5     0  0.0   0.0
got.Ins        4009  3859 10.9  34.2
got.Hyp       27580  8930 74.8  79.1
got.CVD       32539 10313 88.3  91.3
```

2.3 Propensity scoring

We now make a logistic regression of the indicator of SGLT2 assignment versus DPP4 assignment. For convenience we append the just created data frames of the indicators we will use in the analysis:

```
> mset <- cbind( mset, comorb, codisp )
> names( mset )
```

```
  [1] "druggr"        "pnr"           "eksd"          "ATC"           "doDM"
  [6] "epiN"          "doIx"          "Ixdr"          "Ixatc"         "lastpr"
 [11] "doTm"          "doFL"          "FLdr"          "FLatc"         "deCVDD"
 [16] "coD"           "doTIA"         "doAngina"      "doBleed"       "doCOPD"
 [21] "doPAD"         "doHF"          "doCancer"      "doDMcompl"     "doNeuro"
 [26] "doDKD"         "doDiaEye"      "doHypo"        "doAtrFib"      "doMI"
 [31] "doUnstAng"     "doHmStr"       "doDiaFoot"     "doOther"       "doPeriAng"
 [36] "doIscStr"      "doAmp"         "doCKD"         "doPCIsten"     "doCABG"
 [41] "doKeto"        "doDial"        "doBari"        "sex"           "doBth"
 [46] "whBth"         "doDth"         "dSrc"          "dolACE"        "dolSta"
 [51] "dolBBl"        "dolARB"        "dolAlA"        "dolDHP"        "dolWtL"
 [56] "dolRPA"        "dolWrf"        "dolAsp"        "dolHCD"        "dolTHZ"
 [61] "dolCcs"        "dolDXI"        "dolDgo"        "dolAPl"        "dolAmi"
 [66] "dolDTI"        "dolNHP"        "dolFla"        "dolMetformin"  "dolGLP1"
 [71] "dolMetxSGLT2"  "dolMetxDPP4"   "dolSGLT2"      "dollongIns"    "dolmixIns"
 [76] "dolDPP4"       "dolSU"         "dolintIns"     "dolfastIns"    "dolTZD"
 [81] "dolAcarbose"   "dolTZDxDPP4"   "maxH"          "frail"         "recnum"
 [86] "C_ADIAG"       "compl"         "C_OPR"         "D_INDDTO"      "V_SENGDAGE"
 [91] "deHF"          "deMACE"        "deMI"          "deStr"         "deIscStr"
 [96] "deAF"          "deHH"          "deDKD"         "age"           "tff"
[101] "prv.FL"        "prv.TIA"       "prv.Angina"    "prv.Bleed"     "prv.COPD"
[106] "prv.PAD"       "prv.HF"        "prv.Cancer"    "prv.DMcompl"   "prv.Neuro"
[111] "prv.DKD"       "prv.DiaEye"    "prv.Hypo"      "prv.AtrFib"    "prv.MI"
[116] "prv.UnstAng"   "prv.HmStr"     "prv.DiaFoot"   "prv.Other"     "prv.PeriAng"
[121] "prv.IscStr"    "prv.Amp"       "prv.CKD"       "prv.PCIsten"   "prv.CABG"
[126] "prv.Keto"      "prv.Dial"      "pre.CVD"       "pre.Str"       "pre.FPA"
[131] "pre.Mic"       "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"
[136] "had.AlA"       "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"
[141] "had.Asp"       "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"
[146] "had.Dgo"       "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"
[151] "had.Fla"       "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"
[156] "had.SGLT2"     "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"
[161] "had.intIns"    "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"
[166] "got.Ins"       "got.Hyp"       "got.CVD"
```

With this in place it is quite easy to fit a propensity score model because we can easily fish out the relevant variables:

```
> table( mset$Ixdr )
 DPP4 SGLT2
36849 11291
> ( prv <- grep( "prv", names(mset) ) )
 [1] 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122
[23] 123 124 125 126 127
> ( had <- grep( "had", names(mset) ) )
 [1] 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153
[23] 154 155 156 157 158 159 160 161 162 163 164 165
> rmd <- c( grep( "SGL", names( mset )[had] ),
+           grep( "DPP", names( mset )[had] ) )
> had <- had[-rmd]
> names( mset )[had]
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.longIns"   "had.mixIns"    "had.SU"
[26] "had.intIns"    "had.fastIns"   "had.TZD"       "had.Acarbose"
```

```
> names( mset )[prv]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye"
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"
> system.time(
+ pr.0 <- glm( ( Ixdr == "SGLT2" ) ~
+              sex + age + frail + doIx + doFL +
+              as.matrix(mset[,prv]) +  as.matrix(mset[,had]),
+              family = binomial,
+              data = mset, maxit = 100 ) )
   user  system elapsed
   2.22    0.11    2.33
> print( summary( pr.0 ), digits = 3 )
Call:
glm(formula = (Ixdr == "SGLT2") ~ sex + age + frail + doIx +
    doFL + as.matrix(mset[, prv]) + as.matrix(mset[, had]), family = binomial,
    data = mset, maxit = 100)

Deviance Residuals:
   Min      1Q  Median      3Q     Max
-2.784  -0.603  -0.409  -0.170   3.560

Coefficients:
                                    Estimate Std. Error z value Pr(>|z|)
(Intercept)                        -1.04e+03   2.46e+01  -42.29  < 2e-16 ***
sexF                               -8.64e-02   2.75e-02   -3.14  0.00171 **
age                                -3.40e-02   1.29e-03  -26.38  < 2e-16 ***
frail                               8.74e-02   3.05e-02    2.87  0.00417 **
doIx                                5.52e-01   1.24e-02   44.53  < 2e-16 ***
doFL                               -3.55e-02   3.10e-03  -11.44  < 2e-16 ***
as.matrix(mset[, prv])prv.FL        9.31e-01   9.74e-02    9.55  < 2e-16 ***
as.matrix(mset[, prv])prv.TIA       3.79e-02   8.21e-02    0.46  0.64445
as.matrix(mset[, prv])prv.Angina    1.59e-02   4.57e-02    0.35  0.72778
as.matrix(mset[, prv])prv.Bleed    -5.10e-02   6.34e-02   -0.81  0.42060
as.matrix(mset[, prv])prv.COPD     -1.64e-01   7.19e-02   -2.29  0.02226 *
as.matrix(mset[, prv])prv.PAD      -1.21e-01   6.14e-02   -1.98  0.04793 *
as.matrix(mset[, prv])prv.HF       -7.85e-02   7.31e-02   -1.07  0.28281
as.matrix(mset[, prv])prv.Cancer   -1.23e-01   5.80e-02   -2.12  0.03438 *
as.matrix(mset[, prv])prv.DMcompl   1.11e-01   4.15e-02    2.68  0.00729 **
as.matrix(mset[, prv])prv.Neuro     1.93e-01   6.29e-02    3.07  0.00216 **
as.matrix(mset[, prv])prv.DKD      -6.28e-01   7.41e-02   -8.47  < 2e-16 ***
as.matrix(mset[, prv])prv.DiaEye    9.77e-02   4.54e-02    2.15  0.03144 *
as.matrix(mset[, prv])prv.Hypo     -2.54e-01   7.68e-02   -3.30  0.00096 ***
as.matrix(mset[, prv])prv.AtrFib    1.08e-01   7.50e-02    1.44  0.14914
as.matrix(mset[, prv])prv.MI        1.10e-01   5.61e-02    1.95  0.05059 .
as.matrix(mset[, prv])prv.UnstAng  -9.04e-02   7.65e-02   -1.18  0.23731
as.matrix(mset[, prv])prv.HmStr    -4.34e-02   1.41e-01   -0.31  0.75750
as.matrix(mset[, prv])prv.DiaFoot  -2.07e-01   1.49e-01   -1.39  0.16419
as.matrix(mset[, prv])prv.Other    -2.31e-01   6.89e-02   -3.35  0.00080 ***
as.matrix(mset[, prv])prv.PeriAng   2.78e-02   6.78e-02    0.41  0.68244
as.matrix(mset[, prv])prv.IscStr   -2.55e-01   6.79e-02   -3.76  0.00017 ***
as.matrix(mset[, prv])prv.Amp      -1.03e+00   4.13e-01   -2.51  0.01218 *
as.matrix(mset[, prv])prv.CKD      -2.23e+00   1.58e-01  -14.14  < 2e-16 ***
as.matrix(mset[, prv])prv.PCIsten  -1.83e-01   1.45e-01   -1.27  0.20490
```

```
as.matrix(mset[, prv])prv.CABG      -1.01e-01   9.06e-02   -1.11  0.26567
as.matrix(mset[, prv])prv.Keto      -1.90e-01   1.89e-01   -1.00  0.31639
as.matrix(mset[, prv])prv.Dial      -1.34e-01   1.22e+00   -0.11  0.91250
as.matrix(mset[, had])had.ACE        1.96e-01   3.13e-02    6.26  3.9e-10 ***
as.matrix(mset[, had])had.Sta        1.90e-01   3.10e-02    6.13  8.5e-10 ***
as.matrix(mset[, had])had.BBl        2.08e-02   3.46e-02    0.60  0.54800
as.matrix(mset[, had])had.ARB        2.86e-01   3.27e-02    8.74  < 2e-16 ***
as.matrix(mset[, had])had.AlA        3.55e-02   6.37e-02    0.56  0.57687
as.matrix(mset[, had])had.DHP        3.38e-03   3.08e-02    0.11  0.91253
as.matrix(mset[, had])had.WtL        8.78e-01   1.74e-01    5.05  4.5e-07 ***
as.matrix(mset[, had])had.RPA       -1.35e-01   6.12e-02   -2.21  0.02736 *
as.matrix(mset[, had])had.Wrf       -1.62e-01   7.97e-02   -2.04  0.04164 *
as.matrix(mset[, had])had.Asp        9.37e-02   3.20e-02    2.92  0.00346 **
as.matrix(mset[, had])had.HCD       -3.80e-01   4.42e-02   -8.60  < 2e-16 ***
as.matrix(mset[, had])had.THZ        7.31e-02   3.76e-02    1.94  0.05201 .
as.matrix(mset[, had])had.Ccs       -8.56e-02   5.78e-02   -1.48  0.13909
as.matrix(mset[, had])had.DXI       -1.82e-01   1.12e-01   -1.63  0.10226
as.matrix(mset[, had])had.Dgo       -1.30e-01   9.57e-02   -1.36  0.17406
as.matrix(mset[, had])had.APl       -3.24e-02   1.26e-01   -0.26  0.79641
as.matrix(mset[, had])had.Ami       -7.29e-01   2.45e-01   -2.97  0.00296 **
as.matrix(mset[, had])had.DTI        1.30e-01   1.25e-01    1.04  0.29979
as.matrix(mset[, had])had.NHP        2.29e-01   1.05e-01    2.17  0.02981 *
as.matrix(mset[, had])had.Fla       -6.11e-01   4.41e-01   -1.38  0.16609
as.matrix(mset[, had])had.Metformin -1.26e+00   3.72e-02  -33.94  < 2e-16 ***
as.matrix(mset[, had])had.GLP1       2.56e+00   3.72e-02   68.77  < 2e-16 ***
as.matrix(mset[, had])had.longIns    9.45e-01   4.68e-02   20.20  < 2e-16 ***
as.matrix(mset[, had])had.mixIns     6.00e-01   6.04e-02    9.94  < 2e-16 ***
as.matrix(mset[, had])had.SU         2.82e-02   3.23e-02    0.87  0.38287
as.matrix(mset[, had])had.intIns     4.72e-01   6.04e-02    7.81  5.7e-15 ***
as.matrix(mset[, had])had.fastIns    1.28e-01   6.70e-02    1.91  0.05605 .
as.matrix(mset[, had])had.TZD        6.36e-01   2.67e-01    2.38  0.01721 *
as.matrix(mset[, had])had.Acarbose   3.03e-01   3.30e-01    0.92  0.35811
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 52445  on 48139  degrees of freedom
Residual deviance: 38085  on 48078  degrees of freedom
AIC: 38209

Number of Fisher Scoring iterations: 6
```

With this fitted model we can now use the fitted values as propensity scores.

2.4 Propensity score matching

Based on this propensity score we take a matched sample of 1 per SGLT-2 user — note that we explicitly set a seed in order to get a fully reproducible code:

```
> set.seed( 1952 )
> system.time(
+ mt <- Match( Tr = (mset$Ixdr=="SGLT2"),
+               X = fitted( pr.0 ),
+               M = 1,
+         replace = FALSE,
```

```
+           exact = FALSE,
+            ties = FALSE,
+         caliper = 0.2 ) )
   user  system elapsed
  26.74    1.15   27.89
```

```
> str( mt )
```

```
List of 23
 $ est                 : num [1, 1] 0
 $ se                  : NULL
 $ est.noadj           : num 0
 $ se.standard         : num 0
 $ se.cond             : NULL
 $ mdata               :List of 4
  ..$ Y                           : num [1:15774] 0 0 0 0 0 0 0 0 0 0 ...
  ..$ Tr                          : num [1:15774] 1 1 1 1 1 1 1 1 1 1 ...
  ..$ X                           : num [1:2, 1:7887] 0.872 0.872 0.813 0.813 0.957 ...
  .. ..- attr(*, "dimnames")=List of 2
  .. .. ..$ : NULL
  .. .. ..$ : chr [1:7887] "5" "7" "16" "19" ...
  ..$ orig.weighted.treated.nobs: num 11291
 $ index.treated       : num [1:7887] 2 4 6 7 14 17 19 20 24 25 ...
 $ index.control       : num [1:7887] 3883 25566 639 8785 14347 ...
 $ index.dropped       : int [1:3404] 5303 5653 5839 5877 5967 6167 6343 6355 6358 6445 ...
 $ weights             : num [1:7887] 1 1 1 1 1 1 1 1 1 1 ...
 $ orig.nobs           : int 48140
 $ orig.wnobs          : num 48140
 $ orig.treated.nobs: int 11291
 $ nobs                : int 48140
 $ wnobs               : num 7887
 $ caliper             : num 0.2
 $ ecaliper            : num 0.0477
 $ exact               : logi FALSE
 $ ndrops              : num 3404
 $ ndrops.matches      : num 3404
 $ MatchLoopC          : num [1:7887, 1:6] 2 4 6 7 14 17 19 20 24 25 ...
 $ version             : chr "fast"
 $ estimand            : chr "ATT"
 - attr(*, "class")= chr "Match"
```

The resulting matching (`index.`-variables) refers to rows in `mset`:

```
> addmargins( rbind(
+ table( mset$Ixdr[unique(mt$index.treated)] ),
+ table( mset$Ixdr[unique(mt$index.control)] ) ), 2 )
     DPP4 SGLT2  Sum
[1,]    0  7887 7887
[2,] 7887     0 7887
```

We just use the index numbers for the treated as factor levels for the match-factor (we shall not use the factor though):

```
> tnum <- mt$index.treated
> cnum <- mt$index.control
> # a numeric with the index number of SGLT-2 for persons matched up
> mf <- rep( NA, nrow(mset) )
> mf[tnum] <- tnum
```

../rep/matchSGDP.tex

```
> mf[cnum] <- tnum
> # create a factor of this and tabulate
> mset <- transform( mset, mfac = factor(mf),
+                          psco = fitted(pr.0) )
> ( mtab <- with( mset, table( Ixdr, !is.na(mfac), useNA="ifany" ) ) )
Ixdr    FALSE  TRUE
  DPP4  28962  7887
  SGLT2  3404  7887
```

```
> round( cbind( rbind( cbind( mtab,
+                             pctab( mtab ) ),
+                      NA,
+                      NA),
+               pctab( mtab, margin=1 ) )[-3,], 1 )
Ixdr      FALSE    TRUE     All       N
  DPP4     78.6    21.4   100.0 36849.0
  SGLT2    30.1    69.9   100.0 11291.0

Ixdr      FALSE    TRUE
  DPP4     89.5    50.0
  SGLT2    10.5    50.0
  All     100.0   100.0
  N     32366.0 15774.0
      FALSE TRUE FALSE TRUE All     N   FALSE  TRUE
DPP4  28962 7887  78.6 21.4 100 36849    89.5    50
SGLT2  3404 7887  30.1 69.9 100 11291    10.5    50
         NA   NA    NA   NA  NA    NA 32366.0 15774
```

We can see that not all persons can be matched with a caliper of 0.2; we can compare the propensity score among the matched and non-matched SGLT-2 patients:

```
> par( mar=c(3,3,1,1),mgp=c(3,1,0)/1.6,las=1,bty="n" )
> plot( mset$psco[mt$index.treated],
+       mset$psco[mt$index.control],
+       pch=16, cex=0.3 ,
+       xlim=0:1, xlab="SGLT-2i propensity score",
+       ylim=0:1, ylab="DPP-4 propensity score" )
```

For the use in further analyses we save a version for later use:

```
> oset <- mset
> pscore <- table( floor( oset$psco*100 ), oset$Ixdr )
```

Finally we make a dataset restricted to the matched persons:

```
> mset <- subset( oset, !is.na(mfac) )
> psmatch <- table( floor( mset$psco*100 ), mset$Ixdr )
> head( pscore )
   DPP4 SGLT2
  0  468     5
  1  779    13
  2 1289    41
  3 1860    71
  4 2146   117
  5 2186   131
```

```
> head( psmatch )
```

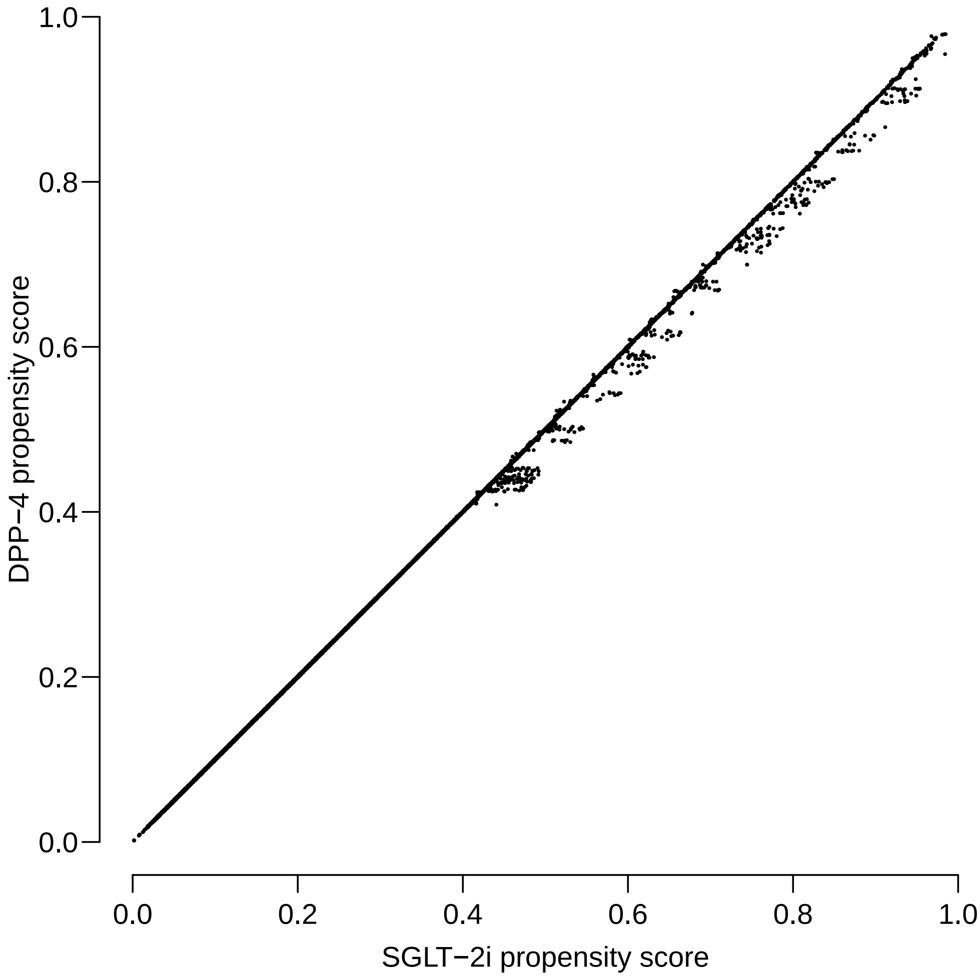

Figure 2.1: *Propensity scores from 1:1 matching; each matched set is represented by a dots.* `./matchSGDP-cmp-ps`

```
   DPP4 SGLT2
 0    5     5
 1   13    13
 2   40    41
 3   74    71
 4  117   117
 5  128   131
> save( oset, mset, pscore, psmatch, file = "adatSGDP.Rda" )
> load( file = "adatSGDP.Rda" )
```

We also make histograms of the propensity scores, both for the original data and for the matched persons

```
> tt <- pscore
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
> head(tt)
                    DPP4      SGLT2
0 -12.70048 12.70048  0.4428306
```

```
1 -21.14033 21.14033  1.1513595
2 -34.98060 34.98060  3.6312107
3 -50.47627 50.47627  6.2881941
4 -58.23767 58.23767 10.3622354
5 -59.32318 59.32318 11.6021610
```

```
> nam <- colnames( tt )[-1]
> clr <- c("transparent","red","blue")
> # we use the undocumented feature of boxplot that you can get stacked
> # bars starting in the negative by giving negative numbers to the first
> # column. But it will mysteriously ignore the first element of col...
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-65,65),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=0 )
```

```
> tt <- psmatch
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-65,65),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=10 )
```

2.5 Baseline tables for propensity matched persons

We have the matched sets in the dataframe `mset`, so we can almost verbatim reuse the code doing the tables for the original sample, except for the names of the resulting tables: `dm.tab` (demographics for matched sample), `cm.tab` (comobidites for matched sample) and `mm.tab` (medication for matched sample).

2.5.1 Demographics

First the tabulations of the baseline demographics:

```
> t.sex <- with( mset, ptab( sex ) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
```

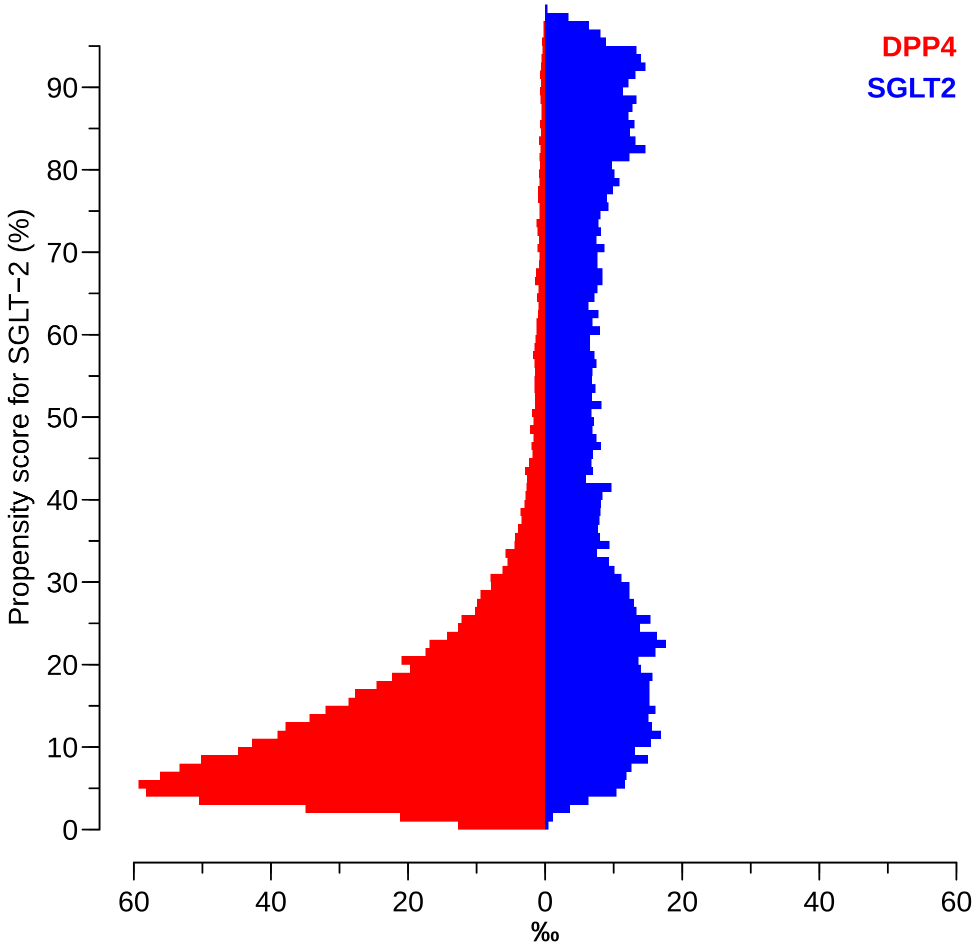

Figure 2.2: *Propensity scores for the SGLT-2 group (left, percent) and other groups (right, %■) in the 1:3 propensity score matched study.* ./matchSGDP-pscoreo

```
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0

                   DPP4 SGLT2 DPP4 SGLT2
Index = First Line  157   151    2   1.9
> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                      tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0

                        [,1] [,2] [,3] [,4]
Index not FL: Mean / SD  8.4  8.3  5.6  5.3
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
+                                tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age

               [,1] [,2] [,3] [,4]
Age: Mean / SD   61 61.1 12.9 11.1
```

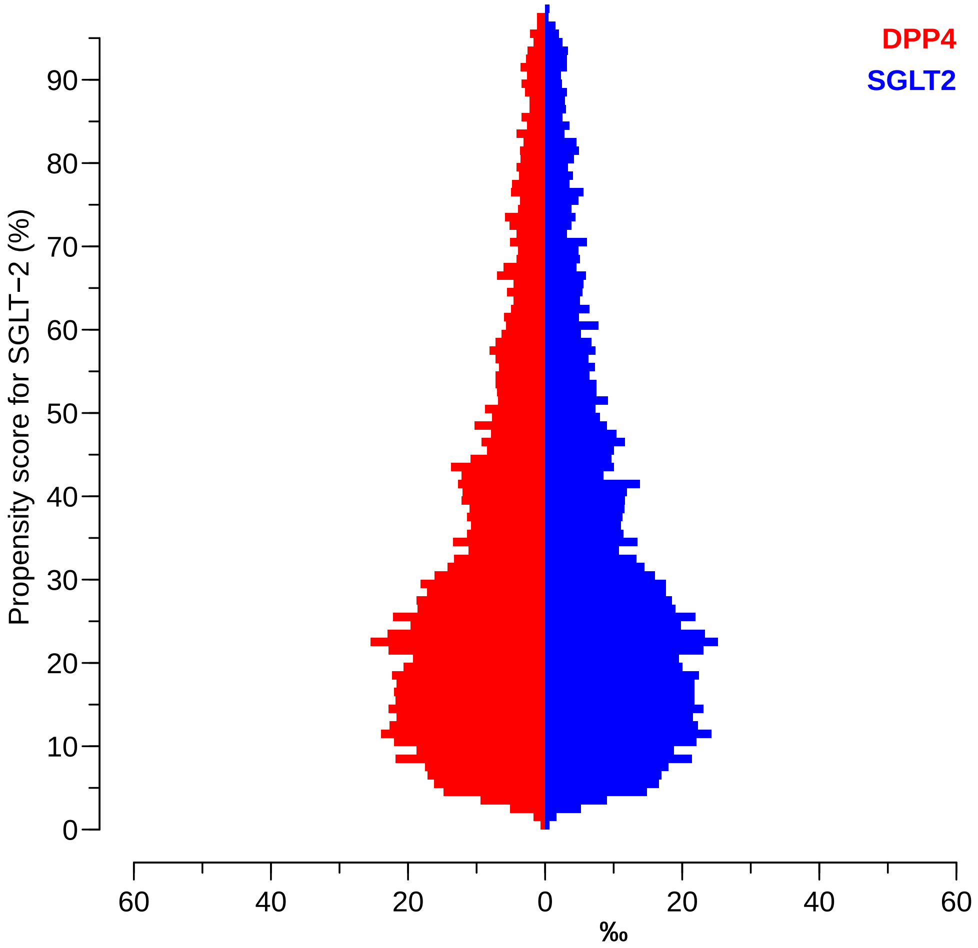

Figure 2.3: *Propensity scores for the SGLT-2 group (left, percent) and other groups in the 1:1 propensity score matched study.* `./matchSGDP-pscorem`

```
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )

       DPP4 SGLT2 DPP4 SGLT2
2012.5   64    15  0.8   0.2
2013    505   556  6.4   7.0
2013.5  592   637  7.5   8.1
2014    787   720 10.0   9.1
2014.5  712   794  9.0  10.1
2015   1055   993 13.4  12.6
2015.5 1124   988 14.3  12.5
2016   1499  1659 19.0  21.0
2016.5 1549  1525 19.6  19.3
```

```
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
```

```
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dm.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dm.tab
                          DPP4  SGLT2 DPP4 SGLT2
Sex M                   4795.0 4818.0 60.8  61.1
F                       3092.0 3069.0 39.2  38.9
Index = First Line       157.0  151.0  2.0   1.9
Index not FL: Mean / SD    8.4    8.3  5.6   5.3
Age at index <40         442.0  257.0  5.6   3.3
40                      1147.0 1010.0 14.5  12.8
50                      2021.0 2198.0 25.6  27.9
60                      2233.0 2674.0 28.3  33.9
70                      1558.0 1518.0 19.8  19.2
80+                      486.0  230.0  6.2   2.9
Age: Mean / SD            61.0   61.1 12.9  11.1
Index date 2012           64.0   15.0  0.8   0.2
2013                    1097.0 1193.0 13.9  15.1
2014                    1499.0 1514.0 19.0  19.2
2015                    2179.0 1981.0 27.6  25.1
2016                    3048.0 3184.0 38.6  40.4
Date of first line 1995  410.0  307.0  5.2   3.9
1996                     153.0  111.0  1.9   1.4
1997                     144.0  130.0  1.8   1.6
1998                     184.0  161.0  2.3   2.0
1999                     198.0  240.0  2.5   3.0
2000                     250.0  248.0  3.2   3.1
2001                     259.0  251.0  3.3   3.2
2002                     297.0  299.0  3.8   3.8
2003                     368.0  369.0  4.7   4.7
2004                     363.0  403.0  4.6   5.1
2005                     408.0  435.0  5.2   5.5
2006                     400.0  511.0  5.1   6.5
2007                     450.0  520.0  5.7   6.6
2008                     533.0  547.0  6.8   6.9
2009                     495.0  585.0  6.3   7.4
2010                     567.0  575.0  7.2   7.3
2011                     573.0  526.0  7.3   6.7
2012                     463.0  404.0  5.9   5.1
2013                     380.0  343.0  4.8   4.3
2014                     367.0  325.0  4.7   4.1
2015                     375.0  323.0  4.8   4.1
2016                     250.0  274.0  3.2   3.5
Frailty 0               5482.0 5474.0 69.5  69.4
1                       2405.0 2413.0 30.5  30.6
```

2.5.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- match( rownames(ct.tab), names( mset ) )
> names( mset )[wh]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"    
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye" 
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
```

```
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"    "pre.CVD"     "pre.Str"     "pre.FPA"
[31] "pre.Mic"
```

```
> comorb <- mset[,wh]
> cm.tab <- cbind(
+ t( sapply( comorb,
+           function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( comorb,
+           function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> cm.tab
```

```
            DPP4 SGLT2 DPP4 SGLT2
prv.FL      7730  7736 98.0  98.1
prv.TIA      220   222  2.8   2.8
prv.Angina  1046  1061 13.3  13.5
prv.Bleed    367   369  4.7   4.7
prv.COPD     269   285  3.4   3.6
prv.PAD      431   413  5.5   5.2
prv.HF       351   364  4.5   4.6
prv.Cancer   448   443  5.7   5.6
prv.DMcompl 1259  1218 16.0  15.4
prv.Neuro    405   395  5.1   5.0
prv.DKD      320   292  4.1   3.7
prv.DiaEye   916   893 11.6  11.3
prv.Hypo     260   268  3.3   3.4
prv.AtrFib   475   486  6.0   6.2
prv.MI       647   655  8.2   8.3
prv.UnstAng 279   285  3.5   3.6
prv.HmStr     62    67  0.8   0.8
prv.DiaFoot   65    62  0.8   0.8
prv.Other    388   379  4.9   4.8
prv.PeriAng  363   378  4.6   4.8
prv.IscStr   394   399  5.0   5.1
prv.Amp        8     7  0.1   0.1
prv.CKD       66    55  0.8   0.7
prv.PCIsten   74    63  0.9   0.8
prv.CABG     211   225  2.7   2.9
prv.Keto      42    37  0.5   0.5
prv.Dial       1     1  0.0   0.0
pre.CVD     2378  2419 30.2  30.7
pre.Str      606   596  7.7   7.6
pre.FPA      410   417  5.2   5.3
pre.Mic     2283  2385 28.9  30.2
```

2.5.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest — well, only in the period after 2011-12-01, one year prior to the first SGLT2 dispensation.

```
> wh <- grep( "had.", names( mset ) )
> names( mset )[wh]
```

```
 [1] "had.ACE"    "had.Sta"    "had.BBl"    "had.ARB"    "had.AlA"
 [6] "had.DHP"    "had.WtL"    "had.RPA"    "had.Wrf"    "had.Asp"
[11] "had.HCD"    "had.THZ"    "had.Ccs"    "had.DXI"    "had.Dgo"
[16] "had.APl"    "had.Ami"    "had.DTI"    "had.NHP"    "had.Fla"
```

```
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"
```

```
> codisp <- mset[,wh]
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )
```

```
[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"
```

```
> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )
```

```
[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> ( names( codisp )[wh.cvd <- c(8,2,wh.hyp)] )
```

```
[1] "had.RPA" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
```

```
> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )
```

```
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"
```

```
> mm.tab <- cbind(
+ t( sapply( codisp,
+             function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+             function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mm.tab
```

```
              DPP4 SGLT2 DPP4 SGLT2
had.ACE       2942  3034 37.3  38.5
had.Sta       5641  5716 71.5  72.5
had.BBl       2159  2178 27.4  27.6
had.ARB       2624  2613 33.3  33.1
had.AlA        424   428  5.4   5.4
had.DHP       2378  2405 30.2  30.5
had.WtL         57    51  0.7   0.6
had.RPA        527   520  6.7   6.6
had.Wrf        353   353  4.5   4.5
had.Asp       2706  2722 34.3  34.5
had.HCD       1150  1116 14.6  14.1
had.THZ       1161  1146 14.7  14.5
had.Ccs        424   434  5.4   5.5
had.DXI        110   130  1.4   1.6
had.Dgo        218   211  2.8   2.7
had.APl         94   101  1.2   1.3
had.Ami         26    23  0.3   0.3
had.DTI         84    97  1.1   1.2
had.NHP        146   132  1.9   1.7
had.Fla          4     8  0.1   0.1
had.Metformin 6181  6267 78.4  79.5
had.GLP1      1477  1516 18.7  19.2
had.MetxSGLT2    0   536  0.0   6.8
had.MetxDPP4  3029  1349 38.4  17.1
```

```
had.SGLT2         0  7352  0.0  93.2
had.longIns    1121  1113 14.2  14.1
had.mixIns      533   539  6.8   6.8
had.DPP4       4857     0 61.6   0.0
had.SU         1980  1907 25.1  24.2
had.intIns      493   483  6.3   6.1
had.fastIns     490   467  6.2   5.9
had.TZD          18    22  0.2   0.3
had.Acarbose     15    13  0.2   0.2
had.TZDxDPP4      3     0  0.0   0.0
got.Ins        1896  1954 24.0  24.8
got.Hyp        5956  6097 75.5  77.3
got.CVD        6930  7055 87.9  89.5
```

2.6 Overview of pre- and post matching

The number of persons and episodes:

```
> addmargins( with( oset, table(table(pnr)) ) )
    1   Sum
48140 48140
> addmargins(
+ with( oset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4      0     1   Sum
  0       0 11291 11291
  1   36849     0 36849
  Sum 36849 11291 48140
> addmargins( with( mset, table(table(pnr)) ) )
    1   Sum
15774 15774
> addmargins(
+ with( mset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4      0     1   Sum
  0       0  7887  7887
  1    7887     0  7887
  Sum  7887  7887 15774
```

The best overview is created if we list the tables for the matched and un-matched next to each other. However we first check that that have the same sets of rows:

```
> identical( rownames(dt.tab), rownames(dm.tab) )
[1] TRUE
> identical( rownames(ct.tab), rownames(cm.tab) )
[1] TRUE
> identical( rownames(mt.tab), rownames(mm.tab) )
[1] TRUE
```

```
> cbind( dt.tab, dm.tab )
```

```
                           DPP4  SGLT2 DPP4 SGLT2   DPP4  SGLT2 DPP4 SGLT2
Sex M                   22246.0 6904.0 60.4  61.1 4795.0 4818.0 60.8  61.1
F                       14603.0 4387.0 39.6  38.9 3092.0 3069.0 39.2  38.9
Index = First Line       1383.0  152.0  3.8   1.3  157.0  151.0  2.0   1.9
Index not FL: Mean / SD     6.9    9.2  5.2   5.4    8.4    8.3  5.6   5.3
Age at index <40         1147.0  431.0  3.1   3.8  442.0  257.0  5.6   3.3
40                       3772.0 1555.0 10.2  13.8 1147.0 1010.0 14.5  12.8
50                       7959.0 3405.0 21.6  30.2 2021.0 2198.0 25.6  27.9
60                      10916.0 3760.0 29.6  33.3 2233.0 2674.0 28.3  33.9
70                       9037.0 1892.0 24.5  16.8 1558.0 1518.0 19.8  19.2
80+                      4018.0  248.0 10.9   2.2  486.0  230.0  6.2   2.9
Age: Mean / SD             64.6   60.1 12.6  10.9   61.0   61.1 12.9  11.1
Index date 2012           673.0   18.0  1.8   0.2   64.0   15.0  0.8   0.2
2013                     8684.0 1494.0 23.6  13.2 1097.0 1193.0 13.9  15.1
2014                     8897.0 2091.0 24.1  18.5 1499.0 1514.0 19.0  19.2
2015                     9392.0 2931.0 25.5  26.0 2179.0 1981.0 27.6  25.1
2016                     9203.0 4757.0 25.0  42.1 3048.0 3184.0 38.6  40.4
Date of first line 1995  1200.0  560.0  3.3   5.0  410.0  307.0  5.2   3.9
1996                      457.0  202.0  1.2   1.8  153.0  111.0  1.9   1.4
1997                      491.0  226.0  1.3   2.0  144.0  130.0  1.8   1.6
1998                      633.0  288.0  1.7   2.6  184.0  161.0  2.3   2.0
1999                      716.0  384.0  1.9   3.4  198.0  240.0  2.5   3.0
2000                      812.0  411.0  2.2   3.6  250.0  248.0  3.2   3.1
2001                      952.0  449.0  2.6   4.0  259.0  251.0  3.3   3.2
2002                     1129.0  499.0  3.1   4.4  297.0  299.0  3.8   3.8
2003                     1447.0  612.0  3.9   5.4  368.0  369.0  4.7   4.7
2004                     1512.0  634.0  4.1   5.6  363.0  403.0  4.6   5.1
2005                     1717.0  688.0  4.7   6.1  408.0  435.0  5.2   5.5
2006                     1862.0  731.0  5.1   6.5  400.0  511.0  5.1   6.5
2007                     2082.0  760.0  5.7   6.7  450.0  520.0  5.7   6.6
2008                     2509.0  780.0  6.8   6.9  533.0  547.0  6.8   6.9
2009                     2551.0  816.0  6.9   7.2  495.0  585.0  6.3   7.4
2010                     2942.0  760.0  8.0   6.7  567.0  575.0  7.2   7.3
2011                     3090.0  660.0  8.4   5.8  573.0  526.0  7.3   6.7
2012                     2897.0  461.0  7.9   4.1  463.0  404.0  5.9   5.1
2013                     2698.0  384.0  7.3   3.4  380.0  343.0  4.8   4.3
2014                     2181.0  357.0  5.9   3.2  367.0  325.0  4.7   4.1
2015                     1922.0  344.0  5.2   3.0  375.0  323.0  4.8   4.1
2016                     1049.0  285.0  2.8   2.5  250.0  274.0  3.2   3.5
Frailty 0               25973.0 7459.0 70.5  66.1 5482.0 5474.0 69.5  69.4
1                       10876.0 3832.0 29.5  33.9 2405.0 2413.0 30.5  30.6
> cbind( ct.tab, cm.tab )
             DPP4 SGLT2 DPP4 SGLT2 DPP4 SGLT2 DPP4 SGLT2
prv.FL      35466 11139 96.2  98.7 7730  7736 98.0  98.1
prv.TIA      1254   301  3.4   2.7  220   222  2.8   2.8
prv.Angina   4864  1574 13.2  13.9 1046  1061 13.3  13.5
prv.Bleed    1827   493  5.0   4.4  367   369  4.7   4.7
prv.COPD     1841   386  5.0   3.4  269   285  3.4   3.6
prv.PAD      2311   562  6.3   5.0  431   413  5.5   5.2
prv.HF       2080   475  5.6   4.2  351   364  4.5   4.6
prv.Cancer   2648   558  7.2   4.9  448   443  5.7   5.6
prv.DMcompl  3563  2307  9.7  20.4 1259  1218 16.0  15.4
prv.Neuro    1278   724  3.5   6.4  405   395  5.1   5.0
prv.DKD      1383   445  3.8   3.9  320   292  4.1   3.7
prv.DiaEye   2798  1569  7.6  13.9  916   893 11.6  11.3
prv.Hypo     1040   425  2.8   3.8  260   268  3.3   3.4
prv.AtrFib   3134   677  8.5   6.0  475   486  6.0   6.2
```

```
prv.MI       3253   956  8.8   8.5  647   655  8.2   8.3
prv.UnstAng  1403   440  3.8   3.9  279   285  3.5   3.6
prv.HmStr     411    85  1.1   0.8   62    67  0.8   0.8
prv.DiaFoot   285   112  0.8   1.0   65    62  0.8   0.8
prv.Other    1855   533  5.0   4.7  388   379  4.9   4.8
prv.PeriAng  1266   637  3.4   5.6  363   378  4.6   4.8
prv.IscStr   2443   535  6.6   4.7  394   399  5.0   5.1
prv.Amp        58    13  0.2   0.1    8     7  0.1   0.1
prv.CKD      1131    56  3.1   0.5   66    55  0.8   0.7
prv.PCIsten   383   105  1.0   0.9   74    63  0.9   0.8
prv.CABG     1128   314  3.1   2.8  211   225  2.7   2.9
prv.Keto      155    67  0.4   0.6   42    37  0.5   0.5
prv.Dial        9     1  0.0   0.0    1     1  0.0   0.0
pre.CVD     12424  3445 33.7  30.5 2378  2419 30.2  30.7
pre.Str      3551   802  9.6   7.1  606   596  7.7   7.6
pre.FPA      1470   703  4.0   6.2  410   417  5.2   5.3
pre.Mic      7800  4132 21.2  36.6 2283  2385 28.9  30.2

> cbind( mt.tab, mm.tab )

               DPP4 SGLT2 DPP4 SGLT2 DPP4 SGLT2 DPP4 SGLT2
had.ACE       13775  4463 37.4  39.5 2942  3034 37.3  38.5
had.Sta       25543  8459 69.3  74.9 5641  5716 71.5  72.5
had.BBl       10977  3124 29.8  27.7 2159  2178 27.4  27.6
had.ARB       10731  3954 29.1  35.0 2624  2613 33.3  33.1
had.AlA        2169   607  5.9   5.4  424   428  5.4   5.4
had.DHP       11043  3529 30.0  31.3 2378  2405 30.2  30.5
had.WtL         109    91  0.3   0.8   57    51  0.7   0.6
had.RPA        2664   716  7.2   6.3  527   520  6.7   6.6
had.Wrf        2498   460  6.8   4.1  353   353  4.5   4.5
had.Asp       12479  4159 33.9  36.8 2706  2722 34.3  34.5
had.HCD        6956  1577 18.9  14.0 1150  1116 14.6  14.1
had.THZ        5651  1735 15.3  15.4 1161  1146 14.7  14.5
had.Ccs        2803   569  7.6   5.0  424   434  5.4   5.5
had.DXI         754   174  2.0   1.5  110   130  1.4   1.6
had.Dgo        1723   277  4.7   2.5  218   211  2.8   2.7
had.APl         645   121  1.8   1.1   94   101  1.2   1.3
had.Ami         240    27  0.7   0.2   26    23  0.3   0.3
had.DTI         592   139  1.6   1.2   84    97  1.1   1.2
had.NHP         620   197  1.7   1.7  146   132  1.9   1.7
had.Fla          48     9  0.1   0.1    4     8  0.1   0.1
had.Metformin 32241  9074 87.5  80.4 6181  6267 78.4  79.5
had.GLP1       1567  4516  4.3  40.0 1477  1516 18.7  19.2
had.MetxSGLT2     0   693  0.0   6.1    0   536  0.0   6.8
had.MetxDPP4  14134  1601 38.4  14.2 3029  1349 38.4  17.1
had.SGLT2         0 10599  0.0  93.9    0  7352  0.0  93.2
had.longIns    1934  2438  5.2  21.6 1121  1113 14.2  14.1
had.mixIns     1109   994  3.0   8.8  533   539  6.8   6.8
had.DPP4      22733     0 61.7   0.0 4857     0 61.6   0.0
had.SU         9683  2622 26.3  23.2 1980  1907 25.1  24.2
had.intIns     1207   890  3.3   7.9  493   483  6.3   6.1
had.fastIns    1002   979  2.7   8.7  490   467  6.2   5.9
had.TZD          54    44  0.1   0.4   18    22  0.2   0.3
had.Acarbose     53    19  0.1   0.2   15    13  0.2   0.2
had.TZDxDPP4      5     0  0.0   0.0    3     0  0.0   0.0
got.Ins        4009  3859 10.9  34.2 1896  1954 24.0  24.8
got.Hyp       27580  8930 74.8  79.1 5956  6097 75.5  77.3
got.CVD       32539 10313 88.3  91.3 6930  7055 87.9  89.5
```

```
> save( dt.tab, dm.tab,
+       ct.tab, cm.tab,
+       mt.tab, mm.tab, file="btabSGDP.Rda" )
```

2.7 Survival analysis datasets: Lexis objects

In this section we take the original and the matched data and set up `Lexis`-objects for the survival analyses; we make separate objects for Death, heart failure (HF) and combined outcomes.

First get the relevant data:

```
> library( Epi )
> library( survival )
> print( sessionInfo(), l=F )
R version 3.4.1 (2017-06-30)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] survival_2.41-3 Epi_2.26

loaded via a namespace (and not attached):
 [1] cmprsk_2.2-7      zoo_1.8-0         MASS_7.3-47       compiler_3.4.1
 [5] Matrix_1.2-11     plyr_1.8.4        parallel_3.4.1    tools_3.4.1
 [9] etm_0.6-2         Rcpp_0.12.12      splines_3.4.1     grid_3.4.1
[13] numDeriv_2016.8-1 lattice_0.20-35
> clear()
> load( file = "adatSGDP.Rda" )
> lls()
  name    mode    class      dim            size(Kb)
1 mset    list    data.frame 15774 170      22,785.3
2 oset    list    data.frame 48140 170      68,613.9
3 pscore  numeric table      100 2               7.2
4 psmatch numeric table      99 2                7.1
```

We will follow persons from date of new use, `doIx`, till either date of event.

For later use we define both the time since index (`tfi`) and current date (period — `per`) and current age (`cua`) as timescales. The latter not to be confused with age at index date, `age`.

2.8 Collecting analysis results and key data

We want to collect analysis results and background data for the analyses. The latter are classified by index drug and PY/events, the former by adjusted/non-adjusted analysis and HR/c.i./s.e. In addition both are classified by endpoint, data, and subset:

```
                                            ...now input from ../rep/anaSGDP.tex
> lst <- list( endp = c("HF","ACD","ACD+HF","CVDD","MI","Str","IscStr",
+                       "CVDD+MI+Str","ACD+MI+Str","DKD"),
+              data = c("OnDr","Total"),
+               sub = c("AllPtt","preCVD","noCVD") )
> dat <- NArray( c( lst, list( ix = c("SGLT2","DPP4"),
+                             dat = c("N","PY","Event") ) ) )
> res <- NArray( c( lst, list( adj = c("Raw","Adj"),
+                              res = c("HR","lo","up","se") ) ) )
> length( dat ) ; str( dat )
[1] 360

 logi [1:10, 1:2, 1:3, 1:2, 1:3] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "DPP4"
  ..$ dat : chr [1:3] "N" "PY" "Event"

> length( res ) ; str( res )

[1] 480

 logi [1:10, 1:2, 1:3, 1:2, 1:4] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ adj : chr [1:2] "Raw" "Adj"
  ..$ res : chr [1:4] "HR" "lo" "up" "se"
```

2.9 Survival dataset: `Lexis` objects

Here is a definition of a function that produces a Lexis object with follow-up till `mset$doX` for the event `D`:

```
> mkLex <-
+ function( )
+    {
+ Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+        exit.status = factor( D, labels=c("OnDr","Event") ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
+ Lx <- cutLexis( Lx, cut = Lx$doTm,
+                 new.state = "OffDr",
+                       pre = "OnDr" )
+ Lx
+    }
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex( )
NOTE: entry.status has been set to "OnDr" for all.
> summary( lxHF )
```

```
Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  10873  4704   197     15774     4901   18245.92     15774
  OffDr     0  4641    63      4704       63    5824.28      4704
  Sum   10873  9345   260     20478     4964   24070.19     15774
```

2.9.1 Follow-up data and events

First we devise a function to extract the person-years and events from the Lexis object:

```
> fill.dat <-
+ function( LexDat, outc )
+ {
+ whc <- c(" Persons:","Risk time:","Event")
+ cat( outc, ":\n" )
+ print( sm <- summary( LexDat, by="Ixdr" ) )
+ s2 <- summary( LexDat, by=c("Ixdr","pre.CVD") )
+ for( ix in c("DPP4","SGLT2") )
+    {
+ dat[outc,,"AllPtt",ix,] <<- sm[[ix]][[1]][c(1,3),whc]
+ dat[outc,,"noCVD" ,ix,] <<- s2[[paste(ix,0,sep=".")]][[1]][c(1,3),whc]
+ dat[outc,,"preCVD",ix,] <<- s2[[paste(ix,1,sep=".")]][[1]][c(1,3),whc]
+    }
+ invisible(NULL)
+ }
> fill.dat( lxHF, "HF" )
HF :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5495  2268   124      7887     2392    9170.43      7887
  OffDr    0  2245    23      2268       23    2775.33      2268
  Sum   5495  4513   147     10155     2415   11945.76      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5378  2436    73      7887     2509    9075.48      7887
  OffDr    0  2396    40      2436       40    3048.95      2436
  Sum   5378  4832   113     10323     2549   12124.43      7887
> round( ftable( dat[1:2,,,,], col.vars=c(4,5) ), 1 )
                  ix     SGLT2                       DPP4
                  dat        N      PY   Event         N      PY   Event
endp data  sub
HF   OnDr  AllPtt       7887.0  9075.5    73.0    7887.0  9170.4   124.0
           preCVD       2419.0  2668.1    60.0    2378.0  2625.3   103.0
           noCVD        5468.0  6407.4    13.0    5509.0  6545.1    21.0
     Total AllPtt       7887.0 12124.4   113.0    7887.0 11945.8   147.0
           preCVD       2419.0  3520.0    87.0    2378.0  3401.4   120.0
           noCVD        5468.0  8604.4    26.0    5509.0  8544.4    27.0
```

```
ACD  OnDr  AllPtt          NA      NA      NA      NA      NA      NA
           preCVD          NA      NA      NA      NA      NA      NA
           noCVD           NA      NA      NA      NA      NA      NA
     Total AllPtt          NA      NA      NA      NA      NA      NA
           preCVD          NA      NA      NA      NA      NA      NA
           noCVD           NA      NA      NA      NA      NA      NA
```

2.9.2 Analysis

Follow-up is now analysed by Cox-models adjusted and non-adjusted, total or on drug and separately for all persons and persons with and without prior CVD. These are named with an `m.` and combination of `r/a` (raw/adjusted), `t/d` (total/on drug) and `p/n/y` (patients/no CVD/yes CVD):

```
> m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
+              I(Ixdr=="SGLT2") + cluster(pnr),
+              data = lxHF )
> m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
+                                + prv.MI + prv.HF + prv.AtrFib + frail
+                                + had.BBl + had.NHP + had.AlA + had.ACE )
> m.dpr <- update( m.tpr, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.dpa <- update( m.tpa, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.tnr <- update( m.tpr, data = subset( lxHF, pre.CVD==1 ) )
> m.tna <- update( m.tpa, data = subset( lxHF, pre.CVD==1  ) )
> m.dnr <- update( m.dpr, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.dna <- update( m.dpa, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.tyr <- update( m.tpr, data = subset( lxHF, pre.CVD==0 ) )
> m.tya <- update( m.tpa, data = subset( lxHF, pre.CVD==0  ) )
> m.dyr <- update( m.dpr, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
> m.dya <- update( m.dpa, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
```

With these models fitted we can now extract the HRs etc. and put into the right slots of `res`:

```
> get4 <- function( m ) ci.lin( m, subset="SGLT2", Exp=TRUE )[,c(5:7,2)]
> res["HF","Total","AllPtt","Raw",] <- get4( m.tpr )
> res["HF","Total","AllPtt","Adj",] <- get4( m.tpa )
> res["HF","OnDr" ,"AllPtt","Raw",] <- get4( m.dpr )
> res["HF","OnDr" ,"AllPtt","Adj",] <- get4( m.dpa )
> res["HF","Total","preCVD","Raw",] <- get4( m.tnr )
> res["HF","Total","preCVD","Adj",] <- get4( m.tna )
> res["HF","OnDr" ,"preCVD","Raw",] <- get4( m.dnr )
> res["HF","OnDr" ,"preCVD","Adj",] <- get4( m.dna )
> res["HF","Total","noCVD" ,"Raw",] <- get4( m.tyr )
> res["HF","Total","noCVD" ,"Adj",] <- get4( m.tya )
> res["HF","OnDr" ,"noCVD" ,"Raw",] <- get4( m.dyr )
> res["HF","OnDr" ,"noCVD" ,"Adj",] <- get4( m.dya )
```

This can now be packed into a function that does this for a given type of event:

```
> fill.res <- function( LexDat, outc )
+     {
+ m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
+              I(Ixdr=="SGLT2") + cluster(pnr),
+              data = LexDat )
+ m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
```

```
+                                + prv.MI + prv.HF + prv.AtrFib + frail
+                                + had.BBl + had.NHP + had.AlA + had.ACE )
+ m.dpr <- update( m.tpr, data = subset( LexDat, lex.Cst=="OnDr" ) )
+ m.dpa <- update( m.tpa, data = subset( LexDat, lex.Cst=="OnDr" ) )
+
+ m.tnr <- update( m.tpr, data = subset( LexDat, pre.CVD==1 ) )
+ m.tna <- update( m.tpa, data = subset( LexDat, pre.CVD==1  ) )
+ m.dnr <- update( m.dpr, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
+ m.dna <- update( m.dpa, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
+
+ m.tyr <- update( m.tpr, data = subset( LexDat, pre.CVD==0 ) )
+ m.tya <- update( m.tpa, data = subset( LexDat, pre.CVD==0  ) )
+ m.dyr <- update( m.dpr, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+ m.dya <- update( m.dpa, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+
+ res[outc,"Total","AllPtt","Raw",] <<- get4( m.tpr )
+ res[outc,"Total","AllPtt","Adj",] <<- get4( m.tpa )
+ res[outc,"OnDr" ,"AllPtt","Raw",] <<- get4( m.dpr )
+ res[outc,"OnDr" ,"AllPtt","Adj",] <<- get4( m.dpa )
+
+ res[outc,"Total","preCVD","Raw",] <<- get4( m.tnr )
+ res[outc,"Total","preCVD","Adj",] <<- get4( m.tna )
+ res[outc,"OnDr" ,"preCVD","Raw",] <<- get4( m.dnr )
+ res[outc,"OnDr" ,"preCVD","Adj",] <<- get4( m.dna )
+
+ res[outc,"Total","noCVD" ,"Raw",] <<- get4( m.tyr )
+ res[outc,"Total","noCVD" ,"Adj",] <<- get4( m.tya )
+ res[outc,"OnDr" ,"noCVD" ,"Raw",] <<- get4( m.dyr )
+ res[outc,"OnDr" ,"noCVD" ,"Adj",] <<- get4( m.dya )
+ invisible( NULL )
+   }
```

So combining this with the function that constructs the Lexis object we get:

```
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxHF, "HF" )
> round( ftable( res[1:2,,,,], col.vars=c(2,5) ), 3 )
                data  OnDr                   Total
                res      HR    lo    up    se    HR    lo    up    se
endp sub    adj
HF   AllPtt Raw      0.593 0.444 0.792 0.148 0.758 0.593 0.969 0.125
            Adj      0.568 0.425 0.760 0.148 0.748 0.585 0.957 0.126
     preCVD Raw      0.574 0.417 0.788 0.162 0.703 0.533 0.926 0.141
            Adj      0.556 0.405 0.762 0.161 0.704 0.536 0.923 0.139
     noCVD  Raw      0.633 0.317 1.267 0.354 0.953 0.557 1.630 0.274
            Adj      0.643 0.314 1.316 0.365 0.944 0.544 1.636 0.281
ACD  AllPtt Raw         NA    NA    NA    NA    NA    NA    NA    NA
            Adj         NA    NA    NA    NA    NA    NA    NA    NA
     preCVD Raw         NA    NA    NA    NA    NA    NA    NA    NA
            Adj         NA    NA    NA    NA    NA    NA    NA    NA
     noCVD  Raw         NA    NA    NA    NA    NA    NA    NA    NA
            Adj         NA    NA    NA    NA    NA    NA    NA    NA
```

So we just repeat this for all types of outcome:

```
> mset$D   <- with( mset, !is.na(doDth) & doDth<2017 )
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
>    lxACD <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxACD, "ACD" )
> fill.dat( lxACD, "ACD" )
ACD :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5337  2297   253      7887     2550    9269.42      7887
  OffDr    0  2218    79      2297       79    2826.14      2297
  Sum   5337  4515   332     10184     2629   12095.56      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5335  2459    93      7887     2552    9133.55      7887
  OffDr    0  2384    75      2459       75    3111.51      2459
  Sum   5335  4843   168     10346     2627   12245.06      7887

> mset$D   <- with( mset, ( !is.na(deHF) | !is.na(doDth) ) &
+                         ( deHF<2017    | doDth<2017 ) )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>   lxACDHF <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxACDHF, "ACD+HF" )
> fill.dat( lxACDHF, "ACD+HF" )
ACD+HF :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5263  2268   356      7887     2624    9170.43      7887
  OffDr    0  2176    92      2268       92    2775.33      2268
  Sum   5263  4444   448     10155     2716   11945.76      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5287  2436   164      7887     2600    9075.48      7887
  OffDr    0  2326   110      2436      110    3048.95      2436
  Sum   5287  4762   274     10323     2710   12124.43      7887

> mset$D   <- with( mset, !is.na(deCVDD) & deCVDD<2017 )
> mset$doX <- with( mset, pmin( doDth, deCVDD, 2017, na.rm=TRUE ) )
>    lxCVDD <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
```

```
> fill.res( lxCVDD, "CVDD" )
> fill.dat( lxCVDD, "CVDD" )

CVDD :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5533  2297    57      7887     2354    9269.42      7887
  OffDr    0  2281    16      2297       16    2826.14      2297
  Sum   5533  4578    73     10184     2370   12095.56      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5411  2459    17      7887     2476    9133.55      7887
  OffDr    0  2445    14      2459       14    3111.51      2459
  Sum   5411  4904    31     10346     2490   12245.06      7887

> mset$D   <- with( mset, !is.na(deMI) & deMI<2017 )
> mset$doX <- with( mset, pmin( doDth, deMI, 2017, na.rm=TRUE ) )
>     lxMI <- mkLex()

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

> fill.res( lxMI, "MI" )
> fill.dat( lxMI, "MI" )

MI :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5533  2276    78      7887     2354    9204.19      7887
  OffDr    0  2251    25      2276       25    2775.85      2276
  Sum   5533  4527   103     10163     2379   11980.04      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5388  2445    54      7887     2499    9093.07      7887
  OffDr    0  2427    18      2445       18    3084.42      2445
  Sum   5388  4872    72     10332     2517   12177.49      7887

> mset$D   <- with( mset, !is.na(deStr) & deStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deStr, 2017, na.rm=TRUE ) )
>    lxStr <- mkLex()

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

> fill.res( lxStr, "Str" )
> fill.dat( lxStr, "Str" )

Str :
$DPP4

Transitions:
```

```
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5523  2279    85      7887     2364    9203.86      7887
  OffDr    0  2267    12      2279       12    2804.17      2279
  Sum   5523  4546    97     10166     2376   12008.03      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5393  2439    55      7887     2494    9086.79      7887
  OffDr    0  2418    21      2439       21    3071.02      2439
  Sum   5393  4857    76     10326     2515   12157.81      7887
```

```
> mset$D   <- with( mset, !is.na(deIscStr) & deIscStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deIscStr, 2017, na.rm=TRUE ) )
>   lxIStr <- mkLex()
```

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

```
> fill.res( lxIStr, "IscStr" )
> fill.dat( lxIStr, "IscStr" )
```

```
IscStr :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5532  2280    75      7887     2355    9211.97      7887
  OffDr    0  2270    10      2280       10    2806.66      2280
  Sum   5532  4550    85     10167     2365   12018.63      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5394  2441    52      7887     2493    9088.84      7887
  OffDr    0  2423    18      2441       18    3074.45      2441
  Sum   5394  4864    70     10328     2511   12163.29      7887
```

```
> mset$D   <- with( mset, ( ( !is.na(deCVDD) & deCVDD < 2017 ) |
+                            ( !is.na(deMI)   & deMI   < 2017 ) |
+                            ( !is.na(deStr)  & deStr  < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deCVDD, deMI, deStr, 2017, na.rm=TRUE ) )
>  lxCVDDx <- mkLex()
```

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

```
> fill.res( lxCVDDx, "CVDD+MI+Str" )
> fill.dat( lxCVDDx, "CVDD+MI+Str" )
```

```
CVDD+MI+Str :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5426  2258   203      7887     2461    9138.64      7887
  OffDr    0  2212    46      2258       46    2754.63      2258
```

```
  Sum   5426  4470   249     10145     2507  11893.27      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5342  2425   120      7887     2545   9047.82      7887
  OffDr    0  2380    45      2425       45   3043.94      2425
  Sum   5342  4805   165     10312     2590  12091.76      7887
```

```
> mset$D   <- with( mset, ( ( !is.na(doDth) & doDth < 2017 ) |
+                           ( !is.na(deMI)  & deMI  < 2017 ) |
+                           ( !is.na(deStr) & deStr < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deMI, deStr, 2017, na.rm=TRUE ) )
>   lxACDx <- mkLex()
```

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

```
> fill.res( lxACDx, "ACD+MI+Str" )
> fill.dat( lxACDx, "ACD+MI+Str" )
```

```
ACD+MI+Str :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5246  2258   383      7887     2641   9138.64      7887
  OffDr    0  2154   104      2258      104   2754.63      2258
  Sum   5246  4412   487     10145     2745  11893.27      7887

$SGLT2

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5269  2425   193      7887     2618   9047.82      7887
  OffDr    0  2323   102      2425      102   3043.94      2425
  Sum   5269  4748   295     10312     2720  12091.76      7887
```

```
> mset$D   <- with( mset, !is.na(deDKD) & deDKD<2017 )
> mset$doX <- with( mset, pmin( doDth, deDKD, 2017, na.rm=TRUE ) )
>    lxKid <- mkLex()
```

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

```
> fill.res( lxKid, "DKD" )
> fill.dat( lxKid, "DKD" )
```

```
DKD :
$DPP4

Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5460  2238   189      7887     2427   9093.73      7887
  OffDr    0  2209    29      2238       29   2732.94      2238
  Sum   5460  4447   218     10125     2456  11826.67      7887

$SGLT2
```

```
Transitions:
     To
From    OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  5399  2433    55      7887     2488    9081.69      7887
  OffDr    0  2407    26      2433       26    3054.16      2433
  Sum   5399  4840    81     10320     2514   12135.85      7887
```

So we can summarize results:

```
> round( ftable( dat, col.vars=c(2,4,5) ), 0 )
                  data  OnDr                                Total
                  ix   SGLT2               DPP4             SGLT2               DPP4
                  dat      N     PY Event     N     PY Event     N     PY Event     N     PY Ever
endp        sub
HF          AllPtt      7887   9075    73  7887   9170   124  7887  12124   113  7887  11946    14
            preCVD      2419   2668    60  2378   2625   103  2419   3520    87  2378   3401    12
            noCVD       5468   6407    13  5509   6545    21  5468   8604    26  5509   8544     2
ACD         AllPtt      7887   9134    93  7887   9269   253  7887  12245   168  7887  12096    33
            preCVD      2419   2714    45  2378   2709   142  2419   3615    90  2378   3526    18
            noCVD       5468   6420    48  5509   6560   111  5468   8630    78  5509   8570    14
ACD+HF      AllPtt      7887   9075   164  7887   9170   356  7887  12124   274  7887  11946    44
            preCVD      2419   2668   103  2378   2625   225  2419   3520   171  2378   3401    27
            noCVD       5468   6407    61  5509   6545   131  5468   8604   103  5509   8544    17
CVDD        AllPtt      7887   9134    17  7887   9269    57  7887  12245    31  7887  12096     7
            preCVD      2419   2714    14  2378   2709    41  2419   3615    23  2378   3526     5
            noCVD       5468   6420     3  5509   6560    16  5468   8630     8  5509   8570     1
MI          AllPtt      7887   9093    54  7887   9204    78  7887  12177    72  7887  11980    10
            preCVD      2419   2692    28  2378   2659    54  2419   3579    39  2378   3440     6
            noCVD       5468   6401    26  5509   6546    24  5468   8599    33  5509   8540     3
Str         AllPtt      7887   9087    55  7887   9204    85  7887  12158    76  7887  12008     9
            preCVD      2419   2696    28  2378   2676    47  2419   3570    41  2378   3480     5
            noCVD       5468   6391    27  5509   6528    38  5468   8588    35  5509   8528     4
IscStr      AllPtt      7887   9089    52  7887   9212    75  7887  12163    70  7887  12019     8
            preCVD      2419   2696    26  2378   2680    42  2419   3574    36  2378   3484     4
            noCVD       5468   6392    26  5509   6532    33  5468   8589    34  5509   8535     3
CVDD+MI+Str AllPtt      7887   9048   120  7887   9139   203  7887  12092   165  7887  11893    24
            preCVD      2419   2674    66  2378   2625   132  2419   3534    94  2378   3395    16
            noCVD       5468   6374    54  5509   6513    71  5468   8558    71  5509   8498     8
ACD+MI+Str  AllPtt      7887   9048   193  7887   9139   383  7887  12092   295  7887  11893    48
            preCVD      2419   2674    95  2378   2625   222  2419   3534   156  2378   3395    27
            noCVD       5468   6374    98  5509   6513   161  5468   8558   139  5509   8498    20
DKD         AllPtt      7887   9082    55  7887   9094   189  7887  12136    81  7887  11827    21
            preCVD      2419   2698    21  2378   2634    83  2419   3573    33  2378   3407     9
            noCVD       5468   6384    34  5509   6460   106  5468   8563    48  5509   8420    11
> round( ftable( res, col.vars=c(2,5) ), 3 )
                        data  OnDr                        Total
                        res     HR    lo    up    se    HR    lo    up    se
endp        sub    adj
HF          AllPtt Raw       0.593 0.444 0.792 0.148 0.758 0.593 0.969 0.125
                   Adj       0.568 0.425 0.760 0.148 0.748 0.585 0.957 0.126
            preCVD Raw       0.574 0.417 0.788 0.162 0.703 0.533 0.926 0.141
                   Adj       0.556 0.405 0.762 0.161 0.704 0.536 0.923 0.139
            noCVD  Raw       0.633 0.317 1.267 0.354 0.953 0.557 1.630 0.274
                   Adj       0.643 0.314 1.316 0.365 0.944 0.544 1.636 0.281
ACD         AllPtt Raw       0.372 0.293 0.472 0.121 0.499 0.414 0.600 0.095
                   Adj       0.471 0.369 0.600 0.124 0.588 0.487 0.711 0.096
            preCVD Raw       0.314 0.224 0.439 0.171 0.471 0.366 0.606 0.128
```

```
                   Adj      0.408 0.290 0.575 0.174 0.581 0.450 0.751 0.131
            noCVD  Raw      0.442 0.315 0.620 0.173 0.531 0.403 0.698 0.140
                   Adj      0.544 0.383 0.772 0.179 0.591 0.447 0.781 0.142
ACD+HF      AllPtt Raw      0.464 0.386 0.559 0.094 0.602 0.518 0.700 0.077
                   Adj      0.528 0.438 0.638 0.096 0.669 0.575 0.779 0.078
            preCVD Raw      0.450 0.356 0.568 0.119 0.597 0.494 0.722 0.097
                   Adj      0.503 0.399 0.635 0.119 0.672 0.555 0.813 0.098
            noCVD  Raw      0.476 0.351 0.645 0.155 0.598 0.468 0.763 0.125
                   Adj      0.560 0.409 0.767 0.160 0.647 0.505 0.829 0.127
CVDD        AllPtt Raw      0.301 0.175 0.518 0.276 0.418 0.275 0.637 0.214
                   Adj      0.430 0.248 0.745 0.280 0.539 0.353 0.825 0.217
            preCVD Raw      0.336 0.183 0.617 0.310 0.412 0.253 0.672 0.249
                   Adj      0.495 0.266 0.923 0.318 0.545 0.330 0.901 0.256
            noCVD  Raw      0.191 0.056 0.654 0.628 0.415 0.182 0.945 0.420
                   Adj      0.265 0.079 0.882 0.614 0.489 0.222 1.076 0.402
MI          AllPtt Raw      0.700 0.494 0.991 0.178 0.692 0.512 0.936 0.154
                   Adj      0.738 0.522 1.044 0.177 0.723 0.535 0.977 0.153
            preCVD Raw      0.510 0.323 0.806 0.233 0.564 0.380 0.836 0.201
                   Adj      0.551 0.346 0.878 0.238 0.598 0.402 0.889 0.202
            noCVD  Raw      1.125 0.643 1.969 0.286 0.915 0.569 1.472 0.242
                   Adj      1.130 0.651 1.959 0.281 0.926 0.578 1.483 0.240
Str         AllPtt Raw      0.656 0.467 0.920 0.173 0.775 0.574 1.047 0.153
                   Adj      0.689 0.491 0.967 0.173 0.810 0.599 1.094 0.154
            preCVD Raw      0.588 0.368 0.939 0.239 0.725 0.484 1.086 0.206
                   Adj      0.626 0.388 1.008 0.243 0.770 0.510 1.162 0.210
            noCVD  Raw      0.729 0.445 1.195 0.252 0.830 0.530 1.300 0.229
                   Adj      0.743 0.453 1.219 0.252 0.835 0.533 1.308 0.229
IscStr      AllPtt Raw      0.703 0.493 1.001 0.180 0.815 0.594 1.118 0.161
                   Adj      0.737 0.518 1.049 0.180 0.849 0.619 1.166 0.162
            preCVD Raw      0.611 0.374 0.997 0.250 0.715 0.465 1.099 0.219
                   Adj      0.644 0.393 1.055 0.252 0.758 0.490 1.171 0.222
            noCVD  Raw      0.809 0.483 1.354 0.263 0.941 0.589 1.504 0.239
                   Adj      0.823 0.490 1.381 0.264 0.945 0.590 1.512 0.240
CVDD+MI+Str AllPtt Raw      0.596 0.476 0.747 0.115 0.654 0.537 0.797 0.100
                   Adj      0.643 0.513 0.806 0.115 0.697 0.573 0.849 0.100
            preCVD Raw      0.489 0.364 0.657 0.151 0.562 0.436 0.725 0.130
                   Adj      0.545 0.403 0.737 0.154 0.618 0.478 0.799 0.131
            noCVD  Raw      0.781 0.548 1.115 0.181 0.803 0.587 1.099 0.160
                   Adj      0.802 0.564 1.141 0.180 0.816 0.597 1.114 0.159
ACD+MI+Str  AllPtt Raw      0.508 0.427 0.604 0.088 0.597 0.516 0.689 0.074
                   Adj      0.576 0.484 0.686 0.089 0.658 0.569 0.761 0.074
            preCVD Raw      0.419 0.329 0.532 0.123 0.540 0.444 0.657 0.100
                   Adj      0.485 0.380 0.619 0.125 0.618 0.506 0.753 0.101
            noCVD  Raw      0.623 0.485 0.802 0.128 0.662 0.534 0.820 0.110
                   Adj      0.683 0.530 0.880 0.130 0.693 0.559 0.860 0.110
DKD         AllPtt Raw      0.291 0.216 0.393 0.153 0.363 0.281 0.468 0.130
                   Adj      0.305 0.225 0.412 0.154 0.378 0.293 0.488 0.130
            preCVD Raw      0.248 0.154 0.401 0.245 0.318 0.215 0.471 0.200
                   Adj      0.278 0.171 0.454 0.250 0.352 0.235 0.528 0.206
            noCVD  Raw      0.324 0.220 0.477 0.197 0.398 0.285 0.556 0.171
                   Adj      0.326 0.222 0.479 0.197 0.398 0.285 0.555 0.170
```

2.10 Exposure tables by drug

We can then produce an overview of the number of persons, risk time and events by index medication; to this end we define functions that uses the `by` argument of the `summary.Lexis` to classify events and follow-up by index drug in various groupings:

```
> tabFU <- ZArray( list( Ix = c("DPP4","SGLT2","Dapa","Empa","Cana"),
+                        wh = c("nPers","FU","meanfu","sdFU","maxFU") ) )
> getFU <-
+ function( lx ) c( length( unique( lx$lex.id ) ),
+                    sum( lx$lex.dur ),
+                   mean( lx$lex.dur ),
+                     sd( lx$lex.dur ),
+                    max( lx$lex.dur ) )
> mset$D   <- 0
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
> Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+        exit.status = factor( D, levels=0:1, labels=c("OnDr","Event") ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
NOTE: entry.status has been set to "OnDr" for all.
```

```
> summary( Lx, by="Ixdr" , simplify=FALSE )
$DPP4

Transitions:
     To
From    OnDr Event  Records:  Events: Risk time:  Persons:
  OnDr  7887     0      7887        0   12095.56      7887
  Event    0     0         0        0         NA        NA
  Sum   7887     0      7887        0   12095.56      7887

$SGLT2

Transitions:
     To
From    OnDr Event  Records:  Events: Risk time:  Persons:
  OnDr  7887     0      7887        0   12245.06      7887
  Event    0     0         0        0         NA        NA
  Sum   7887     0      7887        0   12245.06      7887
```

```
> tabFU["DPP4" ,] <- getFU( subset( Lx, Ixdr=="DPP4") )
> tabFU["SGLT2",] <- getFU( subset( Lx, Ixdr=="SGLT2") )
> tabFU["Dapa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD15","A10BK01") ) )
> tabFU["Cana" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD16","A10BK02") ) )
> tabFU["Empa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD20","A10BK03") ) )
> round( tabFU, 2 )
```

```
       wh
Ix       nPers       FU meanfu sdFU maxFU
  DPP4    7887 12095.56   1.53 1.11  4.08
  SGLT2   7887 12245.06   1.55 1.11  4.05
  Dapa    5094 10088.15   1.98 1.11  4.05
  Empa    2556  1839.65   0.72 0.53  2.35
  Cana     237   317.25   1.34 0.66  2.54
```

2.11 Saving it all

Fially we save all results:

```
> save( res, dat, tabFU, file = "resSGDP.Rda" )
```

2.12 Reformatting

The results are here reformatted to `Excel`-format, `xlsx`, by the `xlsx` pakage of R, so we load that concomitantly with the data.

```
> library( Epi )
> library( xlsx )
> clear()
> load( "btabSGDP.Rda" )
> load( "resSGDP.Rda" )
> lls()
  name   mode    class  dim              size(Kb)
1 cm.tab numeric matrix 31 4                  3.4
2 ct.tab numeric matrix 31 4                  3.4
3 dat    numeric array  10 2 3 2 3            5.5
4 dm.tab numeric matrix 40 4                  3.9
5 dt.tab numeric matrix 40 4                  3.9
6 mm.tab numeric matrix 37 4                  3.8
7 mt.tab numeric matrix 37 4                  3.8
8 res    numeric array  10 2 3 2 4            6.4
9 tabFU  numeric matrix 5 5                   1.7
```

With this in place we can now construct the tables wanted for the sheet in th desided order.

2.12.1 Baseline tables

In order to chack that we get the rows correct we read the rownames from the supplied spreadsheet, in ordet to put these in as a column in the new sheet for control:

```
> cat("Sample size
+ Age, years
+ Women
+ CV-history
+ Myocardial infarction
+ Unstable angina
+ Heart failure
+ Atrial fibrillation
+ Stroke
+ PAD
+ Microvascular disease
+ CKD
+ Frailty (yes)
+ Metformin
+ SU
+ TZD
+ GLP1
+ Insulin
+ Anti hypertensive therapy
```

...now input from ../rep/2xlSGDP.tex

```
+ LOOP diuretics
+ Low ceiling diuretics
+ ACE Inhibitors
+ ARBs
+ Statin therapy
+ Beta blockers
+ Aldosterone antagonists
+ Index year
+ 2012
+ 2013
+ 2014
+ 2015
+ 2016
+ 2017
+ ", file='ol.txt' )
> ol <- read.table('ol.txt',header=FALSE,sep='\t',as.is=TRUE)
```

Baseline pre-matching

We can now construct the pre-matching table

```
> bt <- rbind( "Sample size"= dt.tab[1,2:1]+dt.tab[2,2:1],
+               "Age" = NA,
+               dt.tab["F",2:1,drop=FALSE],
+               ct.tab["pre.CVD",2:1,drop=FALSE],
+               ct.tab["prv.MI",2:1,drop=FALSE],
+               ct.tab["prv.UnstAng",2:1,drop=FALSE],
+               ct.tab["prv.HF",2:1,drop=FALSE],
+               ct.tab["prv.AtrFib",2:1,drop=FALSE],
+               ct.tab["pre.Str",2:1,drop=FALSE],
+               ct.tab["prv.PAD",2:1,drop=FALSE],
+               ct.tab["pre.Mic",2:1,drop=FALSE],
+               ct.tab["prv.CKD",2:1,drop=FALSE],
+               "Frail"=dt.tab["1",2:1],
+               mt.tab["had.Metformin",2:1,drop=FALSE],
+               mt.tab["had.SU",2:1,drop=FALSE],
+               mt.tab["had.TZD",2:1,drop=FALSE],
+               mt.tab["had.GLP1",2:1,drop=FALSE],
+               mt.tab["got.Ins",2:1,drop=FALSE],
+               mt.tab["got.Hyp",2:1,drop=FALSE],
+               mt.tab["had.HCD",2:1,drop=FALSE],
+               mt.tab["had.THZ",2:1,drop=FALSE],
+               mt.tab["had.ACE",2:1,drop=FALSE],
+               mt.tab["had.ARB",2:1,drop=FALSE],
+               mt.tab["had.Sta",2:1,drop=FALSE],
+               mt.tab["had.BBl",2:1,drop=FALSE],
+               mt.tab["had.AlA",2:1,drop=FALSE],
+               "Index year"=NA,
+               dt.tab["Index date 2012",2:1,drop=FALSE],
+               dt.tab["2013",2:1,drop=FALSE],
+               dt.tab["2014",2:1,drop=FALSE],
+               dt.tab["2015",2:1,drop=FALSE],
+               dt.tab["2016",2:1,drop=FALSE],
+               '2017'=NA)
> str(ol)
```

```
'data.frame':        33 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
```

```
> bt <- cbind(bt[,1],NA,NA,bt[,2],NA,NA)
> bt["Age",c(2,3,5,6)] <- dt.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bt ) <- c("SGLT-2","mean","sd","DPP4","mean","sd")
>  cbind( ol, bt )
```

```
                                        V1 SGLT-2 mean   sd  DPP4 mean   sd
Sample size                    Sample size  11291   NA   NA 36849   NA   NA
Age                             Age, years     NA 64.6 12.6    NA 60.1 10.9
F                                    Women   4387   NA   NA 14603   NA   NA
pre.CVD                         CV-history   3445   NA   NA 12424   NA   NA
prv.MI               Myocardial infarction    956   NA   NA  3253   NA   NA
prv.UnstAng                Unstable angina    440   NA   NA  1403   NA   NA
prv.HF                       Heart failure    475   NA   NA  2080   NA   NA
prv.AtrFib             Atrial fibrillation    677   NA   NA  3134   NA   NA
pre.Str                             Stroke    802   NA   NA  3551   NA   NA
prv.PAD                                PAD    562   NA   NA  2311   NA   NA
pre.Mic              Microvascular disease   4132   NA   NA  7800   NA   NA
prv.CKD                                CKD     56   NA   NA  1131   NA   NA
Frail                        Frailty (yes)   3832   NA   NA 10876   NA   NA
had.Metformin                    Metformin   9074   NA   NA 32241   NA   NA
had.SU                                  SU   2622   NA   NA  9683   NA   NA
had.TZD                               TZD      44   NA   NA    54   NA   NA
had.GLP1                             GLP1    4516   NA   NA  1567   NA   NA
got.Ins                           Insulin    3859   NA   NA  4009   NA   NA
got.Hyp         Anti hypertensive therapy    8930   NA   NA 27580   NA   NA
had.HCD                    LOOP diuretics    1577   NA   NA  6956   NA   NA
had.THZ              Low ceiling diuretics   1735   NA   NA  5651   NA   NA
had.ACE                     ACE Inhibitors   4463   NA   NA 13775   NA   NA
had.ARB                               ARBs   3954   NA   NA 10731   NA   NA
had.Sta                     Statin therapy   8459   NA   NA 25543   NA   NA
had.BBl                      Beta blockers   3124   NA   NA 10977   NA   NA
had.AlA            Aldosterone antagonists    607   NA   NA  2169   NA   NA
Index year                      Index year     NA   NA   NA    NA   NA   NA
Index date 2012                       2012     18   NA   NA   673   NA   NA
2013                                  2013   1494   NA   NA  8684   NA   NA
2014                                  2014   2091   NA   NA  8897   NA   NA
2015                                  2015   2931   NA   NA  9392   NA   NA
2016                                  2016   4757   NA   NA  9203   NA   NA
2017                                  2017     NA   NA   NA    NA   NA   NA
```

```
> write.xlsx( cbind( 'Org. labs'=ol, bt ),
+             "SGDP.xlsx",
+ sheetName = "Baseline pre-matching",
+    append = FALSE,
+    showNA = FALSE )
```

Baseline after matching

The data for post matching have exactly the same structure; the tables are just called '`m.tab`' instad of '`t.tab`':

`../rep/2xlSGDP.tex`

```
> bm <- rbind( "Sample size"= dm.tab[1,2:1]+dm.tab[2,2:1],
+               "Age" = NA,
+               dm.tab["F",2:1,drop=FALSE],
+               cm.tab["pre.CVD",2:1,drop=FALSE],
+               cm.tab["prv.MI",2:1,drop=FALSE],
+               cm.tab["prv.UnstAng",2:1,drop=FALSE],
+               cm.tab["prv.HF",2:1,drop=FALSE],
+               cm.tab["prv.AtrFib",2:1,drop=FALSE],
+               cm.tab["pre.Str",2:1,drop=FALSE],
+               cm.tab["prv.PAD",2:1,drop=FALSE],
+               cm.tab["pre.Mic",2:1,drop=FALSE],
+               cm.tab["prv.CKD",2:1,drop=FALSE],
+               "Frail"=dm.tab["1",2:1],
+               mm.tab["had.Metformin",2:1,drop=FALSE],
+               mm.tab["had.SU",2:1,drop=FALSE],
+               mm.tab["had.TZD",2:1,drop=FALSE],
+               mm.tab["had.GLP1",2:1,drop=FALSE],
+               mm.tab["got.Ins",2:1,drop=FALSE],
+               mm.tab["got.Hyp",2:1,drop=FALSE],
+               mm.tab["had.HCD",2:1,drop=FALSE],
+               mm.tab["had.THZ",2:1,drop=FALSE],
+               mm.tab["had.ACE",2:1,drop=FALSE],
+               mm.tab["had.ARB",2:1,drop=FALSE],
+               mm.tab["had.Sta",2:1,drop=FALSE],
+               mm.tab["had.BBl",2:1,drop=FALSE],
+               mm.tab["had.AlA",2:1,drop=FALSE],
+               "Index year"=NA,
+               dm.tab["Index date 2012",2:1,drop=FALSE],
+               dm.tab["2013",2:1,drop=FALSE],
+               dm.tab["2014",2:1,drop=FALSE],
+               dm.tab["2015",2:1,drop=FALSE],
+               dm.tab["2016",2:1,drop=FALSE],
+               '2017'=NA)
> str(ol)
'data.frame':        33 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
> bm <- cbind(bm[,1],NA,NA,bm[,2],NA,NA)
> bm["Age",c(2,3,5,6)] <- dm.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bm ) <- c("SGLT-2","mean","sd","DPP4","mean","sd")
> cbind( ol, bm )
                                        V1 SGLT-2 mean   sd DPP4 mean   sd
Sample size                    Sample size   7887   NA   NA 7887   NA   NA
Age                             Age, years     NA   61 12.9   NA 61.1 11.1
F                                    Women   3069   NA   NA 3092   NA   NA
pre.CVD                         CV-history   2419   NA   NA 2378   NA   NA
prv.MI               Myocardial infarction    655   NA   NA  647   NA   NA
prv.UnstAng                Unstable angina    285   NA   NA  279   NA   NA
prv.HF                       Heart failure    364   NA   NA  351   NA   NA
prv.AtrFib             Atrial fibrillation    486   NA   NA  475   NA   NA
pre.Str                             Stroke    596   NA   NA  606   NA   NA
prv.PAD                               PAD     413   NA   NA  431   NA   NA
pre.Mic              Microvascular disease   2385   NA   NA 2283   NA   NA
prv.CKD                                CKD     55   NA   NA   66   NA   NA
Frail                        Frailty (yes)   2413   NA   NA 2405   NA   NA
had.Metformin                    Metformin   6267   NA   NA 6181   NA   NA
had.SU                                  SU   1907   NA   NA 1980   NA   NA
had.TZD                               TZD      22   NA   NA   18   NA   NA
```

```
had.GLP1                             GLP1    1516   NA   NA 1477   NA   NA
got.Ins                           Insulin    1954   NA   NA 1896   NA   NA
got.Hyp         Anti hypertensive therapy    6097   NA   NA 5956   NA   NA
had.HCD                    LOOP diuretics    1116   NA   NA 1150   NA   NA
had.THZ              Low ceiling diuretics   1146   NA   NA 1161   NA   NA
had.ACE                     ACE Inhibitors   3034   NA   NA 2942   NA   NA
had.ARB                               ARBs   2613   NA   NA 2624   NA   NA
had.Sta                     Statin therapy   5716   NA   NA 5641   NA   NA
had.BBl                      Beta blockers   2178   NA   NA 2159   NA   NA
had.AlA            Aldosterone antagonists    428   NA   NA  424   NA   NA
Index year                      Index year     NA   NA   NA   NA   NA   NA
Index date 2012                       2012     15   NA   NA   64   NA   NA
2013                                  2013   1193   NA   NA 1097   NA   NA
2014                                  2014   1514   NA   NA 1499   NA   NA
2015                                  2015   1981   NA   NA 2179   NA   NA
2016                                  2016   3184   NA   NA 3048   NA   NA
2017                                  2017     NA   NA   NA   NA   NA   NA
> write.xlsx( cbind( 'Org. labs'=ol, bm ),
+             "SGDP.xlsx",
+ sheetName = "Baseline after matching",
+    append = TRUE,
+    showNA = FALSE )
```

2.12.2 Treatment distribution

```
> ( FUtab <- tabFU[c(2:5,rep(NA,4),1),] )
       wh
Ix       nPers         FU    meanfu      sdFU    maxFU
  SGLT2  7887 12245.0575 1.5525621 1.1144939 4.051335
  Dapa   5094 10088.1533 1.9803992 1.1089062 4.051335
  Empa   2556  1839.6496 0.7197377 0.5286949 2.348392
  Cana    237   317.2546 1.3386271 0.6579770 2.542779
  <NA>     NA         NA        NA        NA       NA
  <NA>     NA         NA        NA        NA       NA
  <NA>     NA         NA        NA        NA       NA
  <NA>     NA         NA        NA        NA       NA
  DPP4   7887 12095.5599 1.5336072 1.1129297 4.078713
> colnames(FUtab) <- c(
+ 'Number of patients',
+ 'Total follow-up time',
+ 'Mean follow-up time',
+ 'Sd follow-up time',
+ 'maximum follow-up time')
> rownames( FUtab ) <- c(
+ 'SGLT-2',
+ '   Dapagliflozin',
+ '   Empagliflozin',
+ '   Canagliflozin',
+ '   Ipragliflozin',
+ '   Luseogliflozin',
+ '   Tofugliflozin',
+ '-',
+ 'DPP4')
> FUtab
```

```
                   wh
Ix                  Number of patients Total follow-up time Mean follow-up time Sd follow-up t
  SGLT-2                          7887           12245.0575           1.5525621         1.1144
     Dapagliflozin                5094           10088.1533           1.9803992         1.1089
     Empagliflozin                2556            1839.6496           0.7197377         0.5286
     Canagliflozin                 237             317.2546           1.3386271         0.6579
     Ipragliflozin                  NA                   NA                  NA
     Luseogliflozin                 NA                   NA                  NA
     Tofugliflozin                  NA                   NA                  NA
  -                                 NA                   NA                  NA
  DPP4                            7887           12095.5599           1.5336072         1.1129
                   wh
Ix                  maximum follow-up time
  SGLT-2                          4.051335
     Dapagliflozin                4.051335
     Empagliflozin                2.348392
     Canagliflozin                2.542779
     Ipragliflozin                      NA
     Luseogliflozin                     NA
     Tofugliflozin                      NA
  -                                     NA
  DPP4                            4.078713
```

```
> write.xlsx( FUtab,
+             "SGDP.xlsx",
+ sheetName = "Treatment distribution",
+    append = TRUE,
+    showNA = FALSE )
```

2.12.3 Events

```
> cat(
+ 'Number of patients
+ Total follow-up time - on treatment
+ Number of patients with event - on treatment
+ Total follow-up time - ITT
+ Number of patients with event - ITT
+ ', file='oc' )
> ( oc <- read.table('oc',header=FALSE,sep='\t',as.is=TRUE)[,1] )
```

```
[1] "Number of patients"                           "Total follow-up time - on treatment"
[3] "Number of patients with event - on treatment" "Total follow-up time - ITT"
[5] "Number of patients with event - ITT"
```

```
> cat(
+ 'HHF
+ All-cause death
+ All-cause death or HHF
+ Cardiavascular death
+ Myocardial infarction
+ Stroke
+ Ischemic stroke
+ MACE (cardivascular death, MI or stroke)
+ modified MACE (All-cause death, MI or stroke)
+ Kidney disease
+ ', file='ol' )
> ( ol <- read.table('ol',header=FALSE,sep='\t',as.is=TRUE)[,1] )
```

```
 [1] "HHF"                                         "All-cause death"
 [3] "All-cause death or HHF"                      "Cardiavascular death"
 [5] "Myocardial infarction"                       "Stroke"
 [7] "Ischemic stroke"                             "MACE (cardivascular death, MI or stroke)
 [9] "modified MACE (All-cause death, MI or stroke)" "Kidney disease"
```

The data for this is in the `dat` object:

```
> str( dat )
 num [1:10, 1:2, 1:3, 1:2, 1:3] 7887 7887 7887 7887 7887 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "DPP4"
  ..$ dat : chr [1:3] "N" "PY" "Event"
> cbind( ol, dimnames(dat)[[1]] )
      ol
 [1,] "HHF"                                           "HF"
 [2,] "All-cause death"                               "ACD"
 [3,] "All-cause death or HHF"                        "ACD+HF"
 [4,] "Cardiavascular death"                          "CVDD"
 [5,] "Myocardial infarction"                         "MI"
 [6,] "Stroke"                                        "Str"
 [7,] "Ischemic stroke"                               "IscStr"
 [8,] "MACE (cardivascular death, MI or stroke)"      "CVDD+MI+Str"
 [9,] "modified MACE (All-cause death, MI or stroke)" "ACD+MI+Str"
[10,] "Kidney disease"                                "DKD"
> ft <- ftable( dat[,,1,1:2,,drop=FALSE], col.vars=c(4,2,5) )
> round( ft, 1 )
                   ix     SGLT2                                            DPP4
                   data    OnDr                   Total                    OnDr
                   dat        N      PY   Event       N      PY   Event       N      PY   Ever
endp        sub
HF          AllPtt       7887.0  9075.5    73.0  7887.0 12124.4   113.0  7887.0  9170.4   124.
ACD         AllPtt       7887.0  9133.6    93.0  7887.0 12245.1   168.0  7887.0  9269.4   253.
ACD+HF      AllPtt       7887.0  9075.5   164.0  7887.0 12124.4   274.0  7887.0  9170.4   356.
CVDD        AllPtt       7887.0  9133.6    17.0  7887.0 12245.1    31.0  7887.0  9269.4    57.
MI          AllPtt       7887.0  9093.1    54.0  7887.0 12177.5    72.0  7887.0  9204.2    78.
Str         AllPtt       7887.0  9086.8    55.0  7887.0 12157.8    76.0  7887.0  9203.9    85.
IscStr      AllPtt       7887.0  9088.8    52.0  7887.0 12163.3    70.0  7887.0  9212.0    75.
CVDD+MI+Str AllPtt       7887.0  9047.8   120.0  7887.0 12091.8   165.0  7887.0  9138.6   203.
ACD+MI+Str  AllPtt       7887.0  9047.8   193.0  7887.0 12091.8   295.0  7887.0  9138.6   383.
DKD         AllPtt       7887.0  9081.7    55.0  7887.0 12135.8    81.0  7887.0  9093.7   189.
```

This is the table needed (except for the column on persons, which shoudl not be repeated):

```
> py <- data.frame( as.matrix(ft) )[-c(4,10)]
> py
                   SGLT2_OnDr_N SGLT2_OnDr_PY SGLT2_OnDr_Event SGLT2_Total_PY SGLT2_Total_Ever
HF_AllPtt                  7887      9075.483               73       12124.43               11
ACD_AllPtt                 7887      9133.550               93       12245.06               16
ACD+HF_AllPtt              7887      9075.483              164       12124.43               27
CVDD_AllPtt                7887      9133.550               17       12245.06               3
MI_AllPtt                  7887      9093.067               54       12177.49               7
Str_AllPtt                 7887      9086.789               55       12157.81               7
```

```
IscStr_AllPtt              7887      9088.836               52       12163.29                7
CVDD+MI+Str_AllPtt         7887      9047.824              120       12091.76               16
ACD+MI+Str_AllPtt          7887      9047.824              193       12091.76               29
DKD_AllPtt                 7887      9081.685               55       12135.85                8
                   DPP4_OnDr_N DPP4_OnDr_PY DPP4_OnDr_Event DPP4_Total_PY DPP4_Total_Event
HF_AllPtt                 7887     9170.435             124      11945.76              147
ACD_AllPtt                7887     9269.423             253      12095.56              332
ACD+HF_AllPtt             7887     9170.435             356      11945.76              448
CVDD_AllPtt               7887     9269.423              57      12095.56               73
MI_AllPtt                 7887     9204.194              78      11980.04              103
Str_AllPtt                7887     9203.862              85      12008.03               97
IscStr_AllPtt             7887     9211.971              75      12018.63               85
CVDD+MI+Str_AllPtt        7887     9138.635             203      11893.27              249
ACD+MI+Str_AllPtt         7887     9138.635             383      11893.27              487
DKD_AllPtt                7887     9093.732             189      11826.67              218
> colnames( py )
```

```
 [1] "SGLT2_OnDr_N"      "SGLT2_OnDr_PY"     "SGLT2_OnDr_Event"  "SGLT2_Total_PY"
 [5] "SGLT2_Total_Event" "DPP4_OnDr_N"       "DPP4_OnDr_PY"      "DPP4_OnDr_Event"
 [9] "DPP4_Total_PY"     "DPP4_Total_Event"
```

```
> colnames(py) <- c(oc,oc[-1])
> rownames(py) <- ol
```

With this in order we can now write it to the excel sheet:

```
> write.xlsx( py,
+              "SGDP.xlsx",
+ sheetName = "Events",
+    append = TRUE,
+    showNA = FALSE )
```

2.12.4 Hazard ratios

```
> ft <- ftable((dat[c(1:3,9,5,6),1:2,1,"SGLT2",,drop=FALSE]+
+               dat[c(1:3,9,5,6),1:2,1,"DPP4" ,,drop=FALSE])[,,,c(1,1),],row.vars=c(1,2,3))
> YD <- data.frame(as.matrix(ft))
> HR <- data.frame(as.matrix(ftable(res[c(1:3,9,5,6),1:2,1,1:2,c(1,4)],row.vars=c(1,2,3))))
> Endpoint <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[1] )
> Adjusted <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[3] )
> Analysis <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[2] )
> ( HR <- cbind(Endpoint,Adjusted,Analysis,HR,YD)[,c(1:3,6:8,4:5)] )
```

```
                       Endpoint Adjusted Analysis     N       PY Event        HR         se
HF_OnDr_Raw                  HF      Raw     OnDr 15774 18245.92   197 0.5927892 0.14755802
HF_OnDr_Adj                  HF      Adj     OnDr 15774 18245.92   197 0.5683430 0.14812834
HF_Total_Raw                 HF      Raw    Total 15774 24070.19   260 0.7582214 0.12508638
HF_Total_Adj                 HF      Adj    Total 15774 24070.19   260 0.7481364 0.12563777
ACD_OnDr_Raw                ACD      Raw     OnDr 15774 18402.97   346 0.3719135 0.12136017
ACD_OnDr_Adj                ACD      Adj     OnDr 15774 18402.97   346 0.4705849 0.12416019
ACD_Total_Raw               ACD      Raw    Total 15774 24340.62   500 0.4988829 0.09458513
ACD_Total_Adj               ACD      Adj    Total 15774 24340.62   500 0.5883592 0.09624492
ACD+HF_OnDr_Raw          ACD+HF      Raw     OnDr 15774 18245.92   520 0.4641810 0.09443447
ACD+HF_OnDr_Adj          ACD+HF      Adj     OnDr 15774 18245.92   520 0.5284903 0.09581194
ACD+HF_Total_Raw         ACD+HF      Raw    Total 15774 24070.19   722 0.6023997 0.07662925
ACD+HF_Total_Adj         ACD+HF      Adj    Total 15774 24070.19   722 0.6692084 0.07769434
ACD+MI+Str_OnDr_Raw  ACD+MI+Str      Raw     OnDr 15774 18186.46   576 0.5082130 0.08835286
```

```
ACD+MI+Str_OnDr_Adj  ACD+MI+Str      Adj     OnDr 15774 18186.46   576 0.5760822 0.08900205
ACD+MI+Str_Total_Raw ACD+MI+Str      Raw    Total 15774 23985.03   782 0.5966130 0.07373626
ACD+MI+Str_Total_Adj ACD+MI+Str      Adj    Total 15774 23985.03   782 0.6578412 0.07426376
MI_OnDr_Raw                  MI      Raw     OnDr 15774 18297.26   132 0.6999601 0.17752253
MI_OnDr_Adj                  MI      Adj     OnDr 15774 18297.26   132 0.7383851 0.17686639
MI_Total_Raw                 MI      Raw    Total 15774 24157.53   175 0.6924864 0.15378461
MI_Total_Adj                 MI      Adj    Total 15774 24157.53   175 0.7230674 0.15346243
Str_OnDr_Raw                Str      Raw     OnDr 15774 18290.65   140 0.6556483 0.17297282
Str_OnDr_Adj                Str      Adj     OnDr 15774 18290.65   140 0.6887783 0.17301996
Str_Total_Raw               Str      Raw    Total 15774 24165.84   173 0.7752544 0.15310089
Str_Total_Adj               Str      Adj    Total 15774 24165.84   173 0.8096341 0.15351589
```

```
> write.xlsx( HR,
+             "SGDP.xlsx",
+ sheetName = "Hazard ratios",
+    append = TRUE,
+    showNA = FALSE )
```

2.12.5 Subgroup OT

This is same as above, except the we restrict to “OnDr”, and subclassify by previous CVD:

```
> str(dat)
 num [1:10, 1:2, 1:3, 1:2, 1:3] 7887 7887 7887 7887 7887 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "DPP4"
  ..$ dat : chr [1:3] "N" "PY" "Event"

> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"OnDr",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"OnDr",,"DPP4" ,],row.vars=c(1,2))))
> str( YD )

'data.frame':        18 obs. of  3 variables:
 $ N    : num  15774 4797 10977 15774 4797 ...
 $ PY   : num  18246 5293 12953 18403 5423 ...
 $ Event: num  197 163 34 346 187 159 520 328 192 576 ...

> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"OnDr",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+             "SGDP.xlsx",
+ sheetName = "Subgroups OT",
+    append = TRUE,
+    showNA = FALSE )
```

2.12.6 Subgroup ITT

This is same as above, except the we restrict to “Total”, and subclassify by previous CVD:

```
> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"Total",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"Total",,"DPP4" ,],row.vars=c(1,2))))
> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"Total",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+             "SGDP.xlsx",
+ sheetName = "Subgroups ITT",
+    append = TRUE,
+    showNA = FALSE )
```

Chapter 3

Analysis of SGLT-2i vs. any other drug

3.1 Dataset for analysis od SGLT-2i vs any other drug

First load the relevant package:

```
> options( width=95 )
> library( Epi )
> library( splines )
> library( haven )
> library( Matching )
> clear()
> print( sessionInfo(), l=F )
R version 3.5.0 (2018-04-23)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] Matching_4.9-3 MASS_7.3-49    haven_1.1.1    Epi_2.30

loaded via a namespace (and not attached):
 [1] Rcpp_0.12.16      lattice_0.20-35   zoo_1.8-1         grid_3.5.0        plyr_1.8.4
 [6] magrittr_1.5      etm_0.6-2         pillar_1.2.2      rlang_0.2.0       Matrix_1.2-14
[11] forcats_0.3.0     tools_3.5.0       cmprsk_2.2-7      numDeriv_2016.8-1 survival_2.41-3
[16] parallel_3.5.0    compiler_3.5.0    tibble_1.4.2
```

Then we can read the data:

```
> system.time(
+ mset <- read_sas( "../data/episodes.sas7bdat" ) )
   user  system elapsed
   7.14    0.03   22.25
> dim( mset )
[1] 244715     98
> mset <- subset( mset, is.na(doDth) | doIx<doDth )
> dim( mset )
[1] 244662     98
```

...now input from ../rep/matchSGoth.tex

```
> names( mset )
 [1] "druggr"      "pnr"         "eksd"        "ATC"         "doDM"        "epiN"
 [7] "doIx"        "Ixdr"        "Ixatc"       "lastpr"      "doTm"        "doFL"
[13] "FLdr"        "FLatc"       "deCVDD"      "coD"         "doTIA"       "doAngina"
[19] "doBleed"     "doCOPD"      "doPAD"       "doHF"        "doCancer"    "doDMcompl"
[25] "doNeuro"     "doDKD"       "doDiaEye"    "doHypo"      "doAtrFib"    "doMI"
[31] "doUnstAng"   "doHmStr"     "doDiaFoot"   "doOther"     "doPeriAng"   "doIscStr"
[37] "doAmp"       "doCKD"       "doPCIsten"   "doCABG"      "doKeto"      "doDial"
[43] "doBari"      "sex"         "doBth"       "whBth"       "doDth"       "dSrc"
[49] "dolACE"      "dolSta"      "dolBBl"      "dolARB"      "dolAlA"      "dolDHP"
[55] "dolWtL"      "dolRPA"      "dolWrf"      "dolAsp"      "dolHCD"      "dolTHZ"
[61] "dolCcs"      "dolDXI"      "dolDgo"      "dolAPl"      "dolAmi"      "dolDTI"
[67] "dolNHP"      "dolFla"      "dolMetformin" "dolGLP1"     "dolMetxSGLT2" "dolMetxDPP4"
[73] "dolSGLT2"    "dollongIns"  "dolmixIns"   "dolDPP4"     "dolSU"       "dolintIns"
[79] "dolfastIns"  "dolTZD"      "dolAcarbose" "dolTZDxDPP4" "maxH"        "frail"
[85] "recnum"      "C_ADIAG"     "compl"       "C_OPR"       "D_INDDTO"    "V_SENGDAGE"
[91] "deHF"        "deMACE"      "deMI"        "deStr"       "deIscStr"    "deAF"
[97] "deHH"        "deDKD"
```

```
> addmargins( table( table( mset$pnr ) ) )
     1      2      3      4      5      6      7      8      9     10     11    Sum
 99132  36028  13706   5015   1596    464    143     49     12      2      1 156148
```

We convert all dates to fractions of years to facilitate programming:

```
> mset <- cal.yr( as.data.frame(mset) )
```

To make `FLdr` and `Ixdr` into factors we need some sensible levels:

```
> ( drlab <- read.table( "drlab.txt", header=TRUE, as.is=TRUE ) )
        gr  lab     longlab
1       11  Met   Metformin
2       12   SU Sulfonylurea
3       13  TZD         TZD
4       14  DPP       DPP-4
5       15  GLP       GLP-1
6       16  SGL       SGLT2
7  fastIns fIns     fastIns
8   intIns iIns      intIns
9   mixIns mIns      mixIns
10 longIns lIns     longIns
11      18  Aca    Acarbose
12      19  Meg  Meglitinide
13     212  M+U      Met+SU
14     213  M+T     Met+TZD
15     214  M+D    Met+DPP4
16     216  M+S   Met+SGLT2
17     218  M+A Met+Acarbose
18     223  U+T      SU+TZD
19     234  D+T    TZD+DPP4
20     246  D+S   DPP4+SGLT2
```

Then we can define the first line and the index drug variables as factors:

```
> mset <- transform( mset, doFL = pmax( doFL, 1995 ),
+                          FLdr = factor( FLdr,
+                                         levels = drlab$gr,
+                                         labels = drlab$lab ),
+                          Ixdr = factor( ifelse( is.na(ii<-match(Ixdr,drlab$longlab)),
+                                                 Ixdr,
+                                                 drlab$lab[ii] ) ) )
> with( mset, table(FLdr, Ixdr) )
      Ixdr
FLdr     Aca  DPP4  fIns  GLP1  iIns  lIns   Met  mIns   SGL    SU   TZD
  Met     76 28839  8370 12121  6250 12547 79299  2751 12880 14189    99
  SU      31  8282  7332  3349  3377  7422  7635  1849  3947  4346    43
  TZD      0     6     2     9     4     8    16     0     4     5     9
  DPP      0   727    61    38    56    74   232    17    42    60     0
  GLP      0    30    10  1044     7    22   133     3    31    13     0
  SGL      0    11     2     4     2     3    26     0    94     1     0
  fIns     1   280  2296   302   812  1255   749   245   213   140     2
  iIns     1   265  1118   207  1139   631   590   182   167    91     1
  mIns     1   257   549   175   150   439   569   551   134   116     2
  lIns     1    52   291    26     9   733   177    25    21    18     0
  Aca     68    35    41    23    22    28    49     8    16    18     0
  Meg      0     0     0     0     0     0     0     0     0     0     0
  M+U      0     0     0     0     0     0     0     0     0     0     0
  M+T      0    25    16    21     8    31    21     5    23    13     0
  M+D      0   489    37    51    17    48   498    13    82    84     0
  M+S      0     2     0     0     0     0    23     0    24     0     0
  M+A      0     0     0     0     0     0     0     0     0     0     0
  U+T      0     0     0     0     0     0     0     0     0     0     0
  D+T      0     0     0     0     0     0     0     0     0     0     0
  D+S      0     0     0     0     0     0     0     0     0     0     0
```

We shall use all *episodes*, which means that some persons will contribute more episodes, some of the same type of matching drug (which here is either SGLT2 or Other), so we move the `Ixdr` to the variable `Epdr` (`Ep`isode `dr`ug), and relevel the `Ixdr` to only two levels:

```
> mset$Epdr <- mset$Ixdr
> mset$Ixdr <- factor( 1-(mset$Ixdr=="SGL"), labels=c("SGLT2","Other") )
> with( mset, table( Epdr, Ixdr ) )
      Ixdr
Epdr   SGLT2 Other
  Aca      0   179
  DPP4     0 39300
  fIns     0 20125
  GLP1     0 17370
  iIns     0 11853
  lIns     0 23241
  Met      0 90017
  mIns     0  5649
  SGL  17678     0
  SU       0 19094
  TZD      0   156
```

We tabulate the index drug versus the first-line drug separately for those where the index date and first-line dates are the same:

`../rep/matchSGoth.tex`

```
> print( ftable( with( mset, addmargins(
+                table( "Ix=FL"=abs(doIx-doFL)<0.1, FLdr, E=Epdr ), 2:3 ) ),
+                col.vars=c(3) ),
+        zero = "." )

           E    Aca   DPP4   fIns   GLP1   iIns   lIns    Met   mIns    SGL     SU    TZD    S
Ix=FL FLdr
FALSE Met        75  27758   7918  11901   5606  11833  18599   2605  12748  13198     95 1123
      SU         30   8252   7317   3347   3372   7418   7565   1844   3946   3453     41  465
      TZD         .      6      1      9      4      7     15      .      4      5      1
      DPP         .     51     34     37     40     57    187     14     41     51      .    5
      GLP         .     27      8     73      7     17    118      3     29     13      .    2
      SGL         .      8      1      3      1      2     16      .      2      1      .
      fIns        1    276    758    302    368    784    666    134    213    136      2   36
      iIns        1    262   1056    207    345    625    526    167    167     88      1   34
      mIns        1    256    524    175    148    433    548    166    133    114      2   25
      lIns        1     47    203     25      8     72    113     15     21     16      .    5
      Aca         7     34     41     23     22     28     48      8     16     18      .    2
      Meg         .      .      .      .      .      .      .      .      .      .      .
      M+U         .      .      .      .      .      .      .      .      .      .      .
      M+T         .     25     16     21      8     31     21      5     23     13      .    1
      M+D         .     67     36     50     15     42     76     12     81     70      .    4
      M+S         .      2      .      .      .      .      .      .      1      .      .
      M+A         .      .      .      .      .      .      .      .      .      .      .
      U+T         .      .      .      .      .      .      .      .      .      .      .
      D+T         .      .      .      .      .      .      .      .      .      .      .
      D+S         .      .      .      .      .      .      .      .      .      .      .
      Sum       116  37071  17913  16173   9944  21349  28498   4973  17425  17176    142 1707
TRUE  Met         1   1081    452    220    644    714  60700    146    132    991      4  650
      SU          1     30     15      2      5      4     70      5      1    893      2   10
      TZD         .      .      1      .      .      1      1      .      .      .      8
      DPP         .    676     27      1     16     17     45      3      1      9      .    7
      GLP         .      3      2    971      .      5     15      .      2      .      .    9
      SGL         .      3      1      1      1      1     10      .     92      .      .    1
      fIns        .      4   1538      .    444    471     83    111      .      4      .   26
      iIns        .      3     62      .    794      6     64     15      .      3      .    9
      mIns        .      1     25      .      2      6     21    385      1      2      .    4
      lIns        .      5     88      1      1    661     64     10      .      2      .    8
      Aca        61      1      .      .      .      .      1      .      .      .      .
      Meg         .      .      .      .      .      .      .      .      .      .      .
      M+U         .      .      .      .      .      .      .      .      .      .      .
      M+T         .      .      .      .      .      .      .      .      .      .      .
      M+D         .    422      1      1      2      6    422      1      1     14      .    8
      M+S         .      .      .      .      .      .     23      .     23      .      .
      M+A         .      .      .      .      .      .      .      .      .      .      .
      U+T         .      .      .      .      .      .      .      .      .      .      .
      D+T         .      .      .      .      .      .      .      .      .      .      .
      D+S         .      .      .      .      .      .      .      .      .      .      .
      Sum        63   2229   2212   1197   1909   1892  61519    676    253   1918     14  738
```

We see that among those where the two dates are equal, there are still some where the first line and Index drug are not the same. This is because each initiating *drug* generates its own episode, so they represent episodes where people start more than one drug, or rather different episodes that start the same day.

3.1.1 Persons and episodes

Since we have more episodes for each person we also want to see how many persons contribute how many episodes on index drug SGLT2 resp. Other:

```
> tt <- with( mset, table( pnr, Ixdr ) )
> addmargins( table( SGLT2=tt[,"SGLT2"], Other=tt[,"Other"] ) )
     Other
SGLT2      0      1      2      3      4      5      6      7      8      9     10    Sum
  0        0  94727  30195   9798   3142    847    227     61     12      4      0 139013
  1     4405   5720   3758   1746    678    205     64     24      4      1      1  16606
  2      113    148    124     69     31     15     11      3      1      0      0    515
  3        2      3      2      1      3      2      1      0      0      0      0     14
  Sum   4520 100598  34079  11614   3854   1069    303     88     17      5      1 156148
> addmargins( table( table( mset$pnr ) ) )

     1      2      3      4      5      6      7      8      9     10     11    Sum
 99132  36028  13706   5015   1596    464    143     49     12      2      1 156148
```

Note that the latter table is a tabulation of the diagonals in the former table.

3.2 Baseline tables for all new-starters

We produce an overview of the the exposure status, but first we need a few derived variables, including the indicator of *any* previous CVD:

```
> mset <- transform( mset, age = doIx - doBth,
+                          tff = doIx - doFL,
+                          sex = factor( sex, labels=c("M","F") ),
+                        frail = pmax( frail, 0, na.rm=TRUE ),
+                         maxH = pmax( 0, maxH, na.rm=TRUE ) )
> with( mset, addmargins( table( Ixatc, Ixdr ), 1 ) )
         Ixdr
Ixatc      SGLT2 Other
  A10AB01      0  7136
  A10AB04      0    67
  A10AB05      0 12589
  A10AB06      0   333
  A10AC01      0 11853
  A10AD01      0   642
  A10AD04      0    22
  A10AD05      0  4980
  A10AD06      0     5
  A10AE04      0 15608
  A10AE05      0  5574
  A10AE06      0  2059
  A10BA02      0 89236
  A10BB01      0  1086
  A10BB03      0   326
  A10BB07      0   821
  A10BB09      0  1915
  A10BB12      0 14570
  A10BD03      0    71
  A10BD07      0  7899
  A10BD08      0  7153
  A10BD09      0    15
```

```
  A10BD10      0     22
  A10BD11      0    108
  A10BD13      0    353
  A10BD15    407     12
  A10BD16     13      1
  A10BD20    487     14
  A10BF01      0    179
  A10BG02      0     15
  A10BG03      0    121
  A10BH01      0  14762
  A10BH02      0   2930
  A10BH03      0    908
  A10BH04      0    727
  A10BH05      0   5126
  A10BJ01      0    502
  A10BJ02      0  16499
  A10BJ03      0     79
  A10BJ05      0    290
  A10BK01  10684      0
  A10BK02    465      0
  A10BK03   5622      0
  A10BX02      0    375
  A10BX03      0      1
  Sum      17678 226984
```

We now produce the baseline baseline tables for the entire set of new user episodess; the result is in three tables, `dt.tab` (demographics for total sample), `ct.tab` (comobidites for total sample) and `mt.tab` (medication for total sample).

```
> ptab <- function( var ) cbind( tt <- table( var, mset$Ixdr ),
+                                 round( prop.table( tt, 2 ) * 100, 1 ) )
```

3.2.1 Demographics

First the tabulations of the baseline demographics:

```
> t.sex <- with( mset, ptab(sex) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0
                   SGLT2 Other SGLT2 Other
Index = First Line   157 70185   0.9  30.9
```

```
> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                      tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0
                        [,1] [,2] [,3] [,4]
Index not FL: Mean / SD  8.9  8.4  5.2  5.7
```

```
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
```

```
+                                 tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age
                 [,1] [,2] [,3] [,4]
Age: Mean / SD 60.4 63.2   11 13.6
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )
       SGLT2 Other SGLT2 Other
2012.5    20  4468   0.1   2.0
2013     870 28592   4.9  12.6
2013.5  1059 24531   6.0  10.8
2014    1383 27503   7.8  12.1
2014.5  1655 24758   9.4  10.9
2015    2285 29637  12.9  13.1
2015.5  2476 27216  14.0  12.0
2016    4043 32204  22.9  14.2
2016.5  3887 28075  22.0  12.4
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dt.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dt.tab
                          SGLT2    Other SGLT2 Other
Sex M                   10822.0 132244.0  61.2  58.3
F                        6856.0  94740.0  38.8  41.7
Index = First Line        157.0  70185.0   0.9  30.9
Index not FL: Mean / SD     8.9      8.4   5.2   5.7
Age at index <40          630.0  11106.0   3.6   4.9
40                       2379.0  27582.0  13.5  12.2
50                       5310.0  50352.0  30.0  22.2
60                       5838.0  63988.0  33.0  28.2
70                       3028.0  50123.0  17.1  22.1
80+                       493.0  23833.0   2.8  10.5
Age: Mean / SD             60.4     63.2  11.0  13.6
Index date 2012            20.0   4468.0   0.1   2.0
2013                     1929.0  53123.0  10.9  23.4
2014                     3038.0  52261.0  17.2  23.0
2015                     4761.0  56853.0  26.9  25.0
2016                     7930.0  60279.0  44.9  26.6
Date of first line 1995   739.0  10675.0   4.2   4.7
1996                      294.0   3164.0   1.7   1.4
1997                      306.0   3145.0   1.7   1.4
1998                      415.0   4008.0   2.3   1.8
1999                      525.0   4604.0   3.0   2.0
2000                      564.0   4963.0   3.2   2.2
2001                      652.0   5527.0   3.7   2.4
2002                      753.0   5860.0   4.3   2.6
2003                      919.0   7273.0   5.2   3.2
2004                      953.0   7504.0   5.4   3.3
2005                     1048.0   8005.0   5.9   3.5
```

```
2006                    1173.0   8560.0   6.6   3.8
2007                    1242.0   9342.0   7.0   4.1
2008                    1288.0  10100.0   7.3   4.4
2009                    1315.0  10342.0   7.4   4.6
2010                    1301.0  11079.0   7.4   4.9
2011                    1158.0  11679.0   6.6   5.1
2012                     900.0  11901.0   5.1   5.2
2013                     725.0  25332.0   4.1  11.2
2014                     593.0  21549.0   3.4   9.5
2015                     481.0  21609.0   2.7   9.5
2016                     334.0  20763.0   1.9   9.1
Frailty 0              11663.0 145101.0  66.0  63.9
1                       6015.0  81883.0  34.0  36.1
```

3.2.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- grep( "do[A-Z]", names( mset ) )
> wh <- wh[4:30]
> names( mset )[wh]
 [1] "doFL"      "doTIA"     "doAngina"  "doBleed"   "doCOPD"    "doPAD"     "doHF"
 [8] "doCancer"  "doDMcompl" "doNeuro"   "doDKD"     "doDiaEye"  "doHypo"    "doAtrFib"
[15] "doMI"      "doUnstAng" "doHmStr"   "doDiaFoot" "doOther"   "doPeriAng" "doIscStr"
[22] "doAmp"     "doCKD"     "doPCIsten" "doCABG"    "doKeto"    "doDial"
```

```
> comorb <- data.frame( pmax( mset[,wh] < mset[,"doIx"], 0, na.rm=TRUE ) )
> names( comorb ) <- gsub( "do", "prv.", names(comorb) )
> str( comorb )
'data.frame':        244662 obs. of  27 variables:
 $ prv.FL      : num  1 1 1 1 1 1 1 1 1 1 ...
 $ prv.TIA     : num  0 0 0 0 0 0 0 0 1 1 ...
 $ prv.Angina  : num  0 0 0 0 0 0 1 1 0 0 ...
 $ prv.Bleed   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.COPD    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PAD     : num  0 0 0 0 0 0 0 0 1 1 ...
 $ prv.HF      : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Cancer  : num  1 1 1 1 0 0 0 0 0 0 ...
 $ prv.DMcompl: num  1 1 1 1 0 0 0 0 0 0 ...
 $ prv.Neuro   : num  0 0 0 0 1 0 0 0 0 0 ...
 $ prv.DKD     : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.DiaEye  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Hypo    : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.AtrFib  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.MI      : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.UnstAng: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.HmStr   : num  0 0 0 0 0 0 0 0 1 1 ...
 $ prv.DiaFoot: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Other   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PeriAng: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.IscStr  : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Amp     : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.CKD     : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.PCIsten: num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.CABG    : num  0 0 0 0 0 0 0 0 0 0 ...
```

```
 $ prv.Keto   : num  0 0 0 0 0 0 0 0 0 0 ...
 $ prv.Dial   : num  0 0 0 0 0 0 0 0 0 0 ...
```

Later, in the modeling we will need the indicator of *any* previous CVD as well as *any* type of stroke and micro-vascular complications:

```
> comorb$pre.CVD <- with( comorb, pmax( prv.MI,
+                                       prv.UnstAng,
+                                       prv.Angina,
+                                       prv.HF,
+                                       prv.AtrFib,
+                                       prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA,
+                                       prv.PAD ) )
> comorb$pre.Str <- with( comorb, pmax( prv.HmStr,
+                                       prv.IscStr,
+                                       prv.TIA ) )
> comorb$pre.FPA <- with( comorb, pmax( prv.DiaFoot,
+                                       prv.PeriAng ) )
> comorb$pre.Mic <- with( comorb, pmax( prv.DiaEye,
+                                       prv.DMcompl,
+                                       prv.Neuro,
+                                       prv.DKD,
+                                       prv.DiaFoot,
+                                       prv.PeriAng ) )
```

Note that we name the columns `pre.` to avoid including these in the propensity score estimation.

```
> ct.tab <- cbind(
+ t( sapply( comorb,
+            function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( comorb,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> # remove the dates of recurrent HF
> # wh <- grep( "HF[1-9]", rownames(ct.tab) )
> # ct.tab <- ct.tab[-wh,]
> ct.tab
            SGLT2  Other SGLT2 Other
prv.FL      17521 156799  99.1  69.1
prv.TIA       480   7881   2.7   3.5
prv.Angina   2348  29626  13.3  13.1
prv.Bleed     737  13032   4.2   5.7
prv.COPD      584  12222   3.3   5.4
prv.PAD       861  15553   4.9   6.9
prv.HF        702  13182   4.0   5.8
prv.Cancer    862  20305   4.9   8.9
prv.DMcompl  3297  27477  18.7  12.1
prv.Neuro    1032   9309   5.8   4.1
prv.DKD       671   8484   3.8   3.7
prv.DiaEye   2204  20020  12.5   8.8
prv.Hypo      613   8993   3.5   4.0
prv.AtrFib   1042  18499   5.9   8.1
prv.MI       1412  19911   8.0   8.8
prv.UnstAng   653   8459   3.7   3.7
```

```
prv.HmStr     144   2642   0.8   1.2
prv.DiaFoot   156   2295   0.9   1.0
prv.Other     814  11625   4.6   5.1
prv.PeriAng   902  10607   5.1   4.7
prv.IscStr    828  15774   4.7   6.9
prv.Amp        17    543   0.1   0.2
prv.CKD       101   6537   0.6   2.9
prv.PCIsten   156   2317   0.9   1.0
prv.CABG      477   6534   2.7   2.9
prv.Keto       95   2156   0.5   0.9
prv.Dial        1     80   0.0   0.0
pre.CVD      5268  76805  29.8  33.8
pre.Str      1263  22710   7.1  10.0
pre.FPA      1001  12080   5.7   5.3
pre.Mic      6021  53275  34.1  23.5
```

3.2.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest, restricted to the period after 2011-12-01, one year prior to the first SGLT2 dispensation. We of course also only count the drugs dispensed *before* the index date and not *on* it:

```
> wh <- grep( "dol", names(mset) )
> names( mset )[wh]
 [1] "dolACE"       "dolSta"       "dolBBl"       "dolARB"       "dolAlA"       "dolDHP"
 [7] "dolWtL"       "dolRPA"       "dolWrf"       "dolAsp"       "dolHCD"       "dolTHZ"
[13] "dolCcs"       "dolDXI"       "dolDgo"       "dolAPl"       "dolAmi"       "dolDTI"
[19] "dolNHP"       "dolFla"       "dolMetformin" "dolGLP1"      "dolMetxSGLT2" "dolMetxDPP4"
[25] "dolSGLT2"     "dollongIns"   "dolmixIns"    "dolDPP4"      "dolSU"        "dolintIns"
[31] "dolfastIns"   "dolTZD"       "dolAcarbose"  "dolTZDxDPP4"
> codisp <- data.frame( pmax( mset[,wh] > ( mset[,"doIx"] - 1 ) &
+                             mset[,wh] <   mset[,"doIx"] ,
+                       0, na.rm=TRUE ) )
> names( codisp ) <- gsub( "dol", "had.", names(codisp) )
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )
[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"
> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )
[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
> ( names( codisp )[wh.cvd <- c(10,2,wh.hyp)] )
[1] "had.Asp" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"
> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"
```

```
> mt.tab <- cbind(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+            function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mt.tab
```

```
              SGLT2  Other SGLT2 Other
had.ACE        6830  72133  38.6  31.8
had.Sta       13263 126144  75.0  55.6
had.BBl        4771  63033  27.0  27.8
had.ARB        6104  56367  34.5  24.8
had.AlA         883  14102   5.0   6.2
had.DHP        5354  59189  30.3  26.1
had.WtL         120   1029   0.7   0.5
had.RPA        1134  16626   6.4   7.3
had.Wrf         721  14724   4.1   6.5
had.Asp        6226  68351  35.2  30.1
had.HCD        2330  44177  13.2  19.5
had.THZ        2697  33724  15.3  14.9
had.Ccs         925  21060   5.2   9.3
had.DXI         288   4525   1.6   2.0
had.Dgo         434  10410   2.5   4.6
had.APl         175   3882   1.0   1.7
had.Ami          39   1328   0.2   0.6
had.DTI         218   3451   1.2   1.5
had.NHP         297   3665   1.7   1.6
had.Fla          15    200   0.1   0.1
had.Metformin 11391  80273  64.4  35.4
had.GLP1       4470  13314  25.3   5.9
had.MetxSGLT2     0    215   0.0   0.1
had.MetxDPP4   3192   8967  18.1   4.0
had.SGLT2         0   5432   0.0   2.4
had.longIns    2375  11834  13.4   5.2
had.mixIns      984  11555   5.6   5.1
had.DPP4       3085  14701  17.5   6.5
had.SU         4095  30627  23.2  13.5
had.intIns      932  13647   5.3   6.0
had.fastIns    1034   7846   5.8   3.5
had.TZD          58    224   0.3   0.1
had.Acarbose     32    229   0.2   0.1
had.TZDxDPP4      1      1   0.0   0.0
got.Ins        4067  36359  23.0  16.0
got.Hyp       13819 152904  78.2  67.4
got.CVD       16183 176968  91.5  78.0
```

We also check that there are no episodes with the index drug in the baseline:

```
> print( as.table( t( sapply( codisp,
+                           function( x ) tapply( x, mset$Epdr, sum ) ) ) ),
+        zero.print="-" )
                Aca  DPP4  fIns  GLP1  iIns  lIns   Met  mIns   SGL    SU   TZD
had.ACE          42 14599  7260  6555  4482  8863 21794  2106  6830  6366    66
had.Sta          79 27158 12584 12073  7349 15818 35551  3501 13263 11936    95
had.BBl          40 11633  7023  4756  3857  7615 21127  1825  4771  5106    51
had.ARB          36 11503  5228  5464  2999  6834 17943  1443  6104  4875    42
had.AlA           8  2294  2231  1138   972  1905  4090   506   883   950     8
```

```
had.DHP          27 11676  6133  5080  3529  7225 18853  1653  5354  4975    38
had.WtL           2   118    50   229    26    67   434    16   120    87     -
had.RPA          11  2834  2435  1024  1063  2139  5354   523  1134  1233    10
had.Wrf          11  2621  1869   857  1017  1796  4932   445   721  1167     9
had.Asp          40 13219  8059  5756  4455  8894 19837  2230  6226  5818    43
had.HCD          22  7314  7484  2978  3414  6240 12040  1659  2330  3003    23
had.THZ          28  5939  2917  2788  1811  3404 13202   807  2697  2808    20
had.Ccs          13  2956  3589  1031  1685  2205  7280   849   925  1443     9
had.DXI           -   810   678   252   278   640  1466   121   288   278     2
had.Dgo           6  1796  1448   471   738  1285  3517   341   434   801     7
had.APl           1   665   541   204   325   464  1242   137   175   301     2
had.Ami           -   252   224    90    89   200   341    61    39    70     1
had.DTI           1   621   379   210   210   397  1271    88   218   273     1
had.NHP          10   651   427   256   208   447  1276   100   297   286     4
had.Fla           2    49    13    15     8    13    80     -    15    20     -
had.Metformin    51 29442  8472 10287  5889 12291     -  2814 11391 10939    88
had.GLP1          6  1713  2222     -  1477  4666  1190   834  4470  1176    30
had.MetxSGLT2     -    59    10    45     7    68     -     5     -    21     -
had.MetxDPP4     11     -   783  2631   981  2422     -   368  3192  1759    12
had.SGLT2         3   821   519  1068   388  1615   386   148     -   471    13
had.longIns       6  1622  4592  2115   483     -  1575  1092  2375   333    16
had.mixIns        2  1011  3382  1231   845  3607  1271     -   984   203     3
had.DPP4         18     -  1722  3226  1892  3562  1529   672  3085  2051    29
had.SU           34  9035  2687  3816  3378  5573  4772  1283  4095     -    49
had.intIns        2  1100  3224  1313     -  5068  1496  1134   932   300    10
had.fastIns       6   877     -  1290   825  2482  1468   699  1034   188    11
had.TZD           -    56    15    27    23    34    34    11    58    24     -
had.Acarbose      -    51    17    30    17    25    51     7    32    30     1
had.TZDxDPP4      -     -     -     1     -     -     -     -     1     -     -
got.Ins          11  3643  9882  4457  1854  8949  4340  2342  4067   854    27
got.Hyp         100 29327 14888 12944  8691 17636 51872  4076 13819 13249   121
got.CVD         120 34640 17099 15051  9908 20181 59344  4648 16183 15845   132
```

3.3 Propensity scoring

We now make a logistic regression of the indicator of SGLT2 assignment versus Other assignment. For convenience we append the just created data frames of the indicators we will use in the analysis:

```
> mset <- cbind( mset, comorb, codisp )
> names( mset )
  [1] "druggr"        "pnr"           "eksd"          "ATC"           "doDM"
  [6] "epiN"          "doIx"          "Ixdr"          "Ixatc"         "lastpr"
 [11] "doTm"          "doFL"          "FLdr"          "FLatc"         "deCVDD"
 [16] "coD"           "doTIA"         "doAngina"      "doBleed"       "doCOPD"
 [21] "doPAD"         "doHF"          "doCancer"      "doDMcompl"     "doNeuro"
 [26] "doDKD"         "doDiaEye"      "doHypo"        "doAtrFib"      "doMI"
 [31] "doUnstAng"     "doHmStr"       "doDiaFoot"     "doOther"       "doPeriAng"
 [36] "doIscStr"      "doAmp"         "doCKD"         "doPCIsten"     "doCABG"
 [41] "doKeto"        "doDial"        "doBari"        "sex"           "doBth"
 [46] "whBth"         "doDth"         "dSrc"          "dolACE"        "dolSta"
 [51] "dolBBl"        "dolARB"        "dolAlA"        "dolDHP"        "dolWtL"
 [56] "dolRPA"        "dolWrf"        "dolAsp"        "dolHCD"        "dolTHZ"
 [61] "dolCcs"        "dolDXI"        "dolDgo"        "dolAPl"        "dolAmi"
 [66] "dolDTI"        "dolNHP"        "dolFla"        "dolMetformin"  "dolGLP1"
```

```
 [71] "dolMetxSGLT2"  "dolMetxDPP4"   "dolSGLT2"      "dollongIns"    "dolmixIns"
 [76] "dolDPP4"       "dolSU"         "dolintIns"     "dolfastIns"    "dolTZD"
 [81] "dolAcarbose"   "dolTZDxDPP4"   "maxH"          "frail"         "recnum"
 [86] "C_ADIAG"       "compl"         "C_OPR"         "D_INDDTO"      "V_SENGDAGE"
 [91] "deHF"          "deMACE"        "deMI"          "deStr"         "deIscStr"
 [96] "deAF"          "deHH"          "deDKD"         "Epdr"          "age"
[101] "tff"           "prv.FL"        "prv.TIA"       "prv.Angina"    "prv.Bleed"
[106] "prv.COPD"      "prv.PAD"       "prv.HF"        "prv.Cancer"    "prv.DMcompl"
[111] "prv.Neuro"     "prv.DKD"       "prv.DiaEye"    "prv.Hypo"      "prv.AtrFib"
[116] "prv.MI"        "prv.UnstAng"   "prv.HmStr"     "prv.DiaFoot"   "prv.Other"
[121] "prv.PeriAng"   "prv.IscStr"    "prv.Amp"       "prv.CKD"       "prv.PCIsten"
[126] "prv.CABG"      "prv.Keto"      "prv.Dial"      "pre.CVD"       "pre.Str"
[131] "pre.FPA"       "pre.Mic"       "had.ACE"       "had.Sta"       "had.BBl"
[136] "had.ARB"       "had.AlA"       "had.DHP"       "had.WtL"       "had.RPA"
[141] "had.Wrf"       "had.Asp"       "had.HCD"       "had.THZ"       "had.Ccs"
[146] "had.DXI"       "had.Dgo"       "had.APl"       "had.Ami"       "had.DTI"
[151] "had.NHP"       "had.Fla"       "had.Metformin" "had.GLP1"      "had.MetxSGLT2"
[156] "had.MetxDPP4"  "had.SGLT2"     "had.longIns"   "had.mixIns"    "had.DPP4"
[161] "had.SU"        "had.intIns"    "had.fastIns"   "had.TZD"       "had.Acarbose"
[166] "had.TZDxDPP4"  "got.Ins"       "got.Hyp"       "got.CVD"
```

With this in place it is quite easy to fit a propensity score model because we can easily fish out the relevant variables:

```
> table( mset$Ixdr )
 SGLT2  Other
 17678 226984
> ( prv <- grep( "prv", names(mset) ) )
 [1] 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123
[23] 124 125 126 127 128
> ( had <- grep( "had", names(mset) ) )
 [1] 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154
[23] 155 156 157 158 159 160 161 162 163 164 165 166
> # rmd <- grep( "SGL", names( mset )[had] )
> # had <- had[-rmd]
> names( mset )[had]
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"
> names( mset )[prv]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye"
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"
> system.time(
+ pr.0 <- glm( ( Ixdr == "SGLT2" ) ~
+              sex + age + frail + doIx + doFL +
+              as.matrix(mset[,prv]) +  as.matrix(mset[,had]),
+              family = binomial,
+              data = mset, maxit = 100 ) )
```

```
   user  system elapsed 
  25.75    2.01   27.77 
> print( summary( pr.0 ), digits = 3 )
Call:
glm(formula = (Ixdr == "SGLT2") ~ sex + age + frail + doIx + 
    doFL + as.matrix(mset[, prv]) + as.matrix(mset[, had]), family = binomial, 
    data = mset, maxit = 100)

Deviance Residuals: 
   Min      1Q  Median      3Q     Max  
-2.554  -0.393  -0.217  -0.061   4.273  

Coefficients:
                                     Estimate Std. Error z value Pr(>|z|)    
(Intercept)                         -1.05e+03   1.61e+01  -64.78  < 2e-16 ***
sexF                                -1.05e-01   1.80e-02   -5.85  5.0e-09 ***
age                                 -2.06e-02   8.14e-04  -25.34  < 2e-16 ***
frail                               -2.31e-01   1.93e-02  -11.92  < 2e-16 ***
doIx                                 5.30e-01   8.07e-03   65.61  < 2e-16 ***
doFL                                -1.31e-02   1.95e-03   -6.72  1.8e-11 ***
as.matrix(mset[, prv])prv.FL         3.01e+00   8.28e-02   36.31  < 2e-16 ***
as.matrix(mset[, prv])prv.TIA       -2.40e-02   5.39e-02   -0.45  0.65580    
as.matrix(mset[, prv])prv.Angina    -5.66e-04   2.97e-02   -0.02  0.98479    
as.matrix(mset[, prv])prv.Bleed     -1.65e-01   4.21e-02   -3.93  8.5e-05 ***
as.matrix(mset[, prv])prv.COPD      -1.68e-01   4.78e-02   -3.52  0.00043 ***
as.matrix(mset[, prv])prv.PAD       -2.39e-01   4.03e-02   -5.93  3.1e-09 ***
as.matrix(mset[, prv])prv.HF        -1.05e-01   4.81e-02   -2.18  0.02910 *  
as.matrix(mset[, prv])prv.Cancer    -3.98e-01   3.90e-02  -10.22  < 2e-16 ***
as.matrix(mset[, prv])prv.DMcompl    1.55e-01   2.46e-02    6.32  2.6e-10 ***
as.matrix(mset[, prv])prv.Neuro      1.39e-01   3.82e-02    3.65  0.00026 ***
as.matrix(mset[, prv])prv.DKD       -2.54e-01   4.56e-02   -5.56  2.6e-08 ***
as.matrix(mset[, prv])prv.DiaEye     1.72e-02   2.80e-02    0.61  0.53927    
as.matrix(mset[, prv])prv.Hypo      -2.28e-01   4.70e-02   -4.85  1.2e-06 ***
as.matrix(mset[, prv])prv.AtrFib     4.93e-02   4.90e-02    1.01  0.31487    
as.matrix(mset[, prv])prv.MI         7.01e-03   3.69e-02    0.19  0.84944    
as.matrix(mset[, prv])prv.UnstAng   -2.68e-02   4.94e-02   -0.54  0.58823    
as.matrix(mset[, prv])prv.HmStr     -1.18e-01   9.29e-02   -1.27  0.20367    
as.matrix(mset[, prv])prv.DiaFoot   -1.26e-01   9.14e-02   -1.38  0.16893    
as.matrix(mset[, prv])prv.Other     -1.37e-01   4.41e-02   -3.11  0.00187 ** 
as.matrix(mset[, prv])prv.PeriAng   -4.37e-02   4.13e-02   -1.06  0.29015    
as.matrix(mset[, prv])prv.IscStr    -2.17e-01   4.44e-02   -4.88  1.0e-06 ***
as.matrix(mset[, prv])prv.Amp       -8.48e-01   2.60e-01   -3.27  0.00109 ** 
as.matrix(mset[, prv])prv.CKD       -1.47e+00   1.05e-01  -14.04  < 2e-16 ***
as.matrix(mset[, prv])prv.PCIsten   -1.58e-01   9.35e-02   -1.69  0.09064 .  
as.matrix(mset[, prv])prv.CABG       1.51e-02   5.93e-02    0.25  0.79929    
as.matrix(mset[, prv])prv.Keto      -6.59e-01   1.12e-01   -5.91  3.5e-09 ***
as.matrix(mset[, prv])prv.Dial      -3.16e-01   1.03e+00   -0.31  0.75799    
as.matrix(mset[, had])had.ACE        1.82e-01   2.08e-02    8.77  < 2e-16 ***
as.matrix(mset[, had])had.Sta        3.26e-01   2.08e-02   15.68  < 2e-16 ***
as.matrix(mset[, had])had.BBl        1.28e-02   2.27e-02    0.56  0.57389    
as.matrix(mset[, had])had.ARB        3.31e-01   2.15e-02   15.40  < 2e-16 ***
as.matrix(mset[, had])had.AlA       -2.58e-02   4.17e-02   -0.62  0.53584    
as.matrix(mset[, had])had.DHP        5.88e-04   2.03e-02    0.03  0.97689    
as.matrix(mset[, had])had.WtL        5.03e-01   1.09e-01    4.61  4.0e-06 ***
as.matrix(mset[, had])had.RPA       -6.52e-02   3.93e-02   -1.66  0.09721 .  
as.matrix(mset[, had])had.Wrf       -1.29e-01   5.24e-02   -2.46  0.01394 *  
as.matrix(mset[, had])had.Asp        7.68e-02   2.09e-02    3.67  0.00025 ***
```

```
as.matrix(mset[, had])had.HCD       -3.02e-01   2.85e-02  -10.59  < 2e-16 ***
as.matrix(mset[, had])had.THZ        6.77e-02   2.46e-02    2.75  0.00591 **
as.matrix(mset[, had])had.Ccs       -2.72e-01   3.81e-02   -7.15  8.6e-13 ***
as.matrix(mset[, had])had.DXI       -1.27e-01   7.09e-02   -1.79  0.07408 .
as.matrix(mset[, had])had.Dgo       -1.43e-01   6.37e-02   -2.24  0.02531 *
as.matrix(mset[, had])had.APl       -2.28e-01   8.80e-02   -2.59  0.00962 **
as.matrix(mset[, had])had.Ami       -5.90e-01   1.73e-01   -3.41  0.00064 ***
as.matrix(mset[, had])had.DTI        1.68e-04   8.39e-02    0.00  0.99840
as.matrix(mset[, had])had.NHP        1.90e-01   6.84e-02    2.78  0.00546 **
as.matrix(mset[, had])had.Fla        8.10e-02   2.91e-01    0.28  0.78059
as.matrix(mset[, had])had.Metformin  4.52e-01   1.86e-02   24.25  < 2e-16 ***
as.matrix(mset[, had])had.GLP1       1.32e+00   2.25e-02   58.50  < 2e-16 ***
as.matrix(mset[, had])had.MetxSGLT2 -1.60e+01   2.40e+02   -0.07  0.94688
as.matrix(mset[, had])had.MetxDPP4   1.49e+00   2.54e-02   58.44  < 2e-16 ***
as.matrix(mset[, had])had.SGLT2     -1.64e+01   4.96e+01   -0.33  0.74047
as.matrix(mset[, had])had.longIns    5.57e-01   2.86e-02   19.45  < 2e-16 ***
as.matrix(mset[, had])had.mixIns    -1.67e-01   3.84e-02   -4.34  1.4e-05 ***
as.matrix(mset[, had])had.DPP4       8.77e-01   2.42e-02   36.18  < 2e-16 ***
as.matrix(mset[, had])had.SU         2.20e-01   2.17e-02   10.14  < 2e-16 ***
as.matrix(mset[, had])had.intIns    -5.69e-01   3.84e-02  -14.81  < 2e-16 ***
as.matrix(mset[, had])had.fastIns    3.32e-01   4.01e-02    8.29  < 2e-16 ***
as.matrix(mset[, had])had.TZD        1.01e+00   1.65e-01    6.12  9.5e-10 ***
as.matrix(mset[, had])had.Acarbose   3.04e-01   2.05e-01    1.48  0.13892
as.matrix(mset[, had])had.TZDxDPP4   1.19e+00   1.45e+00    0.82  0.41059
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 126947  on 244661  degrees of freedom
Residual deviance:  95983  on 244595  degrees of freedom
AIC: 96117

Number of Fisher Scoring iterations: 16
```

With this fitted model we can now use the fitted values as propensity scores.

3.4 Propensity score matching

Based on this propensity score we take a matched sample of 1 per SGLT-2 user — note that we explicitly set a seed in order to get a fully reproducible code:

```
> set.seed( 1952 )
> system.time(
+ mt <- Match( Tr = (mset$Ixdr=="SGLT2"),
+               X = fitted( pr.0 ),
+               M = 1,
+         replace = FALSE,
+           exact = FALSE,
+            ties = FALSE,
+         caliper = 0.2 ) )
   user  system elapsed
 198.84  131.68  330.56
```

```
> str( mt )
```

```
List of 23
 $ est              : num [1, 1] 0
 $ se               : NULL
 $ est.noadj        : num 0
 $ se.standard      : num 0
 $ se.cond          : NULL
 $ mdata            :List of 4
  ..$ Y                         : num [1:35220] 0 0 0 0 0 0 0 0 0 0 ...
  ..$ Tr                        : num [1:35220] 1 1 1 1 1 1 1 1 1 1 ...
  ..$ X                         : num [1:2, 1:17610] 0.479 0.479 0.178 0.179 0.46 ...
  .. ..- attr(*, "dimnames")=List of 2
  .. .. ..$ : NULL
  .. .. ..$ : chr [1:17610] "5" "7" "16" "19" ...
  ..$ orig.weighted.treated.nobs: num 17678
 $ index.treated    : num [1:17610] 5 7 16 19 37 56 61 69 77 83 ...
 $ index.control    : num [1:17610] 153842 133038 87125 108397 113006 ...
 $ index.dropped    : int [1:68] 124432 144439 184560 185280 198909 200020 200851 201996 20270
 $ weights          : num [1:17610] 1 1 1 1 1 1 1 1 1 1 ...
 $ orig.nobs        : int 244662
 $ orig.wnobs       : num 244662
 $ orig.treated.nobs: int 17678
 $ nobs             : int 244662
 $ wnobs            : num 17610
 $ caliper          : num 0.2
 $ ecaliper         : num 0.0211
 $ exact            : logi FALSE
 $ ndrops           : num 68
 $ ndrops.matches   : num 68
 $ MatchLoopC       : num [1:17610, 1:6] 5 7 16 19 37 56 61 69 77 83 ...
 $ version          : chr "fast"
 $ estimand         : chr "ATT"
 - attr(*, "class")= chr "Match"
> save( mt, file='mtSGoth.Rda' )
```

```
> load( file='mtSGoth.Rda' )
```

The resulting matching (`index.`-variables) refers to rows in `mset`:

```
> addmargins( rbind(
+ table( mset$Ixdr[unique(mt$index.treated)] ),
+ table( mset$Ixdr[unique(mt$index.control)] ) ), 2 )
     SGLT2 Other   Sum
[1,] 17610     0 17610
[2,]     0 17610 17610
```

We just use the index numbers for the treated as factor levels for the match-factor (we shall not use the factor though):

```
> tnum <- mt$index.treated
> cnum <- mt$index.control
> # a numeric with the index number of SGLT-2 for persons matched up
> mf <- rep( NA, nrow(mset) )
> mf[tnum] <- tnum
> mf[cnum] <- tnum
> # create a factor of this and tabulate
> mset <- transform( mset, mfac = factor(mf),
+                          psco = fitted(pr.0) )
> ( mtab <- with( mset, table( Ixdr, !is.na(mfac), useNA="ifany" ) ) )
```

```
Ixdr      FALSE   TRUE
  SGLT2      68  17610
  Other 209374  17610
```

```
> round( cbind( rbind( cbind( mtab,
+                              pctab( mtab ) ),
+                       NA,
+                       NA),
+                pctab( mtab, margin=1 ) )[-3,], 1 )
```

```
Ixdr        FALSE     TRUE      All         N
  SGLT2       0.4     99.6    100.0   17678.0
  Other      92.2      7.8    100.0  226984.0

Ixdr      FALSE   TRUE
  SGLT2       0     50
  Other     100     50
  All       100    100
  N      209442  35220
       FALSE  TRUE FALSE TRUE All      N  FALSE  TRUE
SGLT2     68 17610   0.4 99.6 100  17678      0    50
Other 209374 17610  92.2  7.8 100 226984    100    50
          NA    NA    NA   NA  NA     NA 209442 35220
```

We can see that we did match all persons, presumably because a lot of persons were matched to themselves:

```
> par( mar=c(3,3,1,1),mgp=c(3,1,0)/1.6,las=1,bty="n" )
> plot( mset$psco[mt$index.treated],
+       mset$psco[mt$index.control],
+       pch=16, cex=0.3 ,
+       xlim=0:1, xlab="SGLT-2i propensity score",
+       ylim=0:1, ylab="Other-drug propensity score" )
```

For the use in further analyses we save a version of the original data for later use:

```
> oset <- mset
> pscore <- table( floor( oset$psco*100 ), oset$Ixdr )
```

Finally we make a dataset restricted to the matched persons:

```
> mset <- subset( oset, !is.na(mfac) )
> psmatch <- table( floor( mset$psco*100 ), mset$Ixdr )
> head( pscore )
   SGLT2 Other
  0   181 83655
  1   170 15493
  2   373 16538
  3   456 14788
  4   517 12308
  5   560 10494
```

```
> head( psmatch )
   SGLT2 Other
  0   181   179
  1   170   169
  2   373   370
  3   456   463
  4   517   516
  5   560   563
```

../rep/matchSGoth.tex

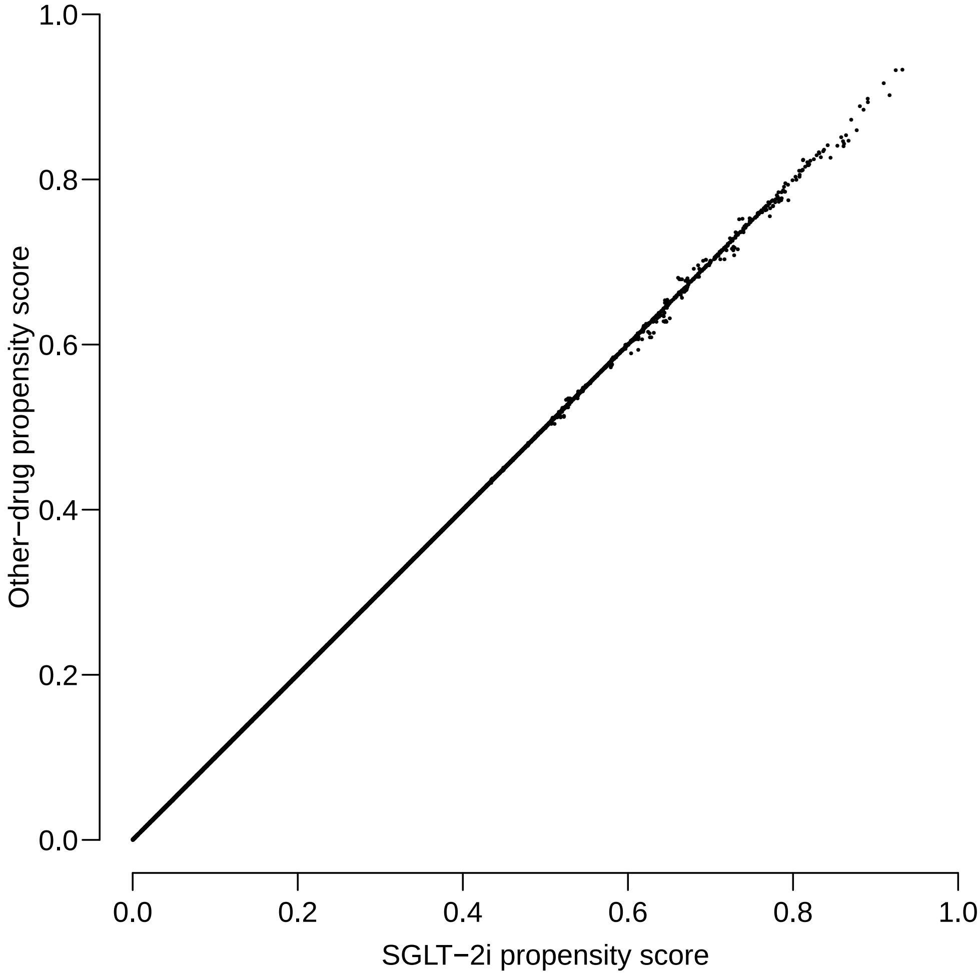

Figure 3.1: *Propensity scores from 1:1 matching; each matched set is represented by a dot.* `./matchSGoth-cmp-ps`

```
> save( oset, mset, pscore, psmatch, file = "adatSGoth.Rda" )
> load( file = "adatSGoth.Rda" )
```

```
> tt <- with( mset, table( pnr, Ixdr ) )
> addmargins( gg <- table( SGLT2=tt[,"SGLT2"], Other=tt[,"Other"] ) )
     Other
SGLT2     0     1     2     3     4     5   Sum
  0       0 12165  1261   137    12     1 13576
  1   14460  1826   228    29     2     1 16546
  2     443    62     6     0     0     0   511
  3      12     1     1     0     0     0    14
  Sum 14915 14054  1496   166    14     2 30647
> sum( gg[-1,-1] )
[1] 2156
> addmargins( table( table( mset$pnr ) ) )
    1     2     3     4     5     6   Sum
26625  3530   439    48     4     1 30647
```

Thus there are 30,647 persons with a total of 2 episodes. Of these persons 2,156 contribute episodes in both groups.

We also make histograms of the propensity scores, both for the original data and for the matched persons

```
> tt <- pscore
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
> head(tt)
                 SGLT2     Other
0 -10.238715 10.238715 368.55021
1  -9.616472  9.616472  68.25591
2 -21.099672 21.099672  72.85976
3 -25.794773 25.794773  65.14997
4 -29.245390 29.245390  54.22409
5 -31.677792 31.677792  46.23233
> nam <- colnames( tt )[-1]
> clr <- c("transparent","red","blue")
> # we use the undocumented feature of boxplot that you can get stacked
> # bars starting in the negative by giving negative numbers to the first
> # column. But it will mysteriously ignore the first element of col...
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-65,65),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=0 )

> tt <- psmatch
> tt[,1] <- tt[,1]/sum(tt[,1]) * 1000
> tt[,2] <- tt[,2]/sum(tt[,2]) * 1000
> tt <- cbind( -tt[,1], tt )
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, bty="n", las=1 )
> barplot( t(tt), space=0, col=clr, border="transparent", xlim=c(-65,65),
+          horiz=T, yaxt="n", ylab="Propensity score for SGLT-2 (%)", xaxt="n" )
> axis( side=2, at=seq(0,95,5), labels=NA, tcl=-0.3 )
> axis( side=2, at=0:9*10 )
> axis( side=1, at=-6:6*10, labels=NA, tcl=-0.3 )
> axis( side=1, at=-3:3*20, labels=abs(-3:3*20) )
> text( rep(60,2), 19:18*5, nam, col=clr[-1], font=2, adj=1 )
> # mtext( "%", side=1, font=2, line=1.5, at=-2.5 )
> mtext( "\211", side=1, font=2, line=1.5, at=10 )
```

3.5 Baseline tables for propensity matched persons

We have the matched sets in the dataframe `mset`, so we can almost verbatim reuse the code doing the tables for the original sample, except for the names of the resulting tables: `dm.tab` (demographics for matched sample), `cm.tab` (comobidites for matched sample) and `mm.tab` (medication for matched sample).

`../rep/matchSGoth.tex`

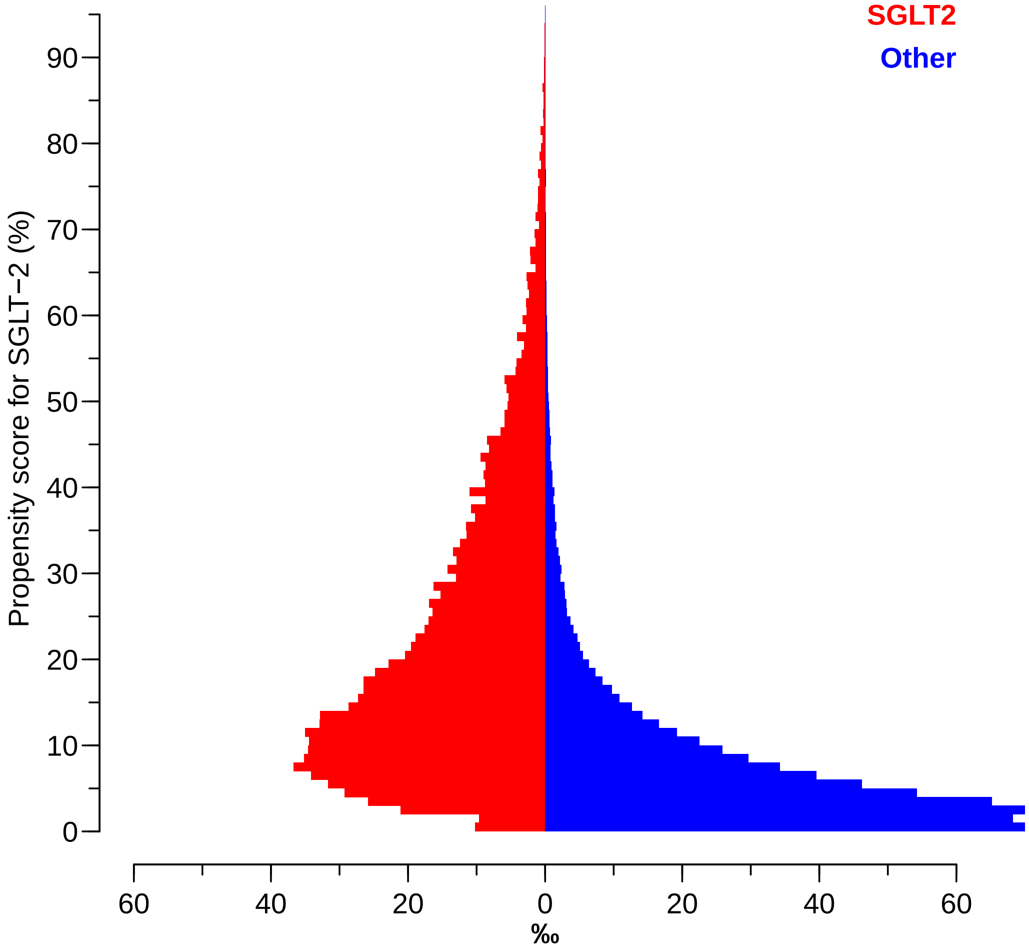

Figure 3.2: *Propensity scores for the SGLT-2 group (left, percent) and other groups (right, %■) in the 1:3 propensity score matched study.* `./matchSGoth-pscoreo`

3.5.1 Demographics

First the tabulations of the baseline demographics for the included *episodes*:

```
> t.sex <- with( mset, ptab( sex ) )
> rownames( t.sex )[1] <- paste("Sex",rownames( t.sex )[1])
> t.age <- with( mset, ptab( floor( pmin(pmax(age,30),89)/10 ) * 10 ) )
> rownames( t.age )[1] <- "Age at index <40"
> rownames( t.age )[nrow(t.age)] <- "80+"
> t.fl0 <- with( mset, ptab( doIx-doFL==0 ) )[-1,,drop=F]
> rownames( t.fl0 )[1] <- "Index = First Line"
> t.fl0
                     SGLT2 Other SGLT2 Other
Index = First Line     157   146   0.9   0.8
```

```
> m.fl0 <- with( subset(mset, doIx-doFL>0 ), round( c( tapply( doIx-doFL, Ixdr, mean ),
+                                                     tapply( doIx-doFL, Ixdr, sd ) ), 1 ) )
> dim( m.fl0 ) <- c(1,4)
> rownames( m.fl0 ) <- c("Index not FL: Mean / SD")
> m.fl0
```

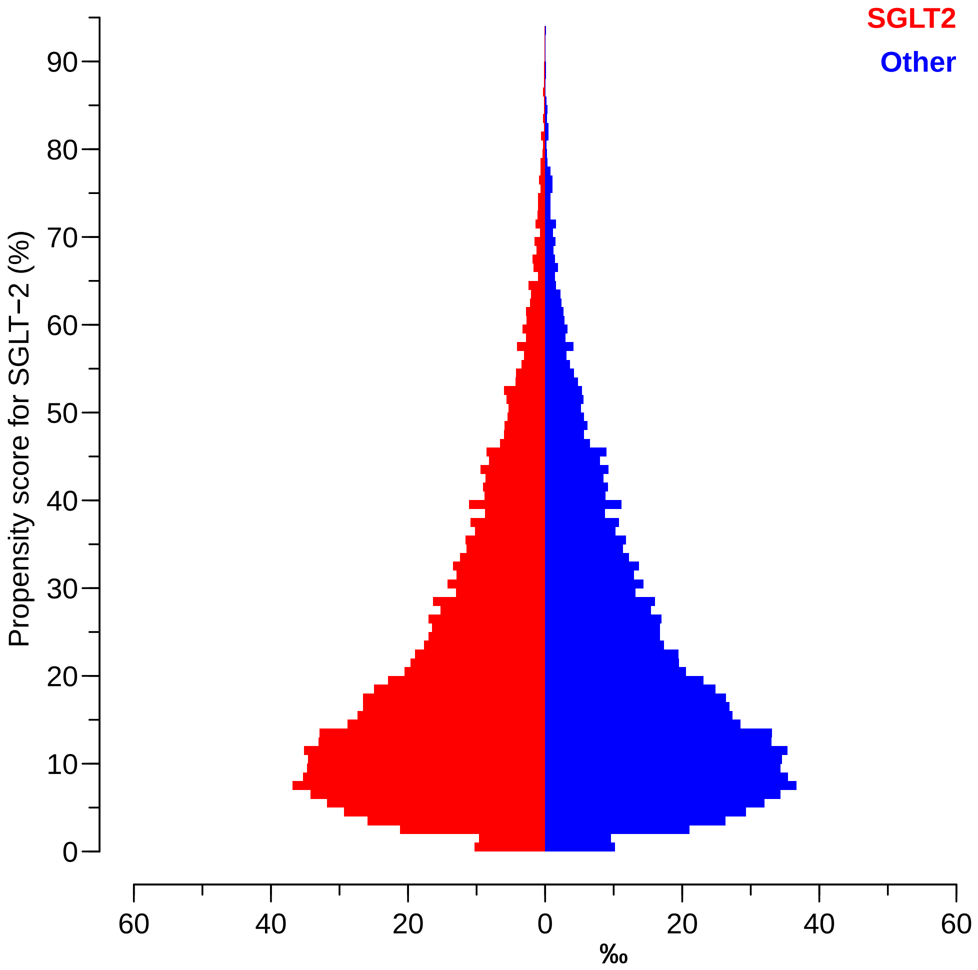

Figure 3.3: *Propensity scores for the SGLT-2 group (left, percent) and other groups in the 1:1 propensity score matched study.* `./matchSGoth-pscorem`

```
                          [,1] [,2] [,3] [,4]
Index not FL: Mean / SD    8.9  8.9  5.2  5.6
```

```
> m.age <- with( mset, round( c( tapply( age, Ixdr, mean ),
+                                tapply( age, Ixdr, sd ) ), 1 ) )
> dim( m.age ) <- c(1,4)
> rownames( m.age ) <- c("Age: Mean / SD")
> m.age
```

```
               [,1] [,2] [,3] [,4]
Age: Mean / SD 60.4 60.4   11 12.7
```

```
> ## Date of index by 6 months and 1 year
> with( mset, ptab( floor( doIx*2 )/2 ) )
```

```
       SGLT2 Other SGLT2 Other
2012.5    20   109   0.1   0.6
2013     870   868   4.9   4.9
2013.5  1059  1007   6.0   5.7
2014    1383  1396   7.9   7.9
2014.5  1655  1485   9.4   8.4
2015    2280  2385  12.9  13.5
```

```
2015.5  2467  2555  14.0  14.5
2016    4020  3745  22.8  21.3
2016.5  3856  4060  21.9  23.1
```

```
> t.dat <- with( mset, ptab( floor( doIx ) ) )
> rownames( t.dat )[1] <- paste("Index date",rownames( t.dat )[1])
> ## Date of First Line
> t.fl <- with( mset, ptab( floor( doFL ) ) )
> rownames( t.fl )[1] <- paste("Date of first line",rownames( t.fl )[1])
> ## Frailty
> t.fr <- with( mset, ptab( frail ) )
> rownames( t.fr )[1] <- paste("Frailty",rownames( t.fr )[1])
> dm.tab <- rbind( t.sex, t.fl0, m.fl0, t.age, m.age, t.dat, t.fl, t.fr )
> dm.tab
```

```
                           SGLT2   Other SGLT2 Other
Sex M                    10777.0 10801.0  61.2  61.3
F                         6833.0  6809.0  38.8  38.7
Index = First Line         157.0   146.0   0.9   0.8
Index not FL: Mean / SD      8.9     8.9   5.2   5.6
Age at index <40           627.0  1023.0   3.6   5.8
40                        2371.0  2600.0  13.5  14.8
50                        5279.0  4704.0  30.0  26.7
60                        5817.0  5160.0  33.0  29.3
70                        3023.0  3153.0  17.2  17.9
80+                        493.0   970.0   2.8   5.5
Age: Mean / SD              60.4    60.4  11.0  12.7
Index date 2012             20.0   109.0   0.1   0.6
2013                      1929.0  1875.0  11.0  10.6
2014                      3038.0  2881.0  17.3  16.4
2015                      4747.0  4940.0  27.0  28.1
2016                      7876.0  7805.0  44.7  44.3
Date of first line 1995    736.0   965.0   4.2   5.5
1996                       293.0   330.0   1.7   1.9
1997                       306.0   308.0   1.7   1.7
1998                       412.0   433.0   2.3   2.5
1999                       525.0   508.0   3.0   2.9
2000                       562.0   595.0   3.2   3.4
2001                       649.0   657.0   3.7   3.7
2002                       750.0   695.0   4.3   3.9
2003                       912.0   870.0   5.2   4.9
2004                       945.0   893.0   5.4   5.1
2005                      1044.0   943.0   5.9   5.4
2006                      1171.0  1022.0   6.6   5.8
2007                      1235.0  1096.0   7.0   6.2
2008                      1284.0  1238.0   7.3   7.0
2009                      1307.0  1190.0   7.4   6.8
2010                      1299.0  1219.0   7.4   6.9
2011                      1155.0  1191.0   6.6   6.8
2012                       895.0  1060.0   5.1   6.0
2013                       724.0   805.0   4.1   4.6
2014                       591.0   664.0   3.4   3.8
2015                       481.0   563.0   2.7   3.2
2016                       334.0   365.0   1.9   2.1
Frailty 0                11622.0 11660.0  66.0  66.2
1                         5988.0  5950.0  34.0  33.8
```

3.5.2 Comorbidities

The data frame contains the dates of the *earliest* recorded comorbidities from the NPR, hence the prefix `.prv`:

```
> wh <- match( rownames(ct.tab), names( mset ) )
> names( mset )[wh]
 [1] "prv.FL"      "prv.TIA"     "prv.Angina"  "prv.Bleed"   "prv.COPD"    "prv.PAD"
 [7] "prv.HF"      "prv.Cancer"  "prv.DMcompl" "prv.Neuro"   "prv.DKD"     "prv.DiaEye"
[13] "prv.Hypo"    "prv.AtrFib"  "prv.MI"      "prv.UnstAng" "prv.HmStr"   "prv.DiaFoot"
[19] "prv.Other"   "prv.PeriAng" "prv.IscStr"  "prv.Amp"     "prv.CKD"     "prv.PCIsten"
[25] "prv.CABG"    "prv.Keto"    "prv.Dial"    "pre.CVD"     "pre.Str"     "pre.FPA"
[31] "pre.Mic"
```

```
> comorb <- mset[,wh]
> cm.tab <- cbind(
+ t( sapply( comorb,
+             function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( comorb,
+             function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> cm.tab
```

```
            SGLT2 Other SGLT2 Other
prv.FL      17453 17464  99.1  99.2
prv.TIA       479   434   2.7   2.5
prv.Angina   2336  2371  13.3  13.5
prv.Bleed     731   692   4.2   3.9
prv.COPD      584   566   3.3   3.2
prv.PAD       861   839   4.9   4.8
prv.HF        701   737   4.0   4.2
prv.Cancer    861   906   4.9   5.1
prv.DMcompl  3274  3272  18.6  18.6
prv.Neuro    1027   998   5.8   5.7
prv.DKD       670   710   3.8   4.0
prv.DiaEye   2191  2271  12.4  12.9
prv.Hypo      613   594   3.5   3.4
prv.AtrFib   1039   991   5.9   5.6
prv.MI       1406  1399   8.0   7.9
prv.UnstAng   647   628   3.7   3.6
prv.HmStr     144   147   0.8   0.8
prv.DiaFoot   156   135   0.9   0.8
prv.Other     811   773   4.6   4.4
prv.PeriAng   898   894   5.1   5.1
prv.IscStr    824   825   4.7   4.7
prv.Amp        17    12   0.1   0.1
prv.CKD       101    81   0.6   0.5
prv.PCIsten   156   167   0.9   0.9
prv.CABG      475   464   2.7   2.6
prv.Keto       95   102   0.5   0.6
prv.Dial        1     0   0.0   0.0
pre.CVD      5248  5195  29.8  29.5
pre.Str      1258  1251   7.1   7.1
pre.FPA       997   975   5.7   5.5
pre.Mic      5988  5899  34.0  33.5
```

3.5.3 Other medication

We have variables that hold the last date of dispensation before index for all drugs of interest — well, only in the period after 2011-12-01, one year prior to the first SGLT2 dispensation.

```
> wh <- grep( "had.", names( mset ) )
> names( mset )[wh]
 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"

> codisp <- mset[,wh]
> ( names( codisp )[wh.ins <- grep("Ins",names(codisp))] )

[1] "had.longIns" "had.mixIns"  "had.intIns"  "had.fastIns"

> ( names( codisp )[wh.hyp <- c(1,4,6,12,3)] )

[1] "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"

> ( names( codisp )[wh.cvd <- c(8,2,wh.hyp)] )

[1] "had.RPA" "had.Sta" "had.ACE" "had.ARB" "had.DHP" "had.THZ" "had.BBl"

> codisp <- transform( codisp, got.Ins = apply( codisp[,wh.ins], 1, max ),
+                              got.Hyp = apply( codisp[,wh.hyp], 1, max ),
+                              got.CVD = apply( codisp[,wh.cvd], 1, max ) )
> names( codisp )

 [1] "had.ACE"       "had.Sta"       "had.BBl"       "had.ARB"       "had.AlA"
 [6] "had.DHP"       "had.WtL"       "had.RPA"       "had.Wrf"       "had.Asp"
[11] "had.HCD"       "had.THZ"       "had.Ccs"       "had.DXI"       "had.Dgo"
[16] "had.APl"       "had.Ami"       "had.DTI"       "had.NHP"       "had.Fla"
[21] "had.Metformin" "had.GLP1"      "had.MetxSGLT2" "had.MetxDPP4"  "had.SGLT2"
[26] "had.longIns"   "had.mixIns"    "had.DPP4"      "had.SU"        "had.intIns"
[31] "had.fastIns"   "had.TZD"       "had.Acarbose"  "had.TZDxDPP4"  "got.Ins"
[36] "got.Hyp"       "got.CVD"

> mm.tab <- cbind(
+ t( sapply( codisp,
+           function( x ) tapply( x, mset$Ixdr, sum ) ) ),
+ round(
+ t( sapply( codisp,
+           function( x ) tapply( x, mset$Ixdr, mean ) ) ) * 100, 1 ) )
> mm.tab

              SGLT2 Other SGLT2 Other
had.ACE        6802  6962  38.6  39.5
had.Sta       13204 13336  75.0  75.7
had.BBl        4755  4740  27.0  26.9
had.ARB        6072  6075  34.5  34.5
had.AlA         883   898   5.0   5.1
had.DHP        5337  5354  30.3  30.4
had.WtL         120   129   0.7   0.7
had.RPA        1131  1165   6.4   6.6
had.Wrf         719   687   4.1   3.9
had.Asp        6205  6309  35.2  35.8
had.HCD        2321  2313  13.2  13.1
had.THZ        2684  2717  15.2  15.4
had.Ccs         925   923   5.3   5.2
```

```
had.DXI         287   274  1.6  1.6
had.Dgo         433   424  2.5  2.4
had.APl         174   182  1.0  1.0
had.Ami          39    36  0.2  0.2
had.DTI         216   213  1.2  1.2
had.NHP         292   269  1.7  1.5
had.Fla          15    13  0.1  0.1
had.Metformin 11333 11345 64.4 64.4
had.GLP1       4419  4296 25.1 24.4
had.MetxSGLT2     0     0  0.0  0.0
had.MetxDPP4   3149  3174 17.9 18.0
had.SGLT2         0     1  0.0  0.0
had.longIns    2351  2315 13.4 13.1
had.mixIns      984  1023  5.6  5.8
had.DPP4       3060  3115 17.4 17.7
had.SU         4074  4116 23.1 23.4
had.intIns      928   939  5.3  5.3
had.fastIns    1027  1008  5.8  5.7
had.TZD          56    58  0.3  0.3
had.Acarbose     32    35  0.2  0.2
had.TZDxDPP4      1     0  0.0  0.0
got.Ins        4042  4241 23.0 24.1
got.Hyp       13759 13641 78.1 77.5
got.CVD       16016 15743 90.9 89.4
```

3.6 Overview of pre- and post matching

The number of persons and episodes:

```
> addmargins( with( oset, table(table(pnr)) ) )
     1      2      3      4      5      6      7      8      9     10     11    Sum
 99132  36028  13706   5015   1596    464    143     49     12      2      1 156148
```

```
> addmargins(
+ with( oset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4       0      1      2      3      4      5      6      7      8      9     10    Sum
  0        0  94727  30195   9798   3142    847    227     61     12      4      0 139013
  1     4405   5720   3758   1746    678    205     64     24      4      1      1  16606
  2      113    148    124     69     31     15     11      3      1      0      0    515
  3        2      3      2      1      3      2      1      0      0      0      0     14
  Sum   4520 100598  34079  11614   3854   1069    303     88     17      5      1 156148
```

```
> addmargins( with( mset, table(table(pnr)) ) )
    1     2     3     4     5     6   Sum
26625  3530   439    48     4     1 30647
```

```
> addmargins(
+ with( mset, table(DPP4=(tt<-table(pnr,Ixdr))[,1],SGLT2=tt[,2]) ) )
     SGLT2
DPP4      0     1     2     3     4     5   Sum
  0       0 12165  1261   137    12     1 13576
  1   14460  1826   228    29     2     1 16546
  2     443    62     6     0     0     0   511
  3      12     1     1     0     0     0    14
  Sum 14915 14054  1496   166    14     2 30647
```

`../rep/matchSGoth.tex`

The best overview is created if we list the tables for the matched and un-matched next to each other. However we first check that that have the same sets of rows:

```
> identical( rownames(dt.tab), rownames(dm.tab) )
[1] TRUE
```

```
> identical( rownames(ct.tab), rownames(cm.tab) )
[1] TRUE
```

```
> identical( rownames(mt.tab), rownames(mm.tab) )
[1] TRUE
```

```
> cbind( dt.tab, dm.tab )
                          SGLT2    Other SGLT2 Other   SGLT2   Other SGLT2 Other
Sex M                   10822.0 132244.0  61.2  58.3 10777.0 10801.0  61.2  61.3
F                        6856.0  94740.0  38.8  41.7  6833.0  6809.0  38.8  38.7
Index = First Line        157.0  70185.0   0.9  30.9   157.0   146.0   0.9   0.8
Index not FL: Mean / SD     8.9      8.4   5.2   5.7     8.9     8.9   5.2   5.6
Age at index <40          630.0  11106.0   3.6   4.9   627.0  1023.0   3.6   5.8
40                       2379.0  27582.0  13.5  12.2  2371.0  2600.0  13.5  14.8
50                       5310.0  50352.0  30.0  22.2  5279.0  4704.0  30.0  26.7
60                       5838.0  63988.0  33.0  28.2  5817.0  5160.0  33.0  29.3
70                       3028.0  50123.0  17.1  22.1  3023.0  3153.0  17.2  17.9
80+                       493.0  23833.0   2.8  10.5   493.0   970.0   2.8   5.5
Age: Mean / SD             60.4     63.2  11.0  13.6    60.4    60.4  11.0  12.7
Index date 2012            20.0   4468.0   0.1   2.0    20.0   109.0   0.1   0.6
2013                     1929.0  53123.0  10.9  23.4  1929.0  1875.0  11.0  10.6
2014                     3038.0  52261.0  17.2  23.0  3038.0  2881.0  17.3  16.4
2015                     4761.0  56853.0  26.9  25.0  4747.0  4940.0  27.0  28.1
2016                     7930.0  60279.0  44.9  26.6  7876.0  7805.0  44.7  44.3
Date of first line 1995   739.0  10675.0   4.2   4.7   736.0   965.0   4.2   5.5
1996                      294.0   3164.0   1.7   1.4   293.0   330.0   1.7   1.9
1997                      306.0   3145.0   1.7   1.4   306.0   308.0   1.7   1.7
1998                      415.0   4008.0   2.3   1.8   412.0   433.0   2.3   2.5
1999                      525.0   4604.0   3.0   2.0   525.0   508.0   3.0   2.9
2000                      564.0   4963.0   3.2   2.2   562.0   595.0   3.2   3.4
2001                      652.0   5527.0   3.7   2.4   649.0   657.0   3.7   3.7
2002                      753.0   5860.0   4.3   2.6   750.0   695.0   4.3   3.9
2003                      919.0   7273.0   5.2   3.2   912.0   870.0   5.2   4.9
2004                      953.0   7504.0   5.4   3.3   945.0   893.0   5.4   5.1
2005                     1048.0   8005.0   5.9   3.5  1044.0   943.0   5.9   5.4
2006                     1173.0   8560.0   6.6   3.8  1171.0  1022.0   6.6   5.8
2007                     1242.0   9342.0   7.0   4.1  1235.0  1096.0   7.0   6.2
2008                     1288.0  10100.0   7.3   4.4  1284.0  1238.0   7.3   7.0
2009                     1315.0  10342.0   7.4   4.6  1307.0  1190.0   7.4   6.8
2010                     1301.0  11079.0   7.4   4.9  1299.0  1219.0   7.4   6.9
2011                     1158.0  11679.0   6.6   5.1  1155.0  1191.0   6.6   6.8
2012                      900.0  11901.0   5.1   5.2   895.0  1060.0   5.1   6.0
2013                      725.0  25332.0   4.1  11.2   724.0   805.0   4.1   4.6
2014                      593.0  21549.0   3.4   9.5   591.0   664.0   3.4   3.8
2015                      481.0  21609.0   2.7   9.5   481.0   563.0   2.7   3.2
2016                      334.0  20763.0   1.9   9.1   334.0   365.0   1.9   2.1
Frailty 0               11663.0 145101.0  66.0  63.9 11622.0 11660.0  66.0  66.2
1                        6015.0  81883.0  34.0  36.1  5988.0  5950.0  34.0  33.8
```

```
> cbind( ct.tab, cm.tab )
```

```
            SGLT2  Other SGLT2 Other SGLT2 Other SGLT2 Other
prv.FL      17521 156799  99.1  69.1 17453 17464  99.1  99.2
prv.TIA       480   7881   2.7   3.5   479   434   2.7   2.5
prv.Angina   2348  29626  13.3  13.1  2336  2371  13.3  13.5
prv.Bleed     737  13032   4.2   5.7   731   692   4.2   3.9
prv.COPD      584  12222   3.3   5.4   584   566   3.3   3.2
prv.PAD       861  15553   4.9   6.9   861   839   4.9   4.8
prv.HF        702  13182   4.0   5.8   701   737   4.0   4.2
prv.Cancer    862  20305   4.9   8.9   861   906   4.9   5.1
prv.DMcompl  3297  27477  18.7  12.1  3274  3272  18.6  18.6
prv.Neuro    1032   9309   5.8   4.1  1027   998   5.8   5.7
prv.DKD       671   8484   3.8   3.7   670   710   3.8   4.0
prv.DiaEye   2204  20020  12.5   8.8  2191  2271  12.4  12.9
prv.Hypo      613   8993   3.5   4.0   613   594   3.5   3.4
prv.AtrFib   1042  18499   5.9   8.1  1039   991   5.9   5.6
prv.MI       1412  19911   8.0   8.8  1406  1399   8.0   7.9
prv.UnstAng  653   8459   3.7   3.7   647   628   3.7   3.6
prv.HmStr     144   2642   0.8   1.2   144   147   0.8   0.8
prv.DiaFoot   156   2295   0.9   1.0   156   135   0.9   0.8
prv.Other     814  11625   4.6   5.1   811   773   4.6   4.4
prv.PeriAng   902  10607   5.1   4.7   898   894   5.1   5.1
prv.IscStr    828  15774   4.7   6.9   824   825   4.7   4.7
prv.Amp        17    543   0.1   0.2    17    12   0.1   0.1
prv.CKD       101   6537   0.6   2.9   101    81   0.6   0.5
prv.PCIsten   156   2317   0.9   1.0   156   167   0.9   0.9
prv.CABG      477   6534   2.7   2.9   475   464   2.7   2.6
prv.Keto       95   2156   0.5   0.9    95   102   0.5   0.6
prv.Dial        1     80   0.0   0.0     1     0   0.0   0.0
pre.CVD      5268  76805  29.8  33.8  5248  5195  29.8  29.5
pre.Str      1263  22710   7.1  10.0  1258  1251   7.1   7.1
pre.FPA      1001  12080   5.7   5.3   997   975   5.7   5.5
pre.Mic      6021  53275  34.1  23.5  5988  5899  34.0  33.5
> cbind( mt.tab, mm.tab )
              SGLT2  Other SGLT2 Other SGLT2 Other SGLT2 Other
had.ACE        6830  72133  38.6  31.8  6802  6962  38.6  39.5
had.Sta       13263 126144  75.0  55.6 13204 13336  75.0  75.7
had.BBl        4771  63033  27.0  27.8  4755  4740  27.0  26.9
had.ARB        6104  56367  34.5  24.8  6072  6075  34.5  34.5
had.AlA         883  14102   5.0   6.2   883   898   5.0   5.1
had.DHP        5354  59189  30.3  26.1  5337  5354  30.3  30.4
had.WtL         120   1029   0.7   0.5   120   129   0.7   0.7
had.RPA        1134  16626   6.4   7.3  1131  1165   6.4   6.6
had.Wrf         721  14724   4.1   6.5   719   687   4.1   3.9
had.Asp        6226  68351  35.2  30.1  6205  6309  35.2  35.8
had.HCD        2330  44177  13.2  19.5  2321  2313  13.2  13.1
had.THZ        2697  33724  15.3  14.9  2684  2717  15.2  15.4
had.Ccs         925  21060   5.2   9.3   925   923   5.3   5.2
had.DXI         288   4525   1.6   2.0   287   274   1.6   1.6
had.Dgo         434  10410   2.5   4.6   433   424   2.5   2.4
had.APl         175   3882   1.0   1.7   174   182   1.0   1.0
had.Ami          39   1328   0.2   0.6    39    36   0.2   0.2
had.DTI         218   3451   1.2   1.5   216   213   1.2   1.2
had.NHP         297   3665   1.7   1.6   292   269   1.7   1.5
had.Fla          15    200   0.1   0.1    15    13   0.1   0.1
had.Metformin 11391  80273  64.4  35.4 11333 11345  64.4  64.4
had.GLP1       4470  13314  25.3   5.9  4419  4296  25.1  24.4
had.MetxSGLT2     0    215   0.0   0.1     0     0   0.0   0.0
```

```
had.MetxDPP4   3192   8967  18.1   4.0  3149  3174  17.9  18.0
had.SGLT2         0   5432   0.0   2.4     0     1   0.0   0.0
had.longIns    2375  11834  13.4   5.2  2351  2315  13.4  13.1
had.mixIns      984  11555   5.6   5.1   984  1023   5.6   5.8
had.DPP4       3085  14701  17.5   6.5  3060  3115  17.4  17.7
had.SU         4095  30627  23.2  13.5  4074  4116  23.1  23.4
had.intIns      932  13647   5.3   6.0   928   939   5.3   5.3
had.fastIns    1034   7846   5.8   3.5  1027  1008   5.8   5.7
had.TZD          58    224   0.3   0.1    56    58   0.3   0.3
had.Acarbose     32    229   0.2   0.1    32    35   0.2   0.2
had.TZDxDPP4      1      1   0.0   0.0     1     0   0.0   0.0
got.Ins        4067  36359  23.0  16.0  4042  4241  23.0  24.1
got.Hyp       13819 152904  78.2  67.4 13759 13641  78.1  77.5
got.CVD       16183 176968  91.5  78.0 16016 15743  90.9  89.4
> save( dt.tab, dm.tab,
+       ct.tab, cm.tab,
+       mt.tab, mm.tab, file="btabSGoth.Rda" )
```

3.7 Survival analysis datasets: Lexis objects

In this section we take the original and the matched data and set up `Lexis`-objects for the survival analyses; we make separate objects for Death, heart failure (HF) and combined outcomes.

First get the relevant data:

```
> library( Epi )
> library( survival )
> print( sessionInfo(), l=F )
R version 3.5.0 (2018-04-23)
Platform: x86_64-w64-mingw32/x64 (64-bit)
Running under: Windows Server 2012 R2 x64 (build 9600)

Matrix products: default

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

other attached packages:
[1] survival_2.41-3 Epi_2.30

loaded via a namespace (and not attached):
 [1] cmprsk_2.2-7      zoo_1.8-1         MASS_7.3-49       compiler_3.5.0
 [5] Matrix_1.2-14     plyr_1.8.4        parallel_3.5.0    tools_3.5.0
 [9] etm_0.6-2         Rcpp_0.12.16      splines_3.5.0     grid_3.5.0
[13] numDeriv_2016.8-1 lattice_0.20-35
> clear()
> load( file = "adatSGoth.Rda" )
> lls()
  name    mode    class      dim                size(Kb)
1 mset    list    data.frame 35220 171          53,136.6
2 oset    list    data.frame 244662 171        355,719.3
3 pscore  numeric table      96 2                    7.8
4 psmatch numeric table      94 2                    7.7
```

...now input from ../rep/anaSGoth.tex

```
> cbind( table( apply( table(mset$pnr,mset$Ixdr), 1, paste, collapse="-") ) )
     [,1]
0-1 12165
0-2  1261
0-3   137
0-4    12
0-5     1
1-0 14460
1-1  1826
1-2   228
1-3    29
1-4     2
1-5     1
2-0   443
2-1    62
2-2     6
3-0    12
3-1     1
3-2     1
```

We will follow persons in episodes from date of new use, `doIx`, till either date of event.

For later use we define both the time since index (`tfi`) and current date (period — `per`) and current age (`cua`) as timescales. The latter not to be confused with age at index date, `age`.

3.8 Collecting analysis results and key data

We want to collect analysis results and background data for the analyses. The latter are classified by index drug and PY/events, the former by adjusted/non-adjusted analysis and HR/c.i./s.e. In addition both are classified by endpoint, data, and subset:

```
> lst <- list( endp = c("HF","ACD","ACD+HF","CVDD","MI","Str","IscStr",
+                        "CVDD+MI+Str","ACD+MI+Str","DKD"),
+              data = c("OnDr","Total"),
+               sub = c("AllPtt","preCVD","noCVD") )
> dat <- NArray( c( lst, list( ix = c("SGLT2","Other"),
+                              dat = c("N","PY","Event") ) ) )
> res <- NArray( c( lst, list( adj = c("Raw","Adj"),
+                               res = c("HR","lo","up","se") ) ) )
> length( dat ) ; str( dat )
[1] 360

 logi [1:10, 1:2, 1:3, 1:2, 1:3] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "Other"
  ..$ dat : chr [1:3] "N" "PY" "Event"

> length( res ) ; str( res )

[1] 480

 logi [1:10, 1:2, 1:3, 1:2, 1:4] NA NA NA NA NA NA ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
```

```
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ adj : chr [1:2] "Raw" "Adj"
  ..$ res : chr [1:4] "HR" "lo" "up" "se"
```

3.9 Survival dataset: `Lexis` objects

Here is a definition of a function that produces a Lexis object with follow-up till `mset$doX` for the event `D`:

```
> mkLex <-
+ function( )
+    {
+ Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+        exit.status = factor( D, labels=c("OnDr","Event") ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
+ Lx <- cutLexis( Lx, cut = Lx$doTm,
+                 new.state = "OffDr",
+                       pre = "OnDr" )
+ Lx
+    }
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex( )
NOTE: entry.status has been set to "OnDr" for all.
```

```
> summary( lxHF )
```

```
Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  25766  9054   400     35220     9454   38479.17     35220
  OffDr     0  8947   107      9054      107   10025.73      9054
  Sum   25766 18001   507     44274     9561   48504.90     35220
```

```
> summary( lxHF, by="Ixdr" )
```

```
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12572  4887   151     17610     5038   18851.19     17610
  OffDr     0  4819    68      4887       68    5592.04      4887
  Sum   12572  9706   219     22497     5106   24443.23     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  13194  4167   249     17610     4416   19627.99     17610
  OffDr     0  4128    39      4167       39    4433.69      4167
  Sum   13194  8295   288     21777     4455   24061.68     17610
```

3.9.1 Follow-up data and events

First we devise a function to extract the person-years and events from the Lexis object:

```
> fill.dat <-
+ function( LexDat, outc )
+ {
+ whc <- c(" Persons:","Risk time:","Event")
+ cat( outc, ":\n" )
+ print( sm <- summary( LexDat, by="Ixdr" ) )
+ s2 <- summary( LexDat, by=c("Ixdr","pre.CVD") )
+ for( ix in c("Other","SGLT2") )
+    {
+ dat[outc,,"AllPtt",ix,] <<- sm[[ix]][[1]][c(1,3),whc]
+ dat[outc,,"noCVD" ,ix,] <<- s2[[paste(ix,0,sep=".")]][[1]][c(1,3),whc]
+ dat[outc,,"preCVD",ix,] <<- s2[[paste(ix,1,sep=".")]][[1]][c(1,3),whc]
+    }
+ invisible(NULL)
+ }
> fill.dat( lxHF, "HF" )
HF :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12572  4887   151     17610     5038   18851.19     17610
  OffDr     0  4819    68      4887       68    5592.04      4887
  Sum   12572  9706   219     22497     5106   24443.23     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  13194  4167   249     17610     4416   19627.99     17610
  OffDr     0  4128    39      4167       39    4433.69      4167
  Sum   13194  8295   288     21777     4455   24061.68     17610

> round( ftable( dat[1:2,,,,], col.vars=c(4,5) ), 1 )

                  ix     SGLT2                      Other
                  dat        N       PY   Event         N       PY   Event
endp data  sub
HF   OnDr  AllPtt      17610.0 18851.2   151.0 17610.0 19628.0   249.0
           preCVD       5248.0  5334.9   124.0  5195.0  5350.6   189.0
           noCVD       12362.0 13516.3    27.0 12415.0 14277.4    60.0
     Total AllPtt      17610.0 24443.2   219.0 17610.0 24061.7   288.0
           preCVD       5248.0  6964.6   173.0  5195.0  6598.4   214.0
           noCVD       12362.0 17478.6    46.0 12415.0 17463.3    74.0
ACD  OnDr  AllPtt           NA      NA      NA      NA      NA      NA
           preCVD           NA      NA      NA      NA      NA      NA
           noCVD            NA      NA      NA      NA      NA      NA
     Total AllPtt           NA      NA      NA      NA      NA      NA
           preCVD           NA      NA      NA      NA      NA      NA
           noCVD            NA      NA      NA      NA      NA      NA
```

3.9.2 Analysis

Follow-up is now analysed by Cox-models adjusted and non-adjusted, total or on drug and separately for all persons and persons with and without prior CVD. These are named with an `m.` and combination of `r/a` (raw/adjusted), `t/d` (total/on drug) and `p/n/y` (patients/no CVD/yes CVD):

```
> m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
+                 I(Ixdr=="SGLT2") + cluster(pnr),
+                 data = lxHF )
> m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
+                               + prv.MI + prv.HF + prv.AtrFib + frail
+                               + had.BBl + had.NHP + had.AlA + had.ACE )
> m.dpr <- update( m.tpr, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.dpa <- update( m.tpa, data = subset( lxHF, lex.Cst=="OnDr" ) )
> m.tnr <- update( m.tpr, data = subset( lxHF, pre.CVD==1 ) )
> m.tna <- update( m.tpa, data = subset( lxHF, pre.CVD==1  ) )
> m.dnr <- update( m.dpr, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.dna <- update( m.dpa, data = subset( lxHF, pre.CVD==1 & lex.Cst=="OnDr" ) )
> m.tyr <- update( m.tpr, data = subset( lxHF, pre.CVD==0 ) )
> m.tya <- update( m.tpa, data = subset( lxHF, pre.CVD==0  ) )
> m.dyr <- update( m.dpr, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
> m.dya <- update( m.dpa, data = subset( lxHF, pre.CVD==0 & lex.Cst=="OnDr" ) )
```

With these models fitted we can now extract the HRs etc. and put into the right slots of `res`:

```
> get4 <- function( m ) ci.lin( m, subset="SGLT2", Exp=TRUE )[,c(5:7,2)]
> res["HF","Total","AllPtt","Raw",] <- get4( m.tpr )
> res["HF","Total","AllPtt","Adj",] <- get4( m.tpa )
> res["HF","OnDr" ,"AllPtt","Raw",] <- get4( m.dpr )
> res["HF","OnDr" ,"AllPtt","Adj",] <- get4( m.dpa )
> res["HF","Total","preCVD","Raw",] <- get4( m.tnr )
> res["HF","Total","preCVD","Adj",] <- get4( m.tna )
> res["HF","OnDr" ,"preCVD","Raw",] <- get4( m.dnr )
> res["HF","OnDr" ,"preCVD","Adj",] <- get4( m.dna )
> res["HF","Total","noCVD" ,"Raw",] <- get4( m.tyr )
> res["HF","Total","noCVD" ,"Adj",] <- get4( m.tya )
> res["HF","OnDr" ,"noCVD" ,"Raw",] <- get4( m.dyr )
> res["HF","OnDr" ,"noCVD" ,"Adj",] <- get4( m.dya )
```

This can now be packed into a function that does this for a given type of event:

```
> fill.res <- function( LexDat, outc )
+     {
+ m.tpr <- coxph( Surv( tfi, tfi+lex.dur, lex.Xst=="Event" ) ~
+              I(Ixdr=="SGLT2") + cluster(pnr),
+              data = LexDat )
+ m.tpa <- update( m.tpr, . ~ . + I(doIx-doBth) + sex + I(doIx-doDM)
+                               + prv.MI + prv.HF + prv.AtrFib + frail
+                               + had.BBl + had.NHP + had.AlA + had.ACE )
+ m.dpr <- update( m.tpr, data = subset( LexDat, lex.Cst=="OnDr" ) )
+ m.dpa <- update( m.tpa, data = subset( LexDat, lex.Cst=="OnDr" ) )
+
+ m.tnr <- update( m.tpr, data = subset( LexDat, pre.CVD==1 ) )
+ m.tna <- update( m.tpa, data = subset( LexDat, pre.CVD==1  ) )
+ m.dnr <- update( m.dpr, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
+ m.dna <- update( m.dpa, data = subset( LexDat, pre.CVD==1 & lex.Cst=="OnDr" ) )
```

```
+
+ m.tyr <- update( m.tpr, data = subset( LexDat, pre.CVD==0 ) )
+ m.tya <- update( m.tpa, data = subset( LexDat, pre.CVD==0  ) )
+ m.dyr <- update( m.dpr, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+ m.dya <- update( m.dpa, data = subset( LexDat, pre.CVD==0 & lex.Cst=="OnDr" ) )
+
+ res[outc,"Total","AllPtt","Raw",] <<- get4( m.tpr )
+ res[outc,"Total","AllPtt","Adj",] <<- get4( m.tpa )
+ res[outc,"OnDr" ,"AllPtt","Raw",] <<- get4( m.dpr )
+ res[outc,"OnDr" ,"AllPtt","Adj",] <<- get4( m.dpa )
+
+ res[outc,"Total","preCVD","Raw",] <<- get4( m.tnr )
+ res[outc,"Total","preCVD","Adj",] <<- get4( m.tna )
+ res[outc,"OnDr" ,"preCVD","Raw",] <<- get4( m.dnr )
+ res[outc,"OnDr" ,"preCVD","Adj",] <<- get4( m.dna )
+
+ res[outc,"Total","noCVD" ,"Raw",] <<- get4( m.tyr )
+ res[outc,"Total","noCVD" ,"Adj",] <<- get4( m.tya )
+ res[outc,"OnDr" ,"noCVD" ,"Raw",] <<- get4( m.dyr )
+ res[outc,"OnDr" ,"noCVD" ,"Adj",] <<- get4( m.dya )
+ invisible( NULL )
+   }
```

So combining this with the function that constructs the Lexis object we get:

```
> mset$D   <- with( mset, !is.na(deHF) & deHF<2017 )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>     lxHF <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxHF, "HF" )
> round( ftable( res[1:2,,,,], col.vars=c(2,5) ), 3 )
                data  OnDr                          Total
                res      HR    lo    up    se    HR    lo    up    se
endp sub    adj
HF   AllPtt Raw       0.621 0.508 0.759 0.102 0.750 0.628 0.894 0.090
            Adj       0.614 0.502 0.752 0.103 0.739 0.617 0.884 0.092
     preCVD Raw       0.653 0.521 0.818 0.115 0.773 0.633 0.942 0.101
            Adj       0.655 0.522 0.822 0.116 0.772 0.631 0.945 0.103
     noCVD  Raw       0.469 0.297 0.740 0.233 0.619 0.424 0.903 0.193
            Adj       0.469 0.297 0.741 0.233 0.616 0.421 0.900 0.194
ACD  AllPtt Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
     preCVD Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
     noCVD  Raw          NA    NA    NA    NA    NA    NA    NA    NA
            Adj          NA    NA    NA    NA    NA    NA    NA    NA
```

So we just repeat this for all types of outcome:

```
> mset$D   <- with( mset, !is.na(doDth) & doDth<2017 )
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
>    lxACD <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxACD, "ACD" )
> fill.dat( lxACD, "ACD" )
```

```
ACD :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12492  4942   176     17610     5118   18960.02     17610
  OffDr     0  4818   124      4942      124    5704.68      4942
  Sum   12492  9760   300     22552     5242   24664.70     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12857  4235   518     17610     4753   19839.60     17610
  OffDr     0  4096   139      4235      139    4523.57      4235
  Sum   12857  8331   657     21845     4892   24363.18     17610
```

```
> mset$D   <- with( mset, ( !is.na(deHF) | !is.na(doDth) ) &
+                         ( deHF<2017    | doDth<2017 ) )
> mset$doX <- with( mset, pmin( doDth, deHF, 2017, na.rm=TRUE ) )
>  lxACDHF <- mkLex()
```

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

```
> fill.res( lxACDHF, "ACD+HF" )
> fill.dat( lxACDHF, "ACD+HF" )
```

```
ACD+HF :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12399  4887   324     17610     5211   18851.19     17610
  OffDr     0  4703   184      4887      184    5592.04      4887
  Sum   12399  9590   508     22497     5395   24443.23     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12719  4167   724     17610     4891   19627.99     17610
  OffDr     0  4002   165      4167      165    4433.69      4167
  Sum   12719  8169   889     21777     5056   24061.68     17610
```

```
> mset$D   <- with( mset, !is.na(deCVDD) & deCVDD<2017 )
> mset$doX <- with( mset, pmin( doDth, deCVDD, 2017, na.rm=TRUE ) )
>   lxCVDD <- mkLex()
```

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

```
> fill.res( lxCVDD, "CVDD" )
> fill.dat( lxCVDD, "CVDD" )
```

```
CVDD :
$SGLT2

Transitions:
     To
```

```
From      OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   12640  4942    28     17610     4970   18960.02     17610
  OffDr      0  4919    23      4942       23    5704.68      4942
  Sum    12640  9861    51     22552     4993   24664.70     17610

$Other

Transitions:
     To
From      OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   13281  4235    94     17610     4329   19839.60     17610
  OffDr      0  4209    26      4235       26    4523.57      4235
  Sum    13281  8444   120     21845     4355   24363.18     17610
```

```
> mset$D   <- with( mset, !is.na(deMI) & deMI<2017 )
> mset$doX <- with( mset, pmin( doDth, deMI, 2017, na.rm=TRUE ) )
>     lxMI <- mkLex()
```

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

```
> fill.res( lxMI, "MI" )
> fill.dat( lxMI, "MI" )
```

```
MI :
$SGLT2

Transitions:
     To
From      OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   12594  4912   104     17610     5016   18884.71     17610
  OffDr      0  4877    35      4912       35    5645.23      4912
  Sum    12594  9789   139     22522     5051   24529.94     17610

$Other

Transitions:
     To
From      OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   13273  4203   134     17610     4337   19726.99     17610
  OffDr      0  4172    31      4203       31    4467.15      4203
  Sum    13273  8375   165     21813     4368   24194.14     17610
```

```
> mset$D   <- with( mset, !is.na(deStr) & deStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deStr, 2017, na.rm=TRUE ) )
>    lxStr <- mkLex()
```

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

```
> fill.res( lxStr, "Str" )
> fill.dat( lxStr, "Str" )
```

```
Str :
$SGLT2

Transitions:
     To
From      OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr   12594  4905   111     17610     5016   18876.26     17610
  OffDr      0  4870    35      4905       35    5638.26      4905
  Sum    12594  9775   146     22515     5051   24514.52     17610

$Other
```

```
Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  13264  4200   146     17610     4346   19731.68     17610
  OffDr     0  4166    34      4200       34    4460.67      4200
  Sum   13264  8366   180     21810     4380   24192.34     17610
```

```
> mset$D   <- with( mset, !is.na(deIscStr) & deIscStr<2017 )
> mset$doX <- with( mset, pmin( doDth, deIscStr, 2017, na.rm=TRUE ) )
>   lxIStr <- mkLex()
```

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

```
> fill.res( lxIStr, "IscStr" )
> fill.dat( lxIStr, "IscStr" )
```

```
IscStr :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12598  4909   103     17610     5012   18880.17     17610
  OffDr     0  4881    28      4909       28    5645.92      4909
  Sum   12598  9790   131     22519     5040   24526.08     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  13275  4206   129     17610     4335   19743.20     17610
  OffDr     0  4174    32      4206       32    4468.83      4206
  Sum   13275  8380   161     21816     4367   24212.03     17610
```

```
> mset$D   <- with( mset, ( ( !is.na(deCVDD) & deCVDD < 2017 ) |
+                           ( !is.na(deMI)   & deMI   < 2017 ) |
+                           ( !is.na(deStr)  & deStr  < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deCVDD, deMI, deStr, 2017, na.rm=TRUE ) )
>  lxCVDDx <- mkLex()
```

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

```
> fill.res( lxCVDDx, "CVDD+MI+Str" )
> fill.dat( lxCVDDx, "CVDD+MI+Str" )
```

```
CVDD+MI+Str :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12499  4876   235     17610     5111   18802.67     17610
  OffDr     0  4793    83      4876       83    5581.85      4876
  Sum   12499  9669   318     22486     5194   24384.52     17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
```

```
  OnDr  13094  4168   348      17610     4516   19621.37      17610
  OffDr     0  4084    84       4168       84    4404.24       4168
  Sum   13094  8252   432      21778     4600   24025.62      17610
> mset$D   <- with( mset, ( ( !is.na(doDth) & doDth < 2017 ) |
+                           ( !is.na(deMI)  & deMI  < 2017 ) |
+                           ( !is.na(deStr) & deStr < 2017 ) ) )
> mset$doX <- with( mset, pmin( doDth, deMI, deStr, 2017, na.rm=TRUE ) )
>   lxACDx <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxACDx, "ACD+MI+Str" )
> fill.dat( lxACDx, "ACD+MI+Str" )
ACD+MI+Str :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12356  4876   378      17610     5254   18802.67      17610
  OffDr     0  4699   177       4876      177    5581.85       4876
  Sum   12356  9575   555      22486     5431   24384.52      17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12684  4168   758      17610     4926   19621.37      17610
  OffDr     0  3976   192       4168      192    4404.24       4168
  Sum   12684  8144   950      21778     5118   24025.62      17610
> mset$D   <- with( mset, !is.na(deDKD) & deDKD<2017 )
> mset$doX <- with( mset, pmin( doDth, deDKD, 2017, na.rm=TRUE ) )
>    lxKid <- mkLex()
NOTE: entry.status has been set to "OnDr" for all.
> fill.res( lxKid, "DKD" )
> fill.dat( lxKid, "DKD" )
DKD :
$SGLT2

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  12583  4890   137      17610     5027   18845.32      17610
  OffDr     0  4845    45       4890       45    5610.39       4890
  Sum   12583  9735   182      22500     5072   24455.71      17610

$Other

Transitions:
     To
From     OnDr OffDr Event  Records:  Events: Risk time:  Persons:
  OnDr  13207  4163   240      17610     4403   19610.92      17610
  OffDr     0  4113    50       4163       50    4415.55       4163
  Sum   13207  8276   290      21773     4453   24026.47      17610
```

So we can summarize results:

```
> round( ftable( dat, col.vars=c(2,4,5) ), 0 )
                   data  OnDr                               Total
                   ix   SGLT2             Other             SGLT2             Other
                   dat      N    PY Event     N    PY Event     N    PY Event     N    PY Even
endp        sub
HF          AllPtt      17610 18851   151 17610 19628   249 17610 24443   219 17610 24062   28
            preCVD       5248  5335   124  5195  5351   189  5248  6965   173  5195  6598   21
            noCVD       12362 13516    27 12415 14277    60 12362 17479    46 12415 17463    7
ACD         AllPtt      17610 18960   176 17610 19840   518 17610 24665   300 17610 24363   65
            preCVD       5248  5426    83  5195  5500   261  5248  7138   149  5195  6813   32
            noCVD       12362 13534    93 12415 14340   257 12362 17527   151 12415 17550   33
ACD+HF      AllPtt      17610 18851   324 17610 19628   724 17610 24443   508 17610 24062   88
            preCVD       5248  5335   204  5195  5351   415  5248  6965   312  5195  6598   49
            noCVD       12362 13516   120 12415 14277   309 12362 17479   196 12415 17463   39
CVDD        AllPtt      17610 18960    28 17610 19840    94 17610 24665    51 17610 24363   12
            preCVD       5248  5426    22  5195  5500    64  5248  7138    34  5195  6813    7
            noCVD       12362 13534     6 12415 14340    30 12362 17527    17 12415 17550    4
MI          AllPtt      17610 18885   104 17610 19727   134 17610 24530   139 17610 24194   16
            preCVD       5248  5389    56  5195  5445    70  5248  7062    80  5195  6730    8
            noCVD       12362 13496    48 12415 14282    64 12362 17468    59 12415 17464    8
Str         AllPtt      17610 18876   111 17610 19732   146 17610 24515   146 17610 24192   18
            preCVD       5248  5391    57  5195  5442    84  5248  7060    79  5195  6715   10
            noCVD       12362 13485    54 12415 14289    62 12362 17455    67 12415 17477    7
IscStr      AllPtt      17610 18880   103 17610 19743   129 17610 24526   131 17610 24212   16
            preCVD       5248  5394    52  5195  5450    73  5248  7069    68  5195  6729    9
            noCVD       12362 13486    51 12415 14293    56 12362 17457    63 12415 17483    7
CVDD+MI+Str AllPtt      17610 18803   235 17610 19621   348 17610 24385   318 17610 24026   43
            preCVD       5248  5354   130  5195  5388   207  5248  6987   182  5195  6633   24
            noCVD       12362 13448   105 12415 14233   141 12362 17397   136 12415 17393   18
ACD+MI+Str  AllPtt      17610 18803   378 17610 19621   758 17610 24385   555 17610 24026   95
            preCVD       5248  5354   188  5195  5388   393  5248  6987   290  5195  6633   48
            noCVD       12362 13448   190 12415 14233   365 12362 17397   265 12415 17393   46
DKD         AllPtt      17610 18845   137 17610 19611   240 17610 24456   182 17610 24026   29
            preCVD       5248  5390    50  5195  5408    98  5248  7062    68  5195  6677   11
            noCVD       12362 13455    87 12415 14203   142 12362 17393   114 12415 17350   17
> round( ftable( res, col.vars=c(2,5) ), 3 )
                       data  OnDr                   Total
                       res     HR    lo    up    se    HR    lo    up    se
endp        sub    adj
HF          AllPtt Raw      0.621 0.508 0.759 0.102 0.750 0.628 0.894 0.090
                   Adj      0.614 0.502 0.752 0.103 0.739 0.617 0.884 0.092
            preCVD Raw      0.653 0.521 0.818 0.115 0.773 0.633 0.942 0.101
                   Adj      0.655 0.522 0.822 0.116 0.772 0.631 0.945 0.103
            noCVD  Raw      0.469 0.297 0.740 0.233 0.619 0.424 0.903 0.193
                   Adj      0.469 0.297 0.741 0.233 0.616 0.421 0.900 0.194
ACD         AllPtt Raw      0.351 0.296 0.417 0.087 0.451 0.394 0.518 0.070
                   Adj      0.417 0.350 0.496 0.088 0.511 0.445 0.586 0.070
            preCVD Raw      0.321 0.251 0.410 0.125 0.436 0.360 0.529 0.098
                   Adj      0.397 0.310 0.508 0.126 0.527 0.435 0.639 0.098
            noCVD  Raw      0.377 0.297 0.479 0.122 0.458 0.377 0.555 0.099
                   Adj      0.427 0.334 0.545 0.125 0.490 0.403 0.595 0.099
ACD+HF      AllPtt Raw      0.460 0.404 0.524 0.067 0.563 0.505 0.629 0.056
                   Adj      0.510 0.447 0.582 0.067 0.609 0.545 0.680 0.056
            preCVD Raw      0.490 0.415 0.579 0.085 0.599 0.520 0.689 0.072
                   Adj      0.541 0.458 0.639 0.085 0.659 0.572 0.760 0.073
            noCVD  Raw      0.404 0.327 0.500 0.108 0.499 0.419 0.593 0.088
                   Adj      0.441 0.356 0.548 0.110 0.521 0.438 0.620 0.089
```

```
CVDD        AllPtt Raw      0.311 0.204 0.474 0.214 0.424 0.306 0.588 0.167
                   Adj      0.373 0.241 0.578 0.223 0.490 0.351 0.684 0.170
            preCVD Raw      0.350 0.217 0.567 0.245 0.417 0.280 0.619 0.202
                   Adj      0.434 0.264 0.715 0.254 0.529 0.353 0.792 0.206
            noCVD  Raw      0.210 0.087 0.506 0.449 0.420 0.236 0.748 0.294
                   Adj      0.237 0.094 0.593 0.469 0.436 0.246 0.773 0.292
MI          AllPtt Raw      0.807 0.624 1.045 0.132 0.831 0.665 1.040 0.114
                   Adj      0.829 0.640 1.074 0.132 0.843 0.674 1.055 0.114
            preCVD Raw      0.804 0.565 1.142 0.179 0.908 0.671 1.228 0.154
                   Adj      0.866 0.608 1.234 0.181 0.959 0.709 1.297 0.154
            noCVD  Raw      0.798 0.546 1.169 0.194 0.731 0.524 1.021 0.170
                   Adj      0.799 0.546 1.168 0.194 0.729 0.523 1.017 0.170
Str         AllPtt Raw      0.785 0.611 1.009 0.128 0.799 0.638 1.001 0.115
                   Adj      0.819 0.636 1.055 0.129 0.819 0.653 1.027 0.116
            preCVD Raw      0.681 0.484 0.958 0.174 0.732 0.542 0.989 0.153
                   Adj      0.719 0.506 1.020 0.179 0.765 0.564 1.039 0.156
            noCVD  Raw      0.914 0.630 1.326 0.190 0.869 0.618 1.222 0.174
                   Adj      0.940 0.648 1.365 0.190 0.876 0.623 1.231 0.174
IscStr      AllPtt Raw      0.823 0.630 1.074 0.136 0.802 0.630 1.019 0.122
                   Adj      0.862 0.660 1.126 0.136 0.822 0.646 1.045 0.123
            preCVD Raw      0.715 0.496 1.030 0.186 0.722 0.522 0.999 0.165
                   Adj      0.754 0.519 1.094 0.190 0.754 0.543 1.048 0.168
            noCVD  Raw      0.953 0.644 1.409 0.200 0.887 0.621 1.267 0.182
                   Adj      0.986 0.667 1.459 0.200 0.896 0.627 1.279 0.182
CVDD+MI+Str AllPtt Raw      0.700 0.593 0.827 0.085 0.727 0.628 0.842 0.075
                   Adj      0.738 0.624 0.872 0.086 0.750 0.647 0.868 0.075
            preCVD Raw      0.631 0.507 0.787 0.112 0.698 0.576 0.846 0.098
                   Adj      0.693 0.554 0.867 0.114 0.752 0.620 0.912 0.099
            noCVD  Raw      0.784 0.607 1.013 0.131 0.746 0.595 0.935 0.115
                   Adj      0.799 0.618 1.033 0.131 0.747 0.596 0.936 0.115
ACD+MI+Str  AllPtt Raw      0.516 0.456 0.584 0.063 0.576 0.518 0.640 0.054
                   Adj      0.570 0.503 0.645 0.064 0.616 0.554 0.684 0.054
            preCVD Raw      0.480 0.404 0.571 0.088 0.572 0.495 0.661 0.074
                   Adj      0.549 0.461 0.653 0.089 0.639 0.552 0.740 0.074
            noCVD  Raw      0.545 0.456 0.651 0.091 0.567 0.487 0.661 0.078
                   Adj      0.581 0.486 0.694 0.091 0.582 0.500 0.678 0.077
DKD         AllPtt Raw      0.585 0.474 0.721 0.107 0.615 0.509 0.743 0.096
                   Adj      0.589 0.477 0.727 0.107 0.618 0.512 0.747 0.097
            preCVD Raw      0.508 0.361 0.714 0.174 0.549 0.405 0.745 0.156
                   Adj      0.533 0.377 0.753 0.177 0.576 0.423 0.785 0.158
            noCVD  Raw      0.634 0.485 0.830 0.137 0.655 0.514 0.834 0.123
                   Adj      0.630 0.481 0.825 0.138 0.652 0.511 0.830 0.124
```

3.10 Exposure tables by drug

We can then produce an overview of the number of persons, risk time and events by index medication; to this end we define functions that uses the `by` argument of the `summary.Lexis` to classify events and follow-up by index drug in various groupings:

```
> odr <- c("Met","SU","GLP1","DPP4","TZD","Aca","fIns","iIns","lIns","mIns")
> tabFU <- ZArray( list( Ix = c("Other",odr,
+                               "SGLT2","Dapa","Empa","Cana"),
+                        wh = c("nPers","FU","meanfu","sdFU","maxFU") ) )
> str( tabFU )
```

```
 num [1:15, 1:5] 0 0 0 0 0 0 0 0 0 0 ...
 - attr(*, "dimnames")=List of 2
  ..$ Ix: chr [1:15] "Other" "Met" "SU" "GLP1" ...
  ..$ wh: chr [1:5] "nPers" "FU" "meanfu" "sdFU" ...
```

```
> getFU <-
+ function( lx ) c( length( unique( lx$lex.id ) ),
+                   sum( lx$lex.dur ),
+                  mean( lx$lex.dur ),
+                    sd( lx$lex.dur ),
+                   max( lx$lex.dur ) )
> mset$doX <- with( mset, pmin( doDth, 2017, na.rm=TRUE ) )
> Lx <- Lexis( entry = list( per = doIx,
+                            cua = doIx-doBth,
+                            tfi = 0 ),
+               exit = list( per = doX ),
+               data = subset( mset, is.na(doDth) | doIx < doDth ) )
> summary( Lx, by="Ixdr", simplify=FALSE )
```

```
$SGLT2

Transitions:
     To
From     0  Records:  Events: Risk time:  Persons:
   0 17610     17610        0    24664.7     17610

$Other

Transitions:
     To
From     0  Records:  Events: Risk time:  Persons:
   0 17610     17610        0   24363.18     17610
```

```
> tabFU["Other",] <- getFU( subset( Lx, Ixdr=="Other") )
> for( oo in odr ) tabFU[oo,] <- getFU( subset( Lx, Epdr==oo) )
> tabFU["SGLT2",] <- getFU( subset( Lx, Ixdr=="SGLT2") )
> tabFU["Dapa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD15","A10BK01") ) )
> tabFU["Cana" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD16","A10BK02") ) )
> tabFU["Empa" ,] <- getFU( subset( Lx, Ixatc %in% c("A10BD20","A10BK03") ) )
> round( tabFU, 2 )
```

```
       wh
Ix       nPers       FU meanfu sdFU maxFU
  Other 17610 24363.18   1.38 1.07  4.08
  Met    1938  2547.93   1.31 1.02  4.07
  SU     2086  3125.47   1.50 1.10  4.07
  GLP1   2606  3609.82   1.39 1.07  4.08
  DPP4   3653  4898.94   1.34 1.04  4.08
  TZD      25    47.80   1.91 1.35  3.98
  Aca      11    16.75   1.52 0.72  3.07
  fIns   1939  2435.78   1.26 1.05  4.08
  iIns   1235  2084.12   1.69 1.13  4.08
  lIns   3488  4452.67   1.28 1.02  4.07
  mIns    629  1143.88   1.82 1.12  4.07
  SGLT2 17610 24664.70   1.40 1.05  4.05
  Dapa  11064 19701.73   1.78 1.09  4.05
  Empa   6070  4308.64   0.71 0.52  2.35
  Cana    477   654.52   1.37 0.65  2.59
```

3.11 Saving it all

Fially we save all results:

```
> save( res, dat, tabFU, file = "resSGoth.Rda" )
```

3.12 Reformatting

The results are here reformatted to `Excel`-format, `xlsx`, by the `xlsx` pakage of R, so we load that concomitantly with the data.

```
> library( Epi )
> library( xlsx )
> clear()
> load( "btabSGoth.Rda" )
> load( "resSGoth.Rda" )
> lls()
  name   mode    class  dim              size(Kb)
1 cm.tab numeric matrix 31 4                  3.4
2 ct.tab numeric matrix 31 4                  3.4
3 dat    numeric array  10 2 3 2 3            5.5
4 dm.tab numeric matrix 40 4                  3.9
5 dt.tab numeric matrix 40 4                  3.9
6 mm.tab numeric matrix 37 4                  3.8
7 mt.tab numeric matrix 37 4                  3.8
8 res    numeric array  10 2 3 2 4            6.4
9 tabFU  numeric matrix 15 5                  2.6
```

With this in place we can now construct the tables wanted for the sheet in th desided order.

3.12.1 Baseline tables

In order to check that we get the rows correct we read the rownames from the supplied spreadsheet, in order to put these in as a column in the new sheet for control:

```
> cat("Sample size
+ Age, years
+ Women
+ CV-history
+ Myocardial infarction
+ Unstable angina
+ Heart failure
+ Atrial fibrillation
+ Stroke
+ PAD
+ Microvascular disease
+ CKD
+ Frailty (yes)
+ Metformin
+ SU
+ TZD
+ GLP1
+ DPP4
+ Insulin
```

```
                                                 ...now input from ../rep/2xlSGoth.tex
+ Anti hypertensive therapy
+ LOOP diuretics
+ Low ceiling diuretics
+ ACE Inhibitors
+ ARBs
+ Statin therapy
+ Beta blockers
+ Aldosterone antagonists
+ Index year
+ 2012
+ 2013
+ 2014
+ 2015
+ 2016
+ 2017
+ ", file='ol.txt' )
> ol <- read.table('ol.txt',header=FALSE,sep='\t',as.is=TRUE)
```

Baseline pre-matching

We can now construct the pre-matching table

```
> bt <- rbind( "Sample size"= dt.tab[1,2:1]+dt.tab[2,2:1],
+               "Age" = NA,
+               dt.tab["F",2:1,drop=FALSE],
+               ct.tab["pre.CVD",2:1,drop=FALSE],
+               ct.tab["prv.MI",2:1,drop=FALSE],
+               ct.tab["prv.UnstAng",2:1,drop=FALSE],
+               ct.tab["prv.HF",2:1,drop=FALSE],
+               ct.tab["prv.AtrFib",2:1,drop=FALSE],
+               ct.tab["pre.Str",2:1,drop=FALSE],
+               ct.tab["prv.PAD",2:1,drop=FALSE],
+               ct.tab["pre.Mic",2:1,drop=FALSE],
+               ct.tab["prv.CKD",2:1,drop=FALSE],
+               "Frail"=dt.tab["1",2:1],
+               mt.tab["had.Metformin",2:1,drop=FALSE],
+               mt.tab["had.SU",2:1,drop=FALSE],
+               mt.tab["had.TZD",2:1,drop=FALSE],
+               mt.tab["had.GLP1",2:1,drop=FALSE],
+               mt.tab["had.DPP4",2:1,drop=FALSE],
+               mt.tab["got.Ins",2:1,drop=FALSE],
+               mt.tab["got.Hyp",2:1,drop=FALSE],
+               mt.tab["had.HCD",2:1,drop=FALSE],
+               mt.tab["had.THZ",2:1,drop=FALSE],
+               mt.tab["had.ACE",2:1,drop=FALSE],
+               mt.tab["had.ARB",2:1,drop=FALSE],
+               mt.tab["had.Sta",2:1,drop=FALSE],
+               mt.tab["had.BBl",2:1,drop=FALSE],
+               mt.tab["had.AlA",2:1,drop=FALSE],
+               "Index year"=NA,
+               dt.tab["Index date 2012",2:1,drop=FALSE],
+               dt.tab["2013",2:1,drop=FALSE],
+               dt.tab["2014",2:1,drop=FALSE],
+               dt.tab["2015",2:1,drop=FALSE],
+               dt.tab["2016",2:1,drop=FALSE],
```

```
+               '2017'=NA)
> str(ol)
'data.frame':        34 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
> bt <- cbind(bt[,2],NA,NA,bt[,1],NA,NA)
> bt["Age",c(2,3,5,6)] <- dt.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bt ) <- c("SGLT-2","mean","sd","Other","mean","sd")
>  cbind( ol, bt )
                                        V1 SGLT-2 mean sd  Other mean   sd
Sample size                    Sample size  17678   NA NA 226984   NA   NA
Age                             Age, years     NA 60.4 11     NA 63.2 13.6
F                                    Women   6856   NA NA  94740   NA   NA
pre.CVD                         CV-history   5268   NA NA  76805   NA   NA
prv.MI               Myocardial infarction   1412   NA NA  19911   NA   NA
prv.UnstAng                Unstable angina    653   NA NA   8459   NA   NA
prv.HF                       Heart failure    702   NA NA  13182   NA   NA
prv.AtrFib             Atrial fibrillation   1042   NA NA  18499   NA   NA
pre.Str                             Stroke   1263   NA NA  22710   NA   NA
prv.PAD                               PAD     861   NA NA  15553   NA   NA
pre.Mic              Microvascular disease   6021   NA NA  53275   NA   NA
prv.CKD                                CKD    101   NA NA   6537   NA   NA
Frail                        Frailty (yes)   6015   NA NA  81883   NA   NA
had.Metformin                    Metformin  11391   NA NA  80273   NA   NA
had.SU                                  SU   4095   NA NA  30627   NA   NA
had.TZD                               TZD      58   NA NA    224   NA   NA
had.GLP1                             GLP1    4470   NA NA  13314   NA   NA
had.DPP4                              DPP4   3085   NA NA  14701   NA   NA
got.Ins                           Insulin    4067   NA NA  36359   NA   NA
got.Hyp         Anti hypertensive therapy   13819   NA NA 152904   NA   NA
had.HCD                    LOOP diuretics    2330   NA NA  44177   NA   NA
had.THZ              Low ceiling diuretics   2697   NA NA  33724   NA   NA
had.ACE                     ACE Inhibitors   6830   NA NA  72133   NA   NA
had.ARB                               ARBs   6104   NA NA  56367   NA   NA
had.Sta                     Statin therapy  13263   NA NA 126144   NA   NA
had.BBl                      Beta blockers   4771   NA NA  63033   NA   NA
had.AlA            Aldosterone antagonists    883   NA NA  14102   NA   NA
Index year                      Index year     NA   NA NA     NA   NA   NA
Index date 2012                       2012     20   NA NA   4468   NA   NA
2013                                  2013   1929   NA NA  53123   NA   NA
2014                                  2014   3038   NA NA  52261   NA   NA
2015                                  2015   4761   NA NA  56853   NA   NA
2016                                  2016   7930   NA NA  60279   NA   NA
2017                                  2017     NA   NA NA     NA   NA   NA

> write.xlsx( cbind( 'Org. labs'=ol, bt ),
+             "SGoth.xlsx",
+ sheetName = "Baseline pre-matching",
+    append = FALSE,
+    showNA = FALSE )
```

Baseline after matching

The data for post matching have exactly the same structure; the tables are just called ’`m.tab`’ instad of ’`t.tab`’:

```
> bm <- rbind( "Sample size"= dm.tab[1,2:1]+dm.tab[2,2:1],
+               "Age" = NA,
+               dm.tab["F",2:1,drop=FALSE],
+               cm.tab["pre.CVD",2:1,drop=FALSE],
+               cm.tab["prv.MI",2:1,drop=FALSE],
+               cm.tab["prv.UnstAng",2:1,drop=FALSE],
+               cm.tab["prv.HF",2:1,drop=FALSE],
+               cm.tab["prv.AtrFib",2:1,drop=FALSE],
+               cm.tab["pre.Str",2:1,drop=FALSE],
+               cm.tab["prv.PAD",2:1,drop=FALSE],
+               cm.tab["pre.Mic",2:1,drop=FALSE],
+               cm.tab["prv.CKD",2:1,drop=FALSE],
+               "Frail"=dm.tab["1",2:1],
+               mm.tab["had.Metformin",2:1,drop=FALSE],
+               mm.tab["had.SU",2:1,drop=FALSE],
+               mm.tab["had.TZD",2:1,drop=FALSE],
+               mm.tab["had.GLP1",2:1,drop=FALSE],
+               mm.tab["had.DPP4",2:1,drop=FALSE],
+               mm.tab["got.Ins",2:1,drop=FALSE],
+               mm.tab["got.Hyp",2:1,drop=FALSE],
+               mm.tab["had.HCD",2:1,drop=FALSE],
+               mm.tab["had.THZ",2:1,drop=FALSE],
+               mm.tab["had.ACE",2:1,drop=FALSE],
+               mm.tab["had.ARB",2:1,drop=FALSE],
+               mm.tab["had.Sta",2:1,drop=FALSE],
+               mm.tab["had.BBl",2:1,drop=FALSE],
+               mm.tab["had.AlA",2:1,drop=FALSE],
+               "Index year"=NA,
+               dm.tab["Index date 2012",2:1,drop=FALSE],
+               dm.tab["2013",2:1,drop=FALSE],
+               dm.tab["2014",2:1,drop=FALSE],
+               dm.tab["2015",2:1,drop=FALSE],
+               dm.tab["2016",2:1,drop=FALSE],
+               '2017'=NA)
> str(ol)
'data.frame':        34 obs. of  1 variable:
 $ V1: chr  "Sample size" "Age, years" "Women" "CV-history" ...
> bm <- cbind(bm[,2],NA,NA,bm[,1],NA,NA)
> bm["Age",c(2,3,5,6)] <- dm.tab["Age: Mean / SD",c(1,3,2,4)]
> colnames( bm ) <- c("SGLT-2","mean","sd","Other","mean","sd")
> cbind( ol, bm )
                                        V1 SGLT-2 mean sd Other mean   sd
Sample size                    Sample size  17610   NA NA 17610   NA   NA
Age                             Age, years     NA 60.4 11    NA 60.4 12.7
F                                    Women   6833   NA NA  6809   NA   NA
pre.CVD                         CV-history   5248   NA NA  5195   NA   NA
prv.MI               Myocardial infarction   1406   NA NA  1399   NA   NA
prv.UnstAng                Unstable angina    647   NA NA   628   NA   NA
prv.HF                       Heart failure    701   NA NA   737   NA   NA
prv.AtrFib             Atrial fibrillation   1039   NA NA   991   NA   NA
pre.Str                             Stroke   1258   NA NA  1251   NA   NA
prv.PAD                               PAD     861   NA NA   839   NA   NA
pre.Mic              Microvascular disease   5988   NA NA  5899   NA   NA
prv.CKD                                CKD    101   NA NA    81   NA   NA
Frail                        Frailty (yes)   5988   NA NA  5950   NA   NA
had.Metformin                    Metformin  11333   NA NA 11345   NA   NA
had.SU                                  SU   4074   NA NA  4116   NA   NA
```

```
had.TZD                               TZD      56   NA NA    58   NA   NA
had.GLP1                              GLP1   4419   NA NA  4296   NA   NA
had.DPP4                              DPP4   3060   NA NA  3115   NA   NA
got.Ins                           Insulin    4042   NA NA  4241   NA   NA
got.Hyp         Anti hypertensive therapy   13759   NA NA 13641   NA   NA
had.HCD                    LOOP diuretics    2321   NA NA  2313   NA   NA
had.THZ              Low ceiling diuretics   2684   NA NA  2717   NA   NA
had.ACE                     ACE Inhibitors   6802   NA NA  6962   NA   NA
had.ARB                               ARBs   6072   NA NA  6075   NA   NA
had.Sta                     Statin therapy  13204   NA NA 13336   NA   NA
had.BBl                      Beta blockers   4755   NA NA  4740   NA   NA
had.AlA            Aldosterone antagonists    883   NA NA   898   NA   NA
Index year                      Index year     NA   NA NA    NA   NA   NA
Index date 2012                       2012     20   NA NA   109   NA   NA
2013                                  2013   1929   NA NA  1875   NA   NA
2014                                  2014   3038   NA NA  2881   NA   NA
2015                                  2015   4747   NA NA  4940   NA   NA
2016                                  2016   7876   NA NA  7805   NA   NA
2017                                  2017     NA   NA NA    NA   NA   NA
> write.xlsx( cbind( 'Org. labs'=ol, bm ),
+             "SGoth.xlsx",
+ sheetName = "Baseline after matching",
+    append = TRUE,
+    showNA = FALSE )
```

3.12.2 Treatment distribution

```
> drnam <- c(
+ 'SGLT-2',
+ '   Dapagliflozin',
+ '   Empagliflozin',
+ '   Canagliflozin',
+ '   Ipragliflozin',
+ '   Luseogliflozin',
+ '   Tofugliflozin',
+ '-',
+ 'Other',
+ '  Metformin',
+ '  SU',
+ '  DPP-4',
+ '  TZD ',
+ '  GLP-1',
+ ' All insulin',
+ '  fast-acting Insulin',
+ '  intermediate-acting Insulin',
+ '  long-acting Insulin',
+ '  mix Insulin',
+ '  Acarbose',
+ '  Amylin alog',
+ '  Metiglinides' )
> FUtab <- tabFU[c(12:15,rep(NA,4),1,2,3,5,6,4,NA,8:11,7,NA,NA),]
> cbind( drnam, rownames(FUtab) )
```

```
      drnam
 [1,] "SGLT-2"                        "SGLT2"
```

```
 [2,] "   Dapagliflozin"              "Dapa"
 [3,] "   Empagliflozin"              "Empa"
 [4,] "   Canagliflozin"              "Cana"
 [5,] "   Ipragliflozin"              NA
 [6,] "   Luseogliflozin"             NA
 [7,] "   Tofugliflozin"              NA
 [8,] "-"                             NA
 [9,] "Other"                         "Other"
[10,] "  Metformin"                   "Met"
[11,] "  SU"                          "SU"
[12,] "  DPP-4"                       "DPP4"
[13,] "  TZD "                        "TZD"
[14,] "  GLP-1"                       "GLP1"
[15,] " All insulin"                  NA
[16,] "  fast-acting Insulin"         "fIns"
[17,] "  intermediate-acting Insulin" "iIns"
[18,] "  long-acting Insulin"         "lIns"
[19,] "  mix Insulin"                 "mIns"
[20,] "  Acarbose"                    "Aca"
[21,] "  Amylin alog"                 NA
[22,] "  Metiglinides"                NA
> FUtab[15,] <- apply( FUtab[16:19,], 2, sum )
> rownames(FUtab) <- drnam
> colnames(FUtab) <- c(
+ 'Number of patients',
+ 'Total follow-up time',
+ 'Mean follow-up time',
+ 'Sd follow-up time',
+ 'maximum follow-up time')
> FUtab
                               wh
Ix                               Number of patients Total follow-up time Mean follow-up time
  SGLT-2                                      17610          24664.69678           1.4006074
     Dapagliflozin                            11064          19701.72553           1.7807055
     Empagliflozin                             6070           4308.63518           0.7098246
     Canagliflozin                              477            654.51882           1.3721569
     Ipragliflozin                               NA                   NA                  NA
     Luseogliflozin                              NA                   NA                  NA
     Tofugliflozin                               NA                   NA                  NA
  -                                              NA                   NA                  NA
  Other                                       17610          24363.17522           1.3834852
    Metformin                                  1938           2547.93361           1.3147232
    SU                                         2086           3125.47023           1.4983079
    DPP-4                                      3653           4898.94251           1.3410738
    TZD                                          25             47.80287           1.9121150
    GLP-1                                      2606           3609.82341           1.3851970
   All insulin                                 7291          10116.45175           6.0388915
    fast-acting Insulin                        1939           2435.78303           1.2562058
    intermediate-acting Insulin                1235           2084.11841           1.6875453
    long-acting Insulin                        3488           4452.66804           1.2765677
    mix Insulin                                 629           1143.88227           1.8185728
    Acarbose                                     11             16.75086           1.5228051
    Amylin alog                                  NA                   NA                  NA
    Metiglinides                                 NA                   NA                  NA
                               wh
Ix                               Sd follow-up time maximum follow-up time
  SGLT-2                                1.0487551               4.051335
```

```
     Dapagliflozin                          1.0865149               4.051335
     Empagliflozin                          0.5157299               2.348392
     Canagliflozin                          0.6478901               2.589322
     Ipragliflozin                                 NA                      NA
     Luseogliflozin                                NA                      NA
     Tofugliflozin                                 NA                      NA
  -                                                NA                      NA
  Other                                     1.0653458               4.078713
    Metformin                               1.0169789               4.073238
    SU                                      1.0963919               4.070500
    DPP-4                                   1.0394548               4.078713
    TZD                                     1.3529273               3.982888
    GLP-1                                   1.0650624               4.075975
   All insulin                              4.3263044              16.303901
    fast-acting Insulin                     1.0514882               4.078713
    intermediate-acting Insulin             1.1338177               4.078713
    long-acting Insulin                     1.0243434               4.073238
    mix Insulin                             1.1166552               4.073238
    Acarbose                                0.7169525               3.068446
    Amylin alog                                    NA                      NA
    Metiglinides                                   NA                      NA
```

```
> write.xlsx( FUtab,
+             "SGoth.xlsx",
+ sheetName = "Treatment distribution",
+    append = TRUE,
+    showNA = FALSE )
```

3.12.3 Events

```
> cat(
+ 'Number of patients
+ Total follow-up time - on treatment
+ Number of patients with event - on treatment
+ Total follow-up time - ITT
+ Number of patients with event - ITT
+ ', file='oc' )
> ( oc <- read.table('oc',header=FALSE,sep='\t',as.is=TRUE)[,1] )
```

```
[1] "Number of patients"                           "Total follow-up time - on treatment"
[3] "Number of patients with event - on treatment" "Total follow-up time - ITT"
[5] "Number of patients with event - ITT"
```

```
> cat(
+ 'HHF
+ All-cause death
+ All-cause death or HHF
+ Cardiavascular death
+ Myocardial infarction
+ Stroke
+ Ischemic stroke
+ MACE (cardivascular death, MI or stroke)
+ modified MACE (All-cause death, MI or stroke)
+ Kidney disease
+ ', file='ol' )
> ( ol <- read.table('ol',header=FALSE,sep='\t',as.is=TRUE)[,1] )
```

```
 [1] "HHF"                                           "All-cause death"
 [3] "All-cause death or HHF"                        "Cardiavascular death"
 [5] "Myocardial infarction"                         "Stroke"
 [7] "Ischemic stroke"                               "MACE (cardivascular death, MI or stroke
 [9] "modified MACE (All-cause death, MI or stroke)" "Kidney disease"
```

The data for this is in the `dat` object:

```
> str( dat )
 num [1:10, 1:2, 1:3, 1:2, 1:3] 17610 17610 17610 17610 17610 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "Other"
  ..$ dat : chr [1:3] "N" "PY" "Event"
> cbind( ol, dimnames(dat)[[1]] )
      ol
 [1,] "HHF"                                            "HF"
 [2,] "All-cause death"                                "ACD"
 [3,] "All-cause death or HHF"                         "ACD+HF"
 [4,] "Cardiavascular death"                           "CVDD"
 [5,] "Myocardial infarction"                          "MI"
 [6,] "Stroke"                                         "Str"
 [7,] "Ischemic stroke"                                "IscStr"
 [8,] "MACE (cardivascular death, MI or stroke)"       "CVDD+MI+Str"
 [9,] "modified MACE (All-cause death, MI or stroke)" "ACD+MI+Str"
[10,] "Kidney disease"                                 "DKD"
> ft <- ftable( dat[,,1,1:2,,drop=FALSE], col.vars=c(4,2,5) )
> round( ft, 1 )
                   ix     SGLT2                                           Other
                   data    OnDr                   Total                    OnDr
                   dat        N      PY   Event       N      PY   Event       N      PY   Ever
endp        sub
HF          AllPtt      17610.0 18851.2   151.0 17610.0 24443.2   219.0 17610.0 19628.0   249.
ACD         AllPtt      17610.0 18960.0   176.0 17610.0 24664.7   300.0 17610.0 19839.6   518.
ACD+HF      AllPtt      17610.0 18851.2   324.0 17610.0 24443.2   508.0 17610.0 19628.0   724.
CVDD        AllPtt      17610.0 18960.0    28.0 17610.0 24664.7    51.0 17610.0 19839.6    94.
MI          AllPtt      17610.0 18884.7   104.0 17610.0 24529.9   139.0 17610.0 19727.0   134.
Str         AllPtt      17610.0 18876.3   111.0 17610.0 24514.5   146.0 17610.0 19731.7   146.
IscStr      AllPtt      17610.0 18880.2   103.0 17610.0 24526.1   131.0 17610.0 19743.2   129.
CVDD+MI+Str AllPtt      17610.0 18802.7   235.0 17610.0 24384.5   318.0 17610.0 19621.4   348.
ACD+MI+Str  AllPtt      17610.0 18802.7   378.0 17610.0 24384.5   555.0 17610.0 19621.4   758.
DKD         AllPtt      17610.0 18845.3   137.0 17610.0 24455.7   182.0 17610.0 19610.9   240.
```

This is the table needed (except for the column on persons, which shoudl not be repeated):

```
> py <- data.frame( as.matrix(ft) )[-c(4,10)]
> py
                   SGLT2_OnDr_N SGLT2_OnDr_PY SGLT2_OnDr_Event SGLT2_Total_PY SGLT2_Total_Ever
HF_AllPtt                 17610      18851.19              151       24443.23               21
ACD_AllPtt                17610      18960.02              176       24664.70               30
ACD+HF_AllPtt             17610      18851.19              324       24443.23               50
CVDD_AllPtt               17610      18960.02               28       24664.70                5
MI_AllPtt                 17610      18884.71              104       24529.94               13
Str_AllPtt                17610      18876.26              111       24514.52               14
```

```
IscStr_AllPtt             17610      18880.17              103       24526.08               13
CVDD+MI+Str_AllPtt        17610      18802.67              235       24384.52               31
ACD+MI+Str_AllPtt         17610      18802.67              378       24384.52               55
DKD_AllPtt                17610      18845.32              137       24455.71               18
                   Other_OnDr_N Other_OnDr_PY Other_OnDr_Event Other_Total_PY Other_Total_Ever
HF_AllPtt                 17610      19627.99              249       24061.68               28
ACD_AllPtt                17610      19839.60              518       24363.18               65
ACD+HF_AllPtt             17610      19627.99              724       24061.68               88
CVDD_AllPtt               17610      19839.60               94       24363.18               12
MI_AllPtt                 17610      19726.99              134       24194.14               16
Str_AllPtt                17610      19731.68              146       24192.34               18
IscStr_AllPtt             17610      19743.20              129       24212.03               16
CVDD+MI+Str_AllPtt        17610      19621.37              348       24025.62               43
ACD+MI+Str_AllPtt         17610      19621.37              758       24025.62               95
DKD_AllPtt                17610      19610.92              240       24026.47               29
> colnames( py )
 [1] "SGLT2_OnDr_N"      "SGLT2_OnDr_PY"     "SGLT2_OnDr_Event"  "SGLT2_Total_PY"
 [5] "SGLT2_Total_Event" "Other_OnDr_N"      "Other_OnDr_PY"     "Other_OnDr_Event"
 [9] "Other_Total_PY"    "Other_Total_Event"
> colnames(py) <- c(oc,oc[-1])
> rownames(py) <- ol
```

With this in order we can now write it to the excel sheet:

```
> write.xlsx( py,
+              "SGoth.xlsx",
+ sheetName = "Events",
+    append = TRUE,
+    showNA = FALSE )
```

3.12.4 Hazard ratios

```
> ft <- ftable((dat[c(1:3,9,5,6),1:2,1,"SGLT2",,drop=FALSE]+
+               dat[c(1:3,9,5,6),1:2,1,"Other",,drop=FALSE])[,,,c(1,1),],row.vars=c(1,2,3))
> YD <- data.frame(as.matrix(ft))
> HR <- data.frame(as.matrix(ftable(res[c(1:3,9,5,6),1:2,1,1:2,c(1,4)],row.vars=c(1,2,3))))
> Endpoint <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[1] )
> Adjusted <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[3] )
> Analysis <- sapply( strsplit( rownames(HR), "_" ), FUN=function(x) x[2] )
> ( HR <- cbind(Endpoint,Adjusted,Analysis,HR,YD)[,c(1:3,6:8,4:5)] )
                       Endpoint Adjusted Analysis     N       PY Event        HR         se
HF_OnDr_Raw                  HF      Raw     OnDr 35220 38479.17   400 0.6211633 0.10232191
HF_OnDr_Adj                  HF      Adj     OnDr 35220 38479.17   400 0.6140398 0.10315404
HF_Total_Raw                 HF      Raw    Total 35220 48504.90   507 0.7497195 0.09005768
HF_Total_Adj                 HF      Adj    Total 35220 48504.90   507 0.7389602 0.09162821
ACD_OnDr_Raw                ACD      Raw     OnDr 35220 38799.62   694 0.3514844 0.08720105
ACD_OnDr_Adj                ACD      Adj     OnDr 35220 38799.62   694 0.4167922 0.08842890
ACD_Total_Raw               ACD      Raw    Total 35220 49027.87   957 0.4513379 0.06982434
ACD_Total_Adj               ACD      Adj    Total 35220 49027.87   957 0.5107222 0.07007331
ACD+HF_OnDr_Raw          ACD+HF      Raw     OnDr 35220 38479.17  1048 0.4598323 0.06662555
ACD+HF_OnDr_Adj          ACD+HF      Adj     OnDr 35220 38479.17  1048 0.5097771 0.06748081
ACD+HF_Total_Raw         ACD+HF      Raw    Total 35220 48504.90  1397 0.5633668 0.05585373
ACD+HF_Total_Adj         ACD+HF      Adj    Total 35220 48504.90  1397 0.6091078 0.05644259
ACD+MI+Str_OnDr_Raw  ACD+MI+Str      Raw     OnDr 35220 38424.05  1136 0.5155899 0.06314070
```

```
ACD+MI+Str_OnDr_Adj  ACD+MI+Str      Adj     OnDr 35220 38424.05  1136 0.5697949 0.06352040
ACD+MI+Str_Total_Raw ACD+MI+Str      Raw    Total 35220 48410.14  1505 0.5760104 0.05374049
ACD+MI+Str_Total_Adj ACD+MI+Str      Adj    Total 35220 48410.14  1505 0.6156372 0.05376023
MI_OnDr_Raw                  MI      Raw     OnDr 35220 38611.70   238 0.8074113 0.13157527
MI_OnDr_Adj                  MI      Adj     OnDr 35220 38611.70   238 0.8292776 0.13214032
MI_Total_Raw                 MI      Raw    Total 35220 48724.08   304 0.8313953 0.11404383
MI_Total_Adj                 MI      Adj    Total 35220 48724.08   304 0.8431956 0.11420636
Str_OnDr_Raw                Str      Raw     OnDr 35220 38607.93   257 0.7849597 0.12799201
Str_OnDr_Adj                Str      Adj     OnDr 35220 38607.93   257 0.8192622 0.12890886
Str_Total_Raw               Str      Raw    Total 35220 48706.87   326 0.7991662 0.11512132
Str_Total_Adj               Str      Adj    Total 35220 48706.87   326 0.8185580 0.11551996
```

```
> write.xlsx( HR,
+              "SGoth.xlsx",
+ sheetName = "Hazard ratios",
+    append = TRUE,
+    showNA = FALSE )
```

3.12.5 Subgroup OT

This is same as above, except the we restrict to “OnDr”, and subclassify by previous CVD:

```
> str(dat)
 num [1:10, 1:2, 1:3, 1:2, 1:3] 17610 17610 17610 17610 17610 ...
 - attr(*, "dimnames")=List of 5
  ..$ endp: chr [1:10] "HF" "ACD" "ACD+HF" "CVDD" ...
  ..$ data: chr [1:2] "OnDr" "Total"
  ..$ sub : chr [1:3] "AllPtt" "preCVD" "noCVD"
  ..$ ix  : chr [1:2] "SGLT2" "Other"
  ..$ dat : chr [1:3] "N" "PY" "Event"
```

```
> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"OnDr",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"OnDr",,"Other" ,],row.vars=c(1,2))))
> str( YD )
```

```
'data.frame':        18 obs. of  3 variables:
 $ N    : num  35220 10443 24777 35220 10443 ...
 $ PY   : num  38479 10686 27794 38800 10926 ...
 $ Event: num  400 313 87 694 344 ...
```

```
> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"OnDr",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+              "SGoth.xlsx",
+ sheetName = "Subgroups OT",
+    append = TRUE,
+    showNA = FALSE )
```

3.12.6 Subgroup ITT

This is same as above, except the we restrict to “Total”, and subclassify by previous CVD:

```
> YD <-
+     data.frame(as.matrix(ftable(dat[c(1:3,9,5,6),"Total",,"SGLT2",] +
+                                 dat[c(1:3,9,5,6),"Total",,"Other" ,],row.vars=c(1,2))))
> HR <-
+     data.frame(as.matrix(ftable(res[c(1:3,9,5,6),"Total",,"Adj",c(1,4)],row.vars=c(1,2))))
```

With this fixed we can now write the table:

```
> write.xlsx( cbind(YD,HR),
+             "SGoth.xlsx",
+ sheetName = "Subgroups ITT",
+    append = TRUE,
+    showNA = FALSE )
```

. . . now input from `../sas/sasdata.tex`

Chapter 4

SAS programs

4.1 Rationale and overview

On the server of Statistics Denmark we constructed a comprehensive Danish Diabetes register, also encompassing persons that are not on drug treatment for their disease. The register is based on existing Danish registers, and crucially contains a classification of patients as T1 / T2, which is most reliable for persons alive after 2005 and increasingly uncertain for patients as the distance from date of death to 2005 increases.

In the process we also constructed a diabetes *drug* register where only drug treated patients were included, with a debut date equal to the first date of drug dispense.

The type 2 patients from this register constitute the base for the current analyses.

The following documented programs sequentially construct analysis data sets, using both register data used for the construction of the diabetes register

All created data will be in the data folder as SAS-data sets.

We have used the following SAS-programs:

`01a-npr` Uses the national patient register (NPR) to generate two data sets:

- `compl` one record per date and complication for all complications of relevant types recorded in the NPR (11.2 mio), not restricted to diabetes patients.
- `wcompl` a dataset with one record per person (not only diabetes patients either) with dates of the *first* complication of each type. Naturally, some of these will be missing if the patients never saw the type of complication, but at least one will be non-missing.

`04d-rmps` Generates two data sets:

- `disp` all dispensations to T2 patients in the period of the Register of Medicine Products Statistics (`rmps`) (1995–2016).
- `xdisp` all dispensed drugs to T2 patients in the period of the Register of Medicine Products Statistics (`rmps`) (1995–2016). This dataset contains separate records for each drug dispensed in combination pills.

`07-newuse` Uses the drug register data to define new user episodes of drugs; that is first use of any drug after a period of at least 180 days. Drug, date of initiation and date of cessation (180 days after last dispense) are recorded.

4.2 Program documentation

The following is a listing of the SAS-programs (that is the `.log` and `.lst` files) used to generate the base datasets. Each is preceded by a very brief description; main technical points are included as comments in the program code, found in the `.log` files.

4.2.1 `optslibs.sas`

This is common set of declarative commands that defines a couple of options, the location of the raw and the derived data sets and some global macro variables holding the follow-up period. It is included as autoexec file in all runs.

```
* This is the autoexec file used throughout ;
* options used thoughout ;
options nocenter nonotes nomprint nosource2
        ps = 10000 /* 105 */
        ls = 90    /* 160 */
       obs = max
  formchar = '           '
/* format libraries we use */
 fmtsearch = ( dsfmt.times_personstatistik
               dsfmt.brancher
               dsfmt.uddannelser
               dsfmt.geokoder
               dsfmt.sundhed
               DMfmt.drugfmt
               ttfmt.ttformat00
               ttfmt.ttformat10
               ttfmt.ttformat20 ) ;

* data libraries ;
libname ekstn  'E:\rawdata\705093\Opdatering_2018\Eksterne data\' ;
libname grund  'E:\rawdata\705093\Opdatering_2018\Grunddata\' ;
libname popul  'E:\rawdata\705093\Opdatering_2018\Population\' ;
libname dmdat  'E:\workdata\705093\BxC\demoDM\DATA\' ;
libname dafdat 'E:\workdata\705093\BxC\daffodil\DATA\' ;

* format libraries ;
libname  ttfmt 'E:\workdata\705093\QSN_MLiJ\' ;
libname daffmt 'E:\workdata\705093\BxC\daffodil\data' ;
libname  DMfmt 'E:\workdata\705093\BxC\demoDM\data' ;
libname  dsfmt 'E:\Formater\SAS formater i Danmarks Statistik\FORMATKATALOG';

* useful constants ;
%let yrf = 1995 ; /* Range of years of population data */
%let yrl = 2017 ;
%let ini = '01JAN1996'd ; /* formerly primo and cutdate */
%let end = '01JAN2017'd ; * we have data including 2016 ;
%let t1oad = 15 ; * Age limit for OAD to define T1 ;
%let t1ins = 30 ; * Age limit for Insulin to define T1 ;
%let pcoslo = 20 ; * Age interval for pcos (years) ;
%let pcoshi = 40 ;
%let gdmint = 200 ; * distance between GDM dates to constitute 2 GDM events (days) ;

* macro to exclude observations with dates in GDM grace period (days) ;
%macro xgdm( xdate,
            gdmpre = 30,
            gdmwin = 365 ) ;
/* this loop should produce a warning to be sure all instances of GDM are covered */
```

```
%do n = 1 %to 12 ;
    if ( doGDM&n. - &gdmpre. ) < &xdate. < ( doGDM&n. + &gdmwin. ) then delete ;
%end ;
%mend ;

* page ;
options notes ;
```

4.3 01a-npr

Reads NPR-records and defines dates of complications or the types relevant for propensity score matching (data set `compl`), as well as a wide-data set with the date of first complication of each type (data set `wcompl`).

```
1                                  "Program: 01a-npr.sas"       11:46 Saturday, May 5, 2018







NOTE: AUTOEXEC processing completed.

1          * all complaications diagnoses ;
2          %macro mold ;
3          data compl1977_93 ;
4            set %do i = 1977 %to 1993 ;
5                grund.lpradm&i. ( keep = pnr recnum c_adiag d_inddto )
6                %end ; ;
7            compl = put( c_adiag, $icd8gr. ) ;
8            if compl ne 'Other' ;
9          run ;
10         %mend ;
11         %mold ;

NOTE: There were 536233 observations read from the data set GRUND.LPRADM1977.
NOTE: There were 576420 observations read from the data set GRUND.LPRADM1978.
NOTE: There were 593268 observations read from the data set GRUND.LPRADM1979.
NOTE: There were 603108 observations read from the data set GRUND.LPRADM1980.
NOTE: There were 602085 observations read from the data set GRUND.LPRADM1981.
NOTE: There were 625460 observations read from the data set GRUND.LPRADM1982.
NOTE: There were 651402 observations read from the data set GRUND.LPRADM1983.
NOTE: There were 669845 observations read from the data set GRUND.LPRADM1984.
NOTE: There were 694325 observations read from the data set GRUND.LPRADM1985.
NOTE: There were 727293 observations read from the data set GRUND.LPRADM1986.
NOTE: There were 754517 observations read from the data set GRUND.LPRADM1987.
NOTE: There were 792697 observations read from the data set GRUND.LPRADM1988.
NOTE: There were 821266 observations read from the data set GRUND.LPRADM1989.
NOTE: There were 852356 observations read from the data set GRUND.LPRADM1990.
NOTE: There were 874072 observations read from the data set GRUND.LPRADM1991.
NOTE: There were 922353 observations read from the data set GRUND.LPRADM1992.
NOTE: There were 989327 observations read from the data set GRUND.LPRADM1993.
NOTE: The data set WORK.COMPL1977_93 has 1108835 observations and 5 variables.
NOTE: DATA statement used (Total process time):
      real time           11.40 seconds
      cpu time            2.09 seconds


12
```

```
13          %macro mnew ;
14          data compl1994_16
15               all94 ( keep = pnr recnum d_inddto v_sengdage c_adiag compl ) ;
16               * the last is for recnum link and hospitalizatiand cancer compl ;
17            set %do i = 1994 %to 2016 ;
18                grund.lpradm&i.        ( keep = pnr recnum d_inddto v_sengdage c_adiag )
19                %end ;
20                grund.lpradm_uafamb16  ( keep = pnr recnum d_inddto v_sengdage c_adiag )
21                ;
22            * sometimes only 3 characters (or none) are given,
23              so we remove trailing blanks and add 0s ;
24             dpad = trim(c_adiag) || '00000' ;
25            compl = put( substr( dpad, 2, 4 ), $icd10gr. ) ;
26            if compl ne 'Other' then output compl1994_16 ;
27            output all94 ;
28          run ;
29          %mend ;
30          %mnew ;

WARNING: Multiple lengths were specified for the variable C_ADIAG by input data set(s).
         This can cause truncation of data.
NOTE: There were 2258243 observations read from the data set GRUND.LPRADM1994.
NOTE: There were 3099173 observations read from the data set GRUND.LPRADM1995.
NOTE: There were 3291605 observations read from the data set GRUND.LPRADM1996.
NOTE: There were 3381335 observations read from the data set GRUND.LPRADM1997.
NOTE: There were 3465118 observations read from the data set GRUND.LPRADM1998.
NOTE: There were 3573088 observations read from the data set GRUND.LPRADM1999.
NOTE: There were 3617722 observations read from the data set GRUND.LPRADM2000.
NOTE: There were 3907990 observations read from the data set GRUND.LPRADM2001.
NOTE: There were 4593801 observations read from the data set GRUND.LPRADM2002.
NOTE: There were 4630558 observations read from the data set GRUND.LPRADM2003.
NOTE: There were 4771082 observations read from the data set GRUND.LPRADM2004.
NOTE: There were 4971541 observations read from the data set GRUND.LPRADM2005.
NOTE: There were 5148309 observations read from the data set GRUND.LPRADM2006.
NOTE: There were 5177044 observations read from the data set GRUND.LPRADM2007.
NOTE: There were 5468126 observations read from the data set GRUND.LPRADM2008.
NOTE: There were 5892938 observations read from the data set GRUND.LPRADM2009.
NOTE: There were 5906084 observations read from the data set GRUND.LPRADM2010.
NOTE: There were 6204182 observations read from the data set GRUND.LPRADM2011.
NOTE: There were 6120611 observations read from the data set GRUND.LPRADM2012.
NOTE: There were 6305317 observations read from the data set GRUND.LPRADM2013.
NOTE: There were 6468603 observations read from the data set GRUND.LPRADM2014.
NOTE: There were 6878652 observations read from the data set GRUND.LPRADM2015.
NOTE: There were 6732177 observations read from the data set GRUND.LPRADM2016.
NOTE: There were 1952252 observations read from the data set GRUND.LPRADM_UAFAMB16.
NOTE: The data set WORK.COMPL1994_16 has 9721906 observations and 7 variables.
NOTE: The data set WORK.ALL94 has 113815551 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           1:48.17
      cpu time            32.34 seconds


31
32          data compl ( keep = pnr d_inddto recnum c_adiag compl ) ;
33            set compl1977_93
34                compl1994_16 ;
35          run ;

WARNING: Multiple lengths were specified for the variable C_ADIAG by input data set(s).
         This can cause truncation of data.
NOTE: There were 1108835 observations read from the data set WORK.COMPL1977_93.
NOTE: There were 9721906 observations read from the data set WORK.COMPL1994_16.
```

```
NOTE: The data set WORK.COMPL has 10830741 observations and 5 variables.
NOTE: DATA statement used (Total process time):
      real time           1.32 seconds
      cpu time            1.32 seconds


36
37         * permanent dataset for hospital stays in the last year
38                                         and cancer in the last 5 years ;
39         data dafdat.hosp ;
40           set all94 ;
41           if d_inddto ge '01dec2011'd or
42            ( d_inddto ge '01dec2007'd and compl eq 'Cancer' ) ;
43         run ;

NOTE: There were 113815551 observations read from the data set WORK.ALL94.
NOTE: The data set DAFDAT.HOSP has 34324010 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           17.62 seconds
      cpu time            10.20 seconds


44
45         * operations and procedures
46           - incomplete, dialysis is in a different table yet to be requested
47           - Bari and PCIsten, CABG not requested (yet) ;
48         %macro mnew ;
49         data opr ( keep = recnum compl c_opr d_odto ) ;
50           set %do i = 1996 %to 2016 ;
51               grund.lprsksop&i.
52               %end ;
53               grund.lprsksop_uafamb16
54               ;
55           if c_oprart eq '+'  then delete ;
56                                     compl = put( substr(c_opr,2,5), $icd5opr. ) ;
57           if compl eq 'Other' then compl = put( substr(c_opr,2,4), $icd4opr. ) ;
58           if compl eq 'Other' then compl = put( substr(c_opr,2,3), $icd3opr. ) ;
59           if compl eq 'Other' or substr(c_opr,2,6) in ('BJFD00','BJFD01')
60                                then delete ;
61         run ;
62         %mend ;
63         %mnew ;

NOTE: There were 26253 observations read from the data set GRUND.LPRSKSOP1996.
NOTE: There were 29149 observations read from the data set GRUND.LPRSKSOP1997.
NOTE: There were 36035 observations read from the data set GRUND.LPRSKSOP1998.
NOTE: There were 40427 observations read from the data set GRUND.LPRSKSOP1999.
NOTE: There were 40704 observations read from the data set GRUND.LPRSKSOP2000.
NOTE: There were 47885 observations read from the data set GRUND.LPRSKSOP2001.
NOTE: There were 55872 observations read from the data set GRUND.LPRSKSOP2002.
NOTE: There were 61537 observations read from the data set GRUND.LPRSKSOP2003.
NOTE: There were 68480 observations read from the data set GRUND.LPRSKSOP2004.
NOTE: There were 64246 observations read from the data set GRUND.LPRSKSOP2005.
NOTE: There were 67259 observations read from the data set GRUND.LPRSKSOP2006.
NOTE: There were 72370 observations read from the data set GRUND.LPRSKSOP2007.
NOTE: There were 92049 observations read from the data set GRUND.LPRSKSOP2008.
NOTE: There were 95820 observations read from the data set GRUND.LPRSKSOP2009.
NOTE: There were 89075 observations read from the data set GRUND.LPRSKSOP2010.
NOTE: There were 132453 observations read from the data set GRUND.LPRSKSOP2011.
NOTE: There were 99757 observations read from the data set GRUND.LPRSKSOP2012.
NOTE: There were 130556 observations read from the data set GRUND.LPRSKSOP2013.
NOTE: There were 128032 observations read from the data set GRUND.LPRSKSOP2014.
```

```
NOTE: There were 319846 observations read from the data set GRUND.LPRSKSOP2015.
NOTE: There were 176484 observations read from the data set GRUND.LPRSKSOP2016.
NOTE: There were 397906 observations read from the data set GRUND.LPRSKSOP_UAFAMB16.
NOTE: The data set WORK.OPR has 373450 observations and 4 variables.
NOTE: DATA statement used (Total process time):
      real time           4.84 seconds
      cpu time            0.48 seconds


64
65          * attach person numbers and dates using recnum ;
66          proc sort data = opr   ; by recnum ; run ;

NOTE: There were 373450 observations read from the data set WORK.OPR.
NOTE: The data set WORK.OPR has 373450 observations and 4 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.07 seconds
      cpu time            0.15 seconds


67          proc sort data = all94 ; by recnum ; run ;

NOTE: There were 113815551 observations read from the data set WORK.ALL94.
NOTE: The data set WORK.ALL94 has 113815551 observations and 6 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           55.79 seconds
      cpu time            1:46.48


68          data opr ;
69            merge opr ( in = op )
70                  all94 ;
71            by recnum ;
72            if op ;
73          run ;

NOTE: There were 373450 observations read from the data set WORK.OPR.
NOTE: There were 113815551 observations read from the data set WORK.ALL94.
NOTE: The data set WORK.OPR has 373450 observations and 8 variables.
NOTE: DATA statement used (Total process time):
      real time           19.34 seconds
      cpu time            19.34 seconds


74
75          * combine with the other complications ;
76          data dafdat.compl ;
77            set compl ( rename = ( d_inddto = doCompl ) )
78                  opr ( rename = ( d_odto   = doCompl ) ) ;
79          run ;

WARNING: Multiple lengths were specified for the variable C_ADIAG by input data set(s).
         This can cause truncation of data.
NOTE: There were 10830741 observations read from the data set WORK.COMPL.
NOTE: There were 373450 observations read from the data set WORK.OPR.
NOTE: The data set DAFDAT.COMPL has 11204191 observations and 8 variables.
NOTE: DATA statement used (Total process time):
      real time           3.07 seconds
      cpu time            1.54 seconds


80
```

```
81         title1 'All recorded complications / diagnoses' ;
82         proc tabulate  data = dafdat.compl  missing  noseps ;
83           where ( doCompl ge '01jan1977'd and
84                   doCompl lt '01jan2016'd ) ;
85           class compl doCompl ;
86           table compl,
87               ( all doCompl="Date" ) * f = comma9.
88               / rts = 9  condense ;
89           format doCompl year4. ;
90           keylabel n = ' ' ;
91         run ;

NOTE: There were 10665972 observations read from the data set DAFDAT.COMPL.
      WHERE (doCompl>='01JAN1977'D and doCompl<'01JAN2016'D);
NOTE: The PROCEDURE TABULATE printed page 1.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           3.93 seconds
      cpu time            5.18 seconds


92         title1 ;
93
94         proc sort  data = dafdat.compl ;
95           by pnr compl doCompl ;
96         run ;

NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set DAFDAT.COMPL has 11204191 observations and 8 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           6.59 seconds
      cpu time            6.06 seconds


97
98         * restrict to first complication of each type ;
99         data compl ;
100          set dafdat.compl ;
101          by pnr compl doCompl ;
102          if first.compl ;
103        run ;

NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL has 3670846 observations and 8 variables.
NOTE: DATA statement used (Total process time):
      real time           4.48 seconds
      cpu time            2.01 seconds


104
105        proc transpose  data = compl
106                         out = dafdat.wcompl ( drop = _NAME_ _LABEL_ )
107                      prefix = do ;
108          by pnr ;
109          var doCompl ;
110          id compl ;
111        run ;

NOTE: There were 3670846 observations read from the data set WORK.COMPL.
NOTE: The data set DAFDAT.WCOMPL has 1997992 observations and 28 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           6.14 seconds
      cpu time            4.70 seconds
```

```
112
113          title1 'First complication dates for each patient' ;
114          proc contents  data = dafdat.wcompl  varnum ; run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.01 seconds
      cpu time            0.00 seconds

NOTE: The PROCEDURE CONTENTS printed page 2.

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414
NOTE: The SAS System used:
      real time           4:03.11
      cpu time            3:12.04
```

4.3.1 01a-npr.lst

```
All recorded complications / diagnoses                    11:46 Saturday, May 5, 2018   1


                                                        Date

                All      1977      1978      1979      1980      1981      1982      1983

 compl
 Amp          3,616         .         .         .         .         .         .         .
 Angina     778,839       727       984     1,191     1,544     1,765     2,231     2,503
 AtrFib     752,964       342       367       440       504       591       647       752
 Bari            14         .         .         .         .         .         .         .
 Bleed      396,063       298       274       318       309       371       308       326
 CABG        44,125         .         .         .         .         .         .         .
 CKD        218,502       398       381       334       395       434       410       429
 COPD       750,894       816     1,019     1,026     1,196     1,180     1,268     1,341
 Cancer   4,079,961     6,552     8,725     9,689    10,745    11,613    13,190    15,189
 DKD         41,429        46        50        53        57        66        82        69
 DMcompl    155,493         4         6         6         6         5        10        11
 DiaEye     229,465     1,833     2,035     2,423     2,727     3,552     4,319     4,814
 DiaFoot     34,012         .         .         .         .         .         .         .
 Dial        15,397         .         .         .         .         .         .         .
 HF         432,557       500       632       701       795       897     1,006     1,237
 HmStr      126,008       598       719       738       772       946     1,031     1,112
 Hypo        97,435       331       363       433       513       440       471       537
 IscStr     516,149       768       932     1,120     1,131     1,316     1,671     1,740
 Keto        26,118         .         .         .         .         .         .         .
 MI         583,196     2,634     3,094     3,064     3,439     3,650     4,290     4,568
 Neuro       62,660     1,016     1,105     1,246     1,340     1,456     1,544     1,670
 Other      108,373         .         .         .         .         .         .         .
 PAD        667,245       511       688       836       930     1,029     1,227     1,544
 PCIsten     20,738         .         .         .         .         .         .         .
 PeriAng    190,503     7,448     8,641     9,278     9,444     9,637     9,937     9,758
 TIA        207,302       558       686       694       788       906     1,091     1,211
 UnstAng    126,914         .         .         .         .         .         .         .

(Continued)
```

```
                                              Date

           1984      1985      1986      1987      1988      1989      1990      1991

 compl
 Amp             .         .         .         .         .         .         .         .
 Angina      2,900     3,694     4,427     5,426     6,815     8,111     8,902    11,267
 AtrFib        847     1,065     1,272     1,613     1,925     2,479     3,021     3,721
 Bari            .         .         .         .         .         .         .         .
 Bleed         330       332       369       354       420       395       502       526
 CABG            .         .         .         .         .         .         .         .
 CKD           523       720       652       464       474       491       463       624
 COPD        1,610     1,884     2,040     2,240     2,544     3,065     3,825     4,724
 Cancer     15,990    17,703    19,903    22,738    25,813    28,629    35,127    40,342
 DKD            70        80       103        96       120       207       171       193
 DMcompl        11        20        39        28       119        91       204       321
 DiaEye      5,119     5,647     6,662     7,152     8,561     9,349     9,251     8,733
 DiaFoot         .         .         *         *         .         .         *         4
 Dial            .         .         .         *         .         .         .         9
 HF          1,335     1,685     1,859     2,320     2,902     3,677     4,936     6,034
 HmStr       1,205     1,256     1,343     1,445     1,468     1,632     1,795     2,101
 Hypo          596       642       663       737       738       818       872       960
 IscStr      1,999     2,101     2,069     2,117     2,207     2,372     2,684     3,085
 Keto            .         .         *         *         *         *         .         *
 MI          5,003     5,813     6,396     7,073     7,547     7,821     8,437     9,564
 Neuro       1,720     1,817     2,062     2,108     2,343     2,291     2,176     2,340
 Other           .         .         .         .         .         .         .         .
 PAD         1,780     1,844     2,043     2,193     2,518     2,753     3,442     4,424
 PCIsten         .         .         .         .         .         .         .         .
 PeriAng     9,989    10,521    11,033     5,431     4,805     4,592     4,497     4,630
 TIA         1,309     1,533     1,710     1,809     2,063     2,324     2,640     3,173
 UnstAng         .         .         .         .         .         *         *         6

(Continued)


                                              Date

           1992      1993      1994      1995      1996      1997      1998      1999

 compl
 Amp             .         .         .         .       159       143       138       146
 Angina     14,179    17,303    23,955    29,454    35,132    39,128    41,720    37,796
 AtrFib      5,099     7,002    11,097    14,221    16,955    19,554    22,436    26,325
 Bari            .         .         .         .         .         .         .         .
 Bleed         617       957    11,698    13,738    13,951    14,152    15,096    15,373
 CABG            .         .         .         .     2,056     2,356     2,662     3,005
 CKD           882       864     2,728     2,187     2,340     2,187     2,265     3,303
 COPD        6,438    10,415    15,188    20,620    23,621    27,418    30,499    33,229
 Cancer     51,739    88,044   142,598   144,761   145,634   150,686   147,842   149,616
 DKD           229       525     1,253     1,097     1,309     1,250     1,368     1,546
 DMcompl       386     3,112     4,588     5,190     5,055     5,836     6,346     7,430
 DiaEye      9,127    10,215     2,689     3,198     3,544     4,091     5,128     5,552
 DiaFoot         8        94       663       771       841     1,184     1,598     1,875
 Dial           17        86       923     2,170     2,044     2,555     2,865     2,519
 HF          7,812    10,528    13,690    15,350    15,454    14,983    16,378    16,904
 HmStr       2,345     2,727     4,065     4,442     4,660     4,712     5,109     5,017
 Hypo        1,098     1,195     2,037     3,288     3,465     3,646     3,552     4,144
 IscStr      3,494     5,111    17,156    20,605    21,323    22,431    24,264    26,631
 Keto            *        46       739       760       766       812       846       804
```

```
 MI          10,339     11,685     16,787     19,303     17,709     17,089     16,819     16,935
 Neuro        1,946      2,431        986        944      1,131      1,122      1,334      1,422
 Other            .          .          .          .      2,558      2,626      2,916      4,750
 PAD          5,379      7,541     23,861     25,570     28,048     26,885     27,251     27,482
 PCIsten          .          .          .          .        134        243        422      1,397
 PeriAng      4,177      4,406      1,586      1,499      2,047      2,016      2,055      2,298
 TIA          3,502      4,129      5,591      7,200      7,168      7,325      7,746      7,193
 UnstAng         11         90      2,835      3,545      4,052      4,505      4,993      6,009

(Continued)


                                                 Date

              2000       2001       2002       2003       2004       2005       2006       2007

 compl
 Amp            134        176        168        200        193        207        192        172
 Angina      36,037     35,094     35,706     33,888     32,354     32,772     31,498     27,318
 AtrFib      28,983     31,385     29,121     27,057     27,030     28,084     30,463     32,232
 Bari             .          .          .          .          .          .          *          *
 Bleed       16,845     17,287     18,080     18,233     18,677     18,219     18,499     18,408
 CABG         2,880      2,774      3,169      2,781      2,329      2,113      2,021      1,970
 CKD          4,129      5,614      7,128      7,765      8,600      9,260     10,339     12,022
 COPD        33,099     35,554     33,565     32,806     32,158     32,299     33,025     31,879
 Cancer     139,347    145,119    150,414    149,286    149,968    151,431    160,431    166,977
 DKD          1,584      1,714      1,590      1,791      1,780      1,809      2,117      1,484
 DMcompl      6,838      7,023      7,435      7,740      7,383      9,317      6,916      5,862
 DiaEye       5,167      5,300      5,097      7,290      7,729      8,849      7,172      7,051
 DiaFoot      1,901      1,594      1,580      1,509      1,392      1,188      1,411      1,407
 Dial         2,103          .          .          8          9          4         16         18
 HF          16,944     16,909     17,364     16,982     16,780     16,517     17,375     15,639
 HmStr        4,874      4,836      4,821      5,061      5,113      4,880      4,582      4,590
 Hypo         3,903      4,262      4,543      4,971      4,708      4,573      4,438      4,148
 IscStr      25,880     25,275     25,248     24,518     23,791     22,325     21,924     19,909
 Keto           830        803        953      1,069      1,070        987      1,084      1,221
 MI          18,325     20,356     23,944     25,263     25,187     24,546     23,264     23,629
 Neuro        1,963      1,806      1,745      1,700      1,319      1,546      1,224      1,057
 Other        5,114      5,076      5,074      5,489      5,865      5,453      5,597      6,057
 PAD         26,249     26,307     27,707     27,599     27,118     28,212     27,879     28,195
 PCIsten        709        831      1,291      1,480      1,715      1,903      1,739      1,723
 PeriAng      2,381      2,575      2,828      2,931      2,992      3,013      3,118      2,621
 TIA          6,863      7,053      7,216      7,226      7,247      7,695      7,882      7,811
 UnstAng      8,030      7,527      8,192      7,572      6,677      6,827      6,802      5,849

(Continued)


                                                 Date

              2008       2009       2010       2011       2012       2013       2014       2015

 compl
 Amp            173        206        225        179        173        218        206        208
 Angina      25,096     28,760     28,972     28,254     27,069     27,519     24,401     22,947
 AtrFib      35,398     40,019     41,170     44,999     48,707     54,362     54,392     57,287
 Bari             *          .          .          .          4          *          4          *
 Bleed       17,734     18,421     19,085     19,021     19,986     21,242     23,286     22,026
```

```
 CABG         1,674     1,810     1,770     1,785     1,627     1,728     1,814     1,801
 CKD         12,621    13,771    14,307    15,910    17,505    19,172    17,529    18,882
 COPD        33,010    34,114    33,751    35,447    35,978    37,977    38,029    40,997
 Cancer     190,242   191,686   189,552   198,961   191,358   199,012   196,123   207,186
 DKD          1,972     1,978     1,491     1,693     1,925     3,342     1,896     3,223
 DMcompl      8,511     7,781     5,657     6,218     6,622     9,581     5,004     8,781
 DiaEye       7,951     6,602     5,427     6,386     6,445     6,269     4,256     6,753
 DiaFoot      1,534     1,679     1,847     1,898     1,766     2,026     2,045     2,194
 Dial            16         8         5         *         *         6        10         *
 HF          16,719    18,154    18,186    19,096    19,544    21,405    20,913    22,415
 HmStr        4,521     4,446     4,484     4,227     4,436     4,586     4,600     4,713
 Hypo         4,349     4,256     4,084     3,698     3,456     3,689     3,490     3,328
 IscStr      19,952    19,835    19,562    18,944    20,031    19,944    20,469    20,215
 Keto         1,351     1,427     1,397     1,478     1,727     1,904     1,992     2,044
 MI          22,956    23,192    23,870    23,151    22,854    23,943    24,890    24,767
 Neuro        1,741     1,398     1,351     1,422     1,579     1,802     1,399     2,058
 Other        5,175     5,980     5,647     6,880     6,864     6,967     6,910     7,375
 PAD         29,546    30,073    30,617    31,186    31,666    32,898    30,575    31,639
 PCIsten      1,470     1,734       793       605       672       604       543       730
 PeriAng      3,002     2,803     2,857     2,985     3,163     4,377     4,118     5,014
 TIA          8,056     8,484     9,165     9,196     9,896    10,310    10,289    10,564
 UnstAng      6,095     5,547     5,399     5,475     5,451     5,321     5,414     4,685

First complication dates for each patient            11:46 Saturday, May 5, 2018   2

The CONTENTS Procedure

Data Set Name          DAFDAT.WCOMPL                 Observations            1997992
Member Type            DATA                          Variables               28
Engine                 V9                            Indexes                 0
Created                05/05/2018 11:50:02           Observation Length      232
Last Modified          05/05/2018 11:50:02           Deleted Observations    0
Protection                                           Compressed              NO
Data Set Type                                        Sorted                  NO
Label
Data Representation    WINDOWS_64
Encoding               wlatin1  Western (Windows)


                       Engine/Host Dependent Information

Data Set Page Size            65536
Number of Data Set Pages      7086
First Data Page               *
Max Obs per Page              282
Obs in First Data Page        265
Number of Data Set Repairs    0
ExtendObsCounter              YES
Filename                      E:\workdata\705093\BxC\daffodil\DATA\wcompl.sas7bdat
Release Created               9.0401M3
Host Created                  X64_SRV12


                     Variables in Creation Order

 #    Variable      Type    Len    Format     Informat    Label

 *    pnr           Char     12    $12.       $10.        Personnummer
 *    doTIA         Num       8    DATE9.
 *    doAngina      Num       8    DATE9.
 4    doBleed       Num       8    DATE9.
```

```
 5    doCOPD       Num       8    DATE9.
 6    doPAD        Num       8    DATE9.
 7    doHF         Num       8    DATE9.
 8    doCancer     Num       8    DATE9.
 9    doDMcompl    Num       8    DATE9.
10    doNeuro      Num       8    DATE9.
11    doDKD        Num       8    DATE9.
12    doDiaEye     Num       8    DATE9.
13    doHypo       Num       8    DATE9.
14    doAtrFib     Num       8    DATE9.
15    doMI         Num       8    DATE9.
16    doUnstAng    Num       8    DATE9.
17    doHmStr      Num       8    DATE9.
18    doDiaFoot    Num       8    DATE9.
19    doOther      Num       8    DATE9.
20    doPeriAng    Num       8    DATE9.
21    doIscStr     Num       8    DATE9.
22    doAmp        Num       8    DATE9.
23    doCKD        Num       8    DATE9.
24    doPCIsten    Num       8    DATE9.
25    doCABG       Num       8    DATE9.
26    doKeto       Num       8    DATE9.
27    doDial       Num       8    DATE9.
28    doBari       Num       8    DATE9.
```

4.4 04a-rmps

Reads all non-DM medication and produces a dataset `wmed` with date of first purchase of a range of medications.

```
1                                "Program: 04a-rmps.sas"         12:25 Friday, May 4, 2018





NOTE: AUTOEXEC processing completed.

1          %macro med ;
2          data med ;
3            set %do i = 1995 %to 2017 ;
4                grund.lmdb&i. ( keep = pnr atc eksd
5                                 where = ( substr(atc,1,3) in
6                       ('A08','B01','C01','C03','C07','C08','C09','C10','H02') ) )
7                %end ; ;
8          * Grouping of non-DM medicines ;
9                                       medgr = put( substr(atc,1,3), $med3oth. ) ;
10         if ( medgr eq "Other" ) then medgr = put( substr(atc,1,4), $med4oth. ) ;
11         if ( medgr eq "Other" ) then medgr = put( substr(atc,1,5), $med5oth. ) ;
12         if ( medgr eq "Other" ) then medgr = put( substr(atc,1,7), $med7oth. ) ;
13         if ( medgr eq "Other" ) then delete ;
14         if ( atc eq "C09DX04" ) then delete ;
15         run ;
16         %mend ;
17         %med ;

NOTE: There were 1569620 observations read from the data set GRUND.LMDB1995.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
```

```
      'H02');
NOTE: There were 1699112 observations read from the data set GRUND.LMDB1996.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 1805191 observations read from the data set GRUND.LMDB1997.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 1936488 observations read from the data set GRUND.LMDB1998.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 2085940 observations read from the data set GRUND.LMDB1999.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 2227335 observations read from the data set GRUND.LMDB2000.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 2441676 observations read from the data set GRUND.LMDB2001.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 2732372 observations read from the data set GRUND.LMDB2002.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 3083882 observations read from the data set GRUND.LMDB2003.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 3468769 observations read from the data set GRUND.LMDB2004.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 3767302 observations read from the data set GRUND.LMDB2005.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4089355 observations read from the data set GRUND.LMDB2006.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4384245 observations read from the data set GRUND.LMDB2007.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4709751 observations read from the data set GRUND.LMDB2008.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4826535 observations read from the data set GRUND.LMDB2009.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4925490 observations read from the data set GRUND.LMDB2010.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4987124 observations read from the data set GRUND.LMDB2011.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 5023355 observations read from the data set GRUND.LMDB2012.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4915248 observations read from the data set GRUND.LMDB2013.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4762917 observations read from the data set GRUND.LMDB2014.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4553864 observations read from the data set GRUND.LMDB2015.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 4327744 observations read from the data set GRUND.LMDB2016.
```

```
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: There were 2090999 observations read from the data set GRUND.LMDB2017.
      WHERE SUBSTR(atc, 1, 3) in ('A08', 'B01', 'C01', 'C03', 'C07', 'C08', 'C09', 'C10',
      'H02');
NOTE: The data set WORK.MED has 75682297 observations and 4 variables.
NOTE: DATA statement used (Total process time):
      real time           1:26.07
      cpu time            1:25.78


18
19         proc sort  data = med ;
20           by pnr medgr eksd ;
21         run ;

NOTE: There were 75682297 observations read from the data set WORK.MED.
NOTE: The data set WORK.MED has 75682297 observations and 4 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           17.40 seconds
      cpu time            41.34 seconds


22
23         * late prescriptions for use with SGLT2 ;
24
25         data dafdat.lmed ;
26           set med ;
27           if eksd ge '01dec2011'd ;
28         run ;

NOTE: There were 75682297 observations read from the data set WORK.MED.
NOTE: The data set DAFDAT.LMED has 25061393 observations and 4 variables.
NOTE: DATA statement used (Total process time):
      real time           8.93 seconds
      cpu time            5.84 seconds


29
30         data med ( keep = pnr eksd medgr ) ;
31           set med ;
32           by pnr medgr ;
33           if first.medgr ;
34         run ;

NOTE: There were 75682297 observations read from the data set WORK.MED.
NOTE: The data set WORK.MED has 2916253 observations and 3 variables.
NOTE: DATA statement used (Total process time):
      real time           7.25 seconds
      cpu time            7.24 seconds


35
36         title1 'All first prescriptions - entire population' ;
37         proc tabulate  data = med  missing  noseps ;
38           class medgr ;
39           table medgr, n * f=comma12. / rts=60 ;
40           format medgr $lmedgr. ;
41         run ;

NOTE: There were 2916253 observations read from the data set WORK.MED.
NOTE: The PROCEDURE TABULATE printed page 1.
```

```
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.50 seconds
      cpu time            0.34 seconds


42           title1 ;
43
44           proc transpose  data = med
45                             out = dafdat.wmed
46                          prefix = do ;
47             by pnr ;
48             var eksd ;
49             id medgr ;
50           run ;

NOTE: There were 2916253 observations read from the data set WORK.MED.
NOTE: The data set DAFDAT.WMED has 549969 observations and 23 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           3.14 seconds
      cpu time            2.18 seconds


51
52           %let meddates =
53           doACE doAPl doARB doAlA doAmi doAsp doBBl doCcs doDHP doDTI
54           doDXI doDgo doFla doHCD doNHP doRPA doSta doTHZ doWrf doWtL ;
55
56           title1 'All medications for persons in DK after 1 dec 2011' ;
57           proc contents  data = dafdat.wmed  ;
58           run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds

NOTE: The PROCEDURE CONTENTS printed page 2.

59
60           title1 'First (other) medication dates for persons in DK' ;
61           proc contents  data = dafdat.wmed  ;
62           run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds

NOTE: The PROCEDURE CONTENTS printed page 3.

63
64           proc tabulate  data = dafdat.wmed  missing  noseps ;
65             class &meddates. ;
66             table all &meddates. ,
67                   n * f=comma12.
68                   / rts = 15 ;
69             format &meddates. year4. ;
70             keylabel n = ' ' ;
71           run ;

NOTE: There were 549969 observations read from the data set DAFDAT.WMED.
NOTE: The PROCEDURE TABULATE printed page 4.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.40 seconds
```

```
      cpu time            1.51 seconds


72         title1 ;

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414
NOTE: The SAS System used:
      real time           2:04.07
      cpu time            2:24.42
```

4.4.1 04a-rmps.lst

```
All first prescriptions - entire population                  12:25 Friday, May 4, 2018   1


                                                                 N

 medgr
 ACE: ACE inhibitors                                             319,467
 APl: Other antiplatelets                                         34,601
 ARB: ARB                                                        187,722
 AlA: Aldosterone antagonists                                     87,902
 Ami: Amiodarone                                                  13,626
 Asp: Low dose aspirin                                           300,987
 BBl: Beta blockers                                              254,657
 Ccs: Corticosteroids                                            223,780
 DHP: Dihydropyridines (calcium channel blockers)                236,240
 DTI: Direct thrombin inhibitor                                   11,465
 DXI: Direct factor Xa inhibitors                                 22,135
 Dgo: Digoxin                                                     76,966
 Fla: Flekanide                                                    1,929
 HCD: High ceiling diuretics (loop-diuretics)                    248,131
 NHP: Non-hydropyridines (calcium channel blockers)               54,401
 RPA: Receptor P2Y12 antagonists                                  80,047
 Sta: Statins                                                    340,655
 THZ: Low ceiling diuretics (thiazides)                          260,951
 Wrf: Warfarin                                                    72,389
 WtL: Weight loss drugs                                           88,202

All medications for persons in DK after * dec 2011           12:25 Friday, May 4, 2018   2

The CONTENTS Procedure

Data Set Name        DAFDAT.WMED                   Observations          549969
Member Type          DATA                          Variables             23
Engine               V9                            Indexes               0
Created              04/05/2018 12:27:15           Observation Length    140
Last Modified        04/05/2018 12:27:15           Deleted Observations  0
Protection                                         Compressed            NO
Data Set Type                                      Sorted                NO
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                      Engine/Host Dependent Information

Data Set Page Size          65536
Number of Data Set Pages    1178
```

```
First Data Page            *
Max Obs per Page           467
Obs in First Data Page     443
Number of Data Set Repairs 0
ExtendObsCounter           YES
Filename                   E:\workdata\705093\BxC\daffodil\DATA\wmed.sas7bdat
Release Created            9.0401M3
Host Created               X64_SRV12


              Alphabetic List of Variables and Attributes

 #    Variable    Type    Len    Format       Label

 *    _LABEL_     Char     40                 LABEL OF FORMER VARIABLE
 *    _NAME_      Char      8                 NAME OF FORMER VARIABLE
 4    doACE       Num       4    YYMMDDN8.
21    doAPl       Num       4    YYMMDDN8.
 7    doARB       Num       4    YYMMDDN8.
14    doAlA       Num       4    YYMMDDN8.
15    doAmi       Num       4    YYMMDDN8.
 8    doAsp       Num       4    YYMMDDN8.
 6    doBBl       Num       4    YYMMDDN8.
 9    doCcs       Num       4    YYMMDDN8.
10    doDHP       Num       4    YYMMDDN8.
22    doDTI       Num       4    YYMMDDN8.
18    doDXI       Num       4    YYMMDDN8.
16    doDgo       Num       4    YYMMDDN8.
23    doFla       Num       4    YYMMDDN8.
11    doHCD       Num       4    YYMMDDN8.
20    doNHP       Num       4    YYMMDDN8.
19    doRPA       Num       4    YYMMDDN8.
 5    doSta       Num       4    YYMMDDN8.
12    doTHZ       Num       4    YYMMDDN8.
17    doWrf       Num       4    YYMMDDN8.
13    doWtL       Num       4    YYMMDDN8.
 *    pnr         Char     12    $12.

First (other) medication dates for persons in DK           12:25 Friday, May 4, 2018   3

The CONTENTS Procedure

Data Set Name        DAFDAT.WMED                    Observations          549969
Member Type          DATA                           Variables             23
Engine               V9                             Indexes               0
Created              04/05/2018 12:27:15            Observation Length    140
Last Modified        04/05/2018 12:27:15            Deleted Observations  0
Protection                                          Compressed            NO
Data Set Type                                       Sorted                NO
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                      Engine/Host Dependent Information

Data Set Page Size         65536
Number of Data Set Pages   1178
First Data Page            *
Max Obs per Page           467
Obs in First Data Page     443
Number of Data Set Repairs 0
```

```
ExtendObsCounter            YES
Filename                    E:\workdata\705093\BxC\daffodil\DATA\wmed.sas7bdat
Release Created             9.0401M3
Host Created                X64_SRV12


              Alphabetic List of Variables and Attributes

 #    Variable    Type    Len    Format       Label

 *    _LABEL_     Char     40                 LABEL OF FORMER VARIABLE
 *    _NAME_      Char      8                 NAME OF FORMER VARIABLE
 4    doACE       Num       4    YYMMDDN8.
21    doAPl       Num       4    YYMMDDN8.
 7    doARB       Num       4    YYMMDDN8.
14    doAlA       Num       4    YYMMDDN8.
15    doAmi       Num       4    YYMMDDN8.
 8    doAsp       Num       4    YYMMDDN8.
 6    doBBl       Num       4    YYMMDDN8.
 9    doCcs       Num       4    YYMMDDN8.
10    doDHP       Num       4    YYMMDDN8.
22    doDTI       Num       4    YYMMDDN8.
18    doDXI       Num       4    YYMMDDN8.
16    doDgo       Num       4    YYMMDDN8.
23    doFla       Num       4    YYMMDDN8.
11    doHCD       Num       4    YYMMDDN8.
20    doNHP       Num       4    YYMMDDN8.
19    doRPA       Num       4    YYMMDDN8.
 5    doSta       Num       4    YYMMDDN8.
12    doTHZ       Num       4    YYMMDDN8.
17    doWrf       Num       4    YYMMDDN8.
13    doWtL       Num       4    YYMMDDN8.
 *    pnr         Char     12    $12.

First (other) medication dates for persons in DK           12:25 Friday, May 4, 2018   4


 All                549,969
 doACE
 .                  230,502
 1995                40,622
 1996                10,823
 1997                10,341
 1998                 9,575
 1999                10,275
 2000                12,099
 2001                13,904
 2002                14,840
 2003                16,752
 2004                18,505
 2005                18,467
 2006                18,256
 2007                18,186
 2008                17,908
 2009                27,156
 2010                15,717
 2011                11,634
 2012                 9,044
 2013                 7,484
 2014                 5,911
 2015                 5,193
 2016                 4,845
```

```
2017                 1,930
doAPl
.                  515,368
1995                   169
1996                   126
1997                   397
1998                 1,422
1999                 2,735
2000                 2,888
2001                 2,969
2002                 3,166
2003                 2,184
2004                 1,980
2005                 2,154
2006                 2,100
2007                 2,115
2008                 2,448
2009                 2,456
2010                 2,053
2011                 1,328
2012                   854
2013                   552
2014                   287
2015                   109
2016                    74
2017                    35
doARB
.                  362,247
1995                 4,189
1996                 3,450
1997                 5,003
1998                 8,096
1999                 7,839
2000                 6,177
2001                 8,137
2002                11,769
2003                11,259
2004                10,249
2005                10,258
2006                10,191
2007                11,193
2008                 9,958
2009                 6,820
2010                10,204
2011                11,567
2012                 9,332
2013                 8,279
2014                 7,377
2015                 6,912
2016                 6,501
2017                 2,962
doAlA
.                  462,067
1995                 6,839
1996                 2,083
1997                 1,896
1998                 1,955
1999                 3,186
2000                 4,859
2001                 4,628
2002                 4,383
2003                 4,100
```

```
2004                 4,188
2005                 4,418
2006                 4,197
2007                 4,035
2008                 4,017
2009                 4,035
2010                 3,922
2011                 4,233
2012                 4,133
2013                 4,206
2014                 3,762
2015                 3,640
2016                 3,488
2017                 1,699
doAmi
.                  536,343
1995                   448
1996                   222
1997                   251
1998                   296
1999                   344
2000                   490
2001                   605
2002                   591
2003                   672
2004                   619
2005                   717
2006                   766
2007                   755
2008                   766
2009                   735
2010                   700
2011                   709
2012                   707
2013                   735
2014                   738
2015                   709
2016                   702
2017                   349
doAsp
.                  248,982
1995                45,554
1996                13,159
1997                12,084
1998                12,098
1999                12,332
2000                13,620
2001                16,633
2002                18,556
2003                18,255
2004                17,032
2005                15,286
2006                15,869
2007                15,117
2008                15,698
2009                12,161
2010                 9,980
2011                 8,666
2012                 6,991
2013                 5,704
2014                 5,120
2015                 4,761
```

```
2016                 4,334
2017                 1,977
doBBl
.                  295,312
1995                41,834
1996                10,354
1997                10,251
1998                10,583
1999                11,352
2000                12,903
2001                13,377
2002                14,818
2003                13,663
2004                13,533
2005                12,237
2006                10,603
2007                10,172
2008                 9,306
2009                 8,934
2010                 8,509
2011                 8,208
2012                 7,654
2013                 6,717
2014                 6,088
2015                 5,766
2016                 5,285
2017                 2,510
doCcs
.                  326,189
1995                28,829
1996                15,454
1997                13,270
1998                12,334
1999                11,269
2000                11,014
2001                10,219
2002                 9,675
2003                 8,967
2004                 8,903
2005                 8,959
2006                 8,676
2007                 8,407
2008                 8,224
2009                 8,187
2010                 7,985
2011                 7,741
2012                 7,124
2013                 6,899
2014                 6,438
2015                 6,229
2016                 5,993
2017                 2,984
doDHP
.                  313,729
1995                28,361
1996                 8,566
1997                 8,536
1998                 8,803
1999                 8,287
2000                 8,028
2001                 8,699
2002                 8,672
```

```
2003                 8,466
2004                 9,750
2005                11,611
2006                12,420
2007                14,051
2008                13,504
2009                13,750
2010                12,950
2011                11,674
2012                 9,564
2013                 8,069
2014                 6,836
2015                 6,549
2016                 6,187
2017                 2,907
doDTI
.                  538,504
2008                    48
2009                   241
2010                   423
2011                 1,770
2012                 3,052
2013                 2,607
2014                 1,891
2015                   737
2016                   515
2017                   181
doDXI
.                  527,834
2009                   236
2010                   419
2011                   420
2012                   758
2013                 2,598
2014                 3,651
2015                 4,823
2016                 5,749
2017                 3,481
doDgo
.                  473,003
1995                22,199
1996                 4,090
1997                 3,572
1998                 3,750
1999                 3,526
2000                 3,222
2001                 3,142
2002                 2,836
2003                 2,820
2004                 2,624
2005                 2,494
2006                 2,306
2007                 2,262
2008                 2,193
2009                 2,162
2010                 2,125
2011                 2,128
2012                 2,032
2013                 1,948
2014                 1,773
2015                 1,602
2016                 1,482
```

```
2017                       678
doFla
.                      548,040
1995                       352
1996                       100
1997                        99
1998                       102
1999                       113
2000                       113
2001                       102
2002                        71
2003                        52
2004                        49
2005                        51
2006                        59
2007                        65
2008                        50
2009                        62
2010                        51
2011                        92
2012                        75
2013                        74
2014                        62
2015                        53
2016                        56
2017                        26
doHCD
.                      301,838
1995                    48,541
1996                    12,361
1997                    10,790
1998                    10,244
1999                    10,065
2000                     9,536
2001                     9,803
2002                     9,618
2003                     9,426
2004                     9,381
2005                     9,702
2006                     9,599
2007                     9,438
2008                     9,169
2009                     9,371
2010                     9,506
2011                     9,239
2012                     8,472
2013                     8,065
2014                     7,793
2015                     7,360
2016                     7,254
2017                     3,398
doNHP
.                      495,568
1995                    20,915
1996                     3,758
1997                     3,157
1998                     3,080
1999                     2,772
2000                     2,503
2001                     2,341
2002                     1,992
2003                     1,916
```

```
2004                     1,880
2005                     1,543
2006                     1,454
2007                     1,269
2008                     1,066
2009                       917
2010                       771
2011                       669
2012                       592
2013                       480
2014                       460
2015                       377
2016                       320
2017                       169
doRPA
.                      469,922
1998                        10
1999                       554
2000                     1,519
2001                     1,939
2002                     3,061
2003                     3,736
2004                     3,816
2005                     3,957
2006                     3,813
2007                     3,824
2008                     3,860
2009                     3,877
2010                     4,917
2011                     6,671
2012                     6,527
2013                     6,321
2014                     6,594
2015                     6,379
2016                     5,926
2017                     2,746
doSta
.                      209,314
1995                     6,291
1996                     3,558
1997                     3,974
1998                     5,617
1999                     7,947
2000                     8,494
2001                    10,861
2002                    17,678
2003                    26,305
2004                    29,372
2005                    26,444
2006                    28,397
2007                    27,031
2008                    26,612
2009                    20,882
2010                    18,586
2011                    16,812
2012                    14,103
2013                    11,402
2014                     9,831
2015                     8,908
2016                     8,225
2017                     3,325
doTHZ
```

```
.                  289,018
1995                47,202
1996                13,633
1997                12,955
1998                13,284
1999                12,888
2000                13,223
2001                13,316
2002                12,932
2003                15,429
2004                14,965
2005                14,620
2006                12,038
2007                10,573
2008                 9,679
2009                 8,692
2010                 7,637
2011                 6,665
2012                 5,342
2013                 4,360
2014                 3,813
2015                 3,326
2016                 2,973
2017                 1,406
doWrf
.                  477,580
1995                 2,849
1996                 1,484
1997                 1,826
1998                 2,474
1999                 3,238
2000                 3,344
2001                 3,565
2002                 3,719
2003                 4,013
2004                 4,108
2005                 4,314
2006                 4,283
2007                 4,113
2008                 3,795
2009                 3,715
2010                 3,761
2011                 3,972
2012                 3,328
2013                 3,175
2014                 2,769
2015                 2,310
2016                 1,666
2017                   568
doWtL
.                  461,767
1995                31,629
1996                14,997
1997                10,068
1998                 7,434
1999                 6,598
2000                 4,432
2001                 3,483
2002                 2,179
2003                   473
2004                   415
2005                   501
```

```
 2006                      698
 2007                    1,342
 2008                      972
 2009                    1,009
 2010                      493
 2011                      354
 2012                      288
 2013                      258
 2014                      188
 2015                      165
 2016                      148
 2017                       78
```

4.5 04d-rmps

Reads and restricts the register-created dataset `prmps` to the type 2 patients.

Processes the records of anti-diabetic medicine from the RMPS and creates three files; one with one record per T2 patient (`pRMPS`) with dates of first purchase of each group of diabetes drugs. There are separate first purchase dates for any type of a given drug which also includes combination pills, and first purchase date for single drug pills.

The other data sets created, (`disp`) has one record per anti-diabetic prescription, respectively one record per drug-type dispensation (`xdisp`). The latter means that combination pills contribute one record per drug in the pill.

```
1                                "Program: 04d-rmps.sas"        19:40 Tuesday, May 8, 2018






NOTE: AUTOEXEC processing completed.

1          * Base population of persons that we use ( DMdreg ) ;
2          * including the first dates of mono drug (donlXX) or any (danyXX) ;
3          data dafdat.pRMPS ;
4            merge DMdat.prmps  ( in = drug )
5                  DMdat.DMdreg ( in = t2dm
6                                 where = ( DMtp eq "T2" ) ) ;
7            by pnr ;
8            if drug and t2dm ;
9          run ;

NOTE: There were 426299 observations read from the data set DMDAT.PRMPS.
NOTE: There were 383033 observations read from the data set DMDAT.DMDREG.
      WHERE DMtp='T2';
NOTE: The data set DAFDAT.PRMPS has 383033 observations and 30 variables.
NOTE: DATA statement used (Total process time):
      real time           2.34 seconds
      cpu time            0.21 seconds


10
11         %let drdates = donlMet   danyMet
12                        donlSU    danySU
13                        donlTZD   danyTZD
```

```
14                        donlDPP4  danyDPP4
15                                  danyGLP1
16                        donlSGLT2 danySGLT2
17                        donlAca   danyAca
18                                  danyMeg
19                        dofIns doiIns domIns dolIns ;
20
21         title1 "T2 patients from the RPMS" ;
22         proc tabulate  data = dafdat.pRMPS  missing  noseps ;
23           class &drdates. doOAD doRMPS ;
24           table all &drdates. doOAD doRMPS,
25                 n * f=comma10.
26                 / rts = 15 ;
27           format &drdates. doOAD doRMPS year4. ;
28           keylabel n = ' ' ;
29         run ;

NOTE: There were 383033 observations read from the data set DAFDAT.PRMPS.
NOTE: The PROCEDURE TABULATE printed page 1.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.39 seconds
      cpu time            1.03 seconds


30         title1 ;
31
32         * Read the entire drug register files (again) and match dispensations to
32       ! persons;
33         %macro med ;
34         data rmps ;
35           length druggr $ 7 ;
36           set %do i = 1995 %to 2017 ;
37               grund.lmdb&i. ( keep = pnr ATC eksd apk volume packsize doso
38                               where = ( substr(atc,1,3) eq 'A10' ) )
39               %end ; ;
40           * Grouping of drugs as a character ;
41                                       druggr = put(        atc     , $atc5grp. ) ;
42           if ( druggr eq "Other" ) then druggr = put( substr(atc,1,5), $atc4grp. ) ;
43         run ;
44         %mend ;
45         %med ;

NOTE: There were 561710 observations read from the data set GRUND.LMDB1995.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 626242 observations read from the data set GRUND.LMDB1996.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 670823 observations read from the data set GRUND.LMDB1997.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 732412 observations read from the data set GRUND.LMDB1998.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 795111 observations read from the data set GRUND.LMDB1999.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 826954 observations read from the data set GRUND.LMDB2000.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 906834 observations read from the data set GRUND.LMDB2001.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 985199 observations read from the data set GRUND.LMDB2002.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1067000 observations read from the data set GRUND.LMDB2003.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1179974 observations read from the data set GRUND.LMDB2004.
      WHERE SUBSTR(atc, 1, 3)='A10';
```

```
NOTE: There were 1290910 observations read from the data set GRUND.LMDB2005.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1407903 observations read from the data set GRUND.LMDB2006.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1519940 observations read from the data set GRUND.LMDB2007.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1659418 observations read from the data set GRUND.LMDB2008.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1751050 observations read from the data set GRUND.LMDB2009.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1875341 observations read from the data set GRUND.LMDB2010.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2003132 observations read from the data set GRUND.LMDB2011.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2101706 observations read from the data set GRUND.LMDB2012.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2130959 observations read from the data set GRUND.LMDB2013.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2152197 observations read from the data set GRUND.LMDB2014.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2164328 observations read from the data set GRUND.LMDB2015.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 2252557 observations read from the data set GRUND.LMDB2016.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: There were 1130278 observations read from the data set GRUND.LMDB2017.
      WHERE SUBSTR(atc, 1, 3)='A10';
NOTE: The data set WORK.RMPS has 31791978 observations and 8 variables.
NOTE: DATA statement used (Total process time):
      real time           8:17.41
      cpu time            50.09 seconds


46
47         proc sort  data = rmps ;
48           by pnr druggr eksd ;
49         run ;

NOTE: There were 31791978 observations read from the data set WORK.RMPS.
NOTE: The data set WORK.RMPS has 31791978 observations and 8 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           7.85 seconds
      cpu time            18.76 seconds


50
51         * file of dispensations in the T2 drug-treated pateints ;
52         data dafdat.disp ;
53           merge rmps
54                 dafdat.pRMPS ( keep = pnr doDM
55                                  in = ok ) ;
56           by pnr ;
57           if ok ;
58         run ;

NOTE: There were 31791978 observations read from the data set WORK.RMPS.
NOTE: There were 383033 observations read from the data set DAFDAT.PRMPS.
NOTE: The data set DAFDAT.DISP has 26205558 observations and 9 variables.
NOTE: DATA statement used (Total process time):
      real time           10.75 seconds
      cpu time            6.96 seconds
```

```
59
60         * dataset where combination pills are sorted to components ;
61         data dafdat.xdisp ;
62           set dafdat.disp ;
63           if druggr eq '212' then do ;
64              druggr = '11' ; output ;
65              druggr = '12' ; output ;
66              end  ; else
67           if druggr eq '213' then do ;
68              druggr = '11' ; output ;
69              druggr = '13' ; output ;
70              end  ; else
71           if druggr eq '214' then do ;
72              druggr = '11' ; output ;
73              druggr = '14' ; output ;
74              end  ; else
75           if druggr eq '216' then do ;
76              druggr = '11' ; output ;
77              druggr = '16' ; output ;
78              end  ; else
79           if druggr eq '218' then do ;
80              druggr = '11' ; output ;
81              druggr = '18' ; output ;
82              end  ; else
83           if druggr eq '223' then do ;
84              druggr = '12' ; output ;
85              druggr = '13' ; output ;
86              end  ; else
87           if druggr eq '234' then do ;
88              druggr = '13' ; output ;
89              druggr = '14' ; output ;
90              end  ; else
91           if druggr eq '246' then do ;
92              druggr = '14' ; output ;
93              druggr = '16' ; output ;
94              end  ; else
95           output ;
96         run ;

NOTE: There were 26205558 observations read from the data set DAFDAT.DISP.
NOTE: The data set DAFDAT.XDISP has 26878885 observations and 9 variables.
NOTE: DATA statement used (Total process time):
      real time           21.59 seconds
      cpu time            5.03 seconds


97
98         title1 "Dispensations on T2 from the RPMS" ;
99         proc tabulate  data = dafdat.disp  missing  noseps ;
100          class eksd druggr atc ;
101          table all eksd = "Date",
102               ( all druggr ) * f=comma12.
103               / rts = 6  condense ;
104          table druggr * atc,
105                n * f=comma10.
106                / indent=2  rts = 53 ;
107          keylabel n = ' ' ;
108          format eksd year4.
109               druggr $druggr.
110                  atc $atc_L1L1_kt. ;
111        run ;
```

```
NOTE: There were 26205558 observations read from the data set DAFDAT.DISP.
NOTE: The PROCEDURE TABULATE printed pages 2-3.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           6.68 seconds
      cpu time            10.15 seconds


112
113        title1 "Dispensed *drugs* to T2 ptt. from the RPMS" ;
114        proc tabulate  data = dafdat.xdisp  missing  noseps ;
115          class eksd druggr ;
116          table all eksd = "Date",
117              ( all druggr ) * f=comma12.
118              / rts = 6  condense ;
119          format eksd year4.
120               druggr $druggr. ;
121        run ;

NOTE: There were 26878885 observations read from the data set DAFDAT.XDISP.
NOTE: The PROCEDURE TABULATE printed page 4.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           25.32 seconds
      cpu time            8.51 seconds


122        title1 ;
123
124        proc contents  data = dafdat.pRMPS ; run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.10 seconds
      cpu time            0.01 seconds

NOTE: The PROCEDURE CONTENTS printed page 5.

125        proc contents  data = dafdat.disp  ; run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.10 seconds
      cpu time            0.00 seconds

NOTE: The PROCEDURE CONTENTS printed page 6.

126        proc contents  data = dafdat.xdisp  ; run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds

NOTE: The PROCEDURE CONTENTS printed page 7.

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414
NOTE: The SAS System used:
      real time           9:32.83
      cpu time            1:40.92
```

4.5.1 04d-rmps.lst

```
T2 patients from the RPMS                              19:40 Tuesday, May 8, 2018   1
```

```
All               383,033
donlMet
.                  78,235
1995               11,973
1996                4,138
1997                3,867
1998                4,750
1999                6,524
2000                8,577
2001                9,114
2002                9,674
2003               11,451
2004               13,032
2005               13,052
2006               14,161
2007               16,496
2008               19,000
2009               20,802
2010               22,635
2011               26,920
2012               23,094
2013               16,548
2014               15,044
2015               16,507
2016               17,439
danyMet
.                  77,135
1995               11,973
1996                4,138
1997                3,867
1998                4,750
1999                6,524
2000                8,577
2001                9,114
2002                9,674
2003               11,451
2004               13,090
2005               13,111
2006               14,307
2007               16,622
2008               19,106
2009               20,931
2010               22,751
2011               26,960
2012               23,160
2013               16,616
2014               15,088
2015               16,580
2016               17,508
donlSU
.                 194,558
1995               40,775
1996                9,707
1997                9,155
1998                9,975
1999                9,731
2000                8,765
2001                9,086
2002                8,470
2003                9,750
2004                9,349
```

```
2005               8,913
2006               8,109
2007               8,009
2008               7,101
2009               5,931
2010               5,846
2011               4,591
2012               3,579
2013               3,206
2014               2,888
2015               2,940
2016               2,599
danySU
.                194,557
1995              40,775
1996               9,707
1997               9,155
1998               9,975
1999               9,731
2000               8,765
2001               9,086
2002               8,470
2003               9,750
2004               9,349
2005               8,913
2006               8,109
2007               8,010
2008               7,102
2009               5,932
2010               5,845
2011               4,590
2012               3,579
2013               3,206
2014               2,888
2015               2,940
2016               2,599
donlTZD
.                378,464
2000                  89
2001                 625
2002                 405
2003                 326
2004                 414
2005                 458
2006                 563
2007                 566
2008                 382
2009                 303
2010                 177
2011                  91
2012                  51
2013                  38
2014                  36
2015                  25
2016                  20
danyTZD
.                373,107
2000                  89
2001                 625
2002                 405
2003                 327
2004               1,092
```

```
2005                1,397
2006                2,080
2007                1,826
2008                  938
2009                  615
2010                  311
2011                   57
2012                   42
2013                   35
2014                   37
2015                   25
2016                   25
donlDPP4
.                 337,192
2007                2,258
2008                4,403
2009                3,198
2010                4,372
2011                4,617
2012                4,432
2013                5,016
2014                5,379
2015                6,029
2016                6,137
danyDPP4
.                 314,315
2007                2,258
2008                5,094
2009                5,403
2010                7,462
2011                7,688
2012                7,387
2013                7,767
2014                8,057
2015                8,683
2016                8,919
danyGLP1
.                 346,850
2007                  171
2008                1,015
2009                2,179
2010                7,125
2011                6,379
2012                5,124
2013                3,492
2014                2,890
2015                3,576
2016                4,232
donlSGLT2
.                 366,795
2012                   20
2013                1,928
2014                2,922
2015                4,459
2016                6,909
danySGLT2
.                 365,916
2012                   20
2013                1,928
2014                3,003
2015                4,615
2016                7,551
```

```
donlAca
.                375,997
1995                 620
1996               1,147
1997               1,071
1998               1,096
1999                 671
2000                 436
2001                 400
2002                 237
2003                 210
2004                 186
2005                 163
2006                 132
2007                 112
2008                 108
2009                  70
2010                  96
2011                  56
2012                  75
2013                  55
2014                  42
2015                  38
2016                  15
danyAca
.                375,997
1995                 620
1996               1,147
1997               1,071
1998               1,096
1999                 671
2000                 436
2001                 400
2002                 237
2003                 210
2004                 186
2005                 163
2006                 132
2007                 112
2008                 108
2009                  70
2010                  96
2011                  56
2012                  75
2013                  55
2014                  42
2015                  38
2016                  15
danyMeg
.                383,033
dofIns
.                337,947
1995               4,177
1996               1,114
1997                 978
1998               1,060
1999               1,115
2000               1,179
2001               1,192
2002               1,268
2003               1,412
2004               1,532
```

```
2005                1,653
2006                1,743
2007                1,825
2008                1,983
2009                2,213
2010                2,330
2011                2,468
2012                2,683
2013                2,965
2014                3,182
2015                3,416
2016                3,598
doiIns
.                 314,553
1995               10,500
1996                2,388
1997                2,272
1998                2,531
1999                2,959
2000                3,205
2001                3,113
2002                3,411
2003                3,952
2004                3,839
2005                3,555
2006                3,312
2007                3,289
2008                2,436
2009                2,138
2010                2,206
2011                2,204
2012                2,208
2013                2,727
2014                2,449
2015                2,160
2016                1,626
domIns
.                 336,762
1995                3,740
1996                1,236
1997                1,239
1998                1,628
1999                1,803
2000                1,846
2001                1,915
2002                1,943
2003                2,682
2004                3,288
2005                3,328
2006                3,700
2007                3,913
2008                2,845
2009                2,357
2010                1,784
2011                1,621
2012                1,434
2013                1,330
2014                1,134
2015                  924
2016                  581
dolIns
.                 340,944
```

```
1997                   *
1998                   *
1999                   *
2000                   *
2004                 494
2005                 926
2006                 598
2007                 738
2008               3,510
2009               4,289
2010               3,666
2011               3,754
2012               3,894
2013               3,595
2014               4,209
2015               5,209
2016               7,202
doOAD
.                 19,528
1995              43,675
1996              10,343
1997               9,642
1998              10,670
1999              10,990
2000              11,113
2001              11,847
2002              11,718
2003              13,935
2004              14,412
2005              14,319
2006              14,844
2007              16,285
2008              18,011
2009              18,975
2010              21,135
2011              24,885
2012              21,739
2013              15,851
2014              14,669
2015              16,527
2016              17,920
doRMPS
1995              54,189
1996              10,785
1997              10,032
1998              11,056
1999              11,365
2000              11,552
2001              12,226
2002              12,089
2003              14,392
2004              14,969
2005              14,814
2006              15,394
2007              16,751
2008              18,495
2009              19,347
2010              21,475
2011              25,159
2012              22,024
2013              16,368
2014              15,164
```

```
 2015              16,966
 2016              18,421


Dispensations on T2 from the RPMS                           19:40 Tuesday, May 8, 2018   2


                                                druggr

          All       Metformin        SU          TZD          DPP4         GLP1

 All   26,205,558   11,743,209    6,010,980       62,122      605,015    1,050,971
 Date
 1995      364,856       68,573      209,175            .            .            .
 1996      420,944       82,128      236,688            .            .            .
 1997      454,555       91,503      250,638            .            .            .
 1998      504,996      104,375      271,182            .            .            .
 1999      563,147      127,803      290,980            .            .            .
 2000      608,447      164,539      293,860          115            .            .
 2001      679,074      205,400      303,689        2,734            .            .
 2002      748,965      252,127      307,795        3,725            .            .
 2003      834,071      303,458      321,128        4,286            .            .
 2004      943,171      368,259      334,014        5,064            .            .
 2005    1,039,651      425,324      339,883        5,835            .            .
 2006    1,148,795      497,333      341,096        7,207            .            .
 2007    1,256,261      565,912      340,288        8,394        5,375          371
 2008    1,390,371      657,116      336,426        7,677       27,297        5,169
 2009    1,484,065      729,019      315,244        7,236       33,489       14,312
 2010    1,604,634      809,837      291,733        4,928       40,926       58,850
 2011    1,736,175      909,317      265,320        1,469       49,903      108,984
 2012    1,832,221      981,406      231,891        1,192       57,354      137,962
 2013    1,861,340      993,609      200,590          950       66,300      150,395
 2014    1,881,166      988,958      175,371          525       79,009      151,692
 2015    1,890,045      956,713      155,239          355       90,592      160,477
 2016    1,971,181      982,643      137,500          276      101,147      172,492
 2017      987,427      477,857       61,250          154       53,623       90,267

(Continued)


                                         druggr

         SGLT2       Acarbose     MetxTZD      MetxDPP4    MetxSGLT2      SUxTZD

 All       144,566      109,318      115,942      547,406        9,605          271
 Date
 1995            .        1,870            .            .            .            .
 1996            .        6,338            .            .            .            .
 1997            .        9,438            .            .            .            .
 1998            .       11,337            .            .            .            .
 1999            .       11,262            .            .            .            .
 2000            .       10,017            .            .            .            .
 2001            .        8,997            .            .            .            .
 2002            .        7,373            .            .            .            .
 2003            .        6,358            *            .            .            .
 2004            .        5,555        3,392            .            .            .
 2005            .        5,067        9,671            .            .            .
 2006            .        4,674       18,141            .            .            .
 2007            .        4,201       25,239            .            .           49
 2008            .        3,820       23,459        2,026            .           65
```

```
2009            .        3,044       20,612       16,103            .           87
2010            .        2,473       15,339       30,713            .           70
2011            .        2,125           88       48,139            .            .
2012           20        1,810            .       59,664            .            .
2013        6,241        1,566            .       70,564            .            .
2014       16,046          916            .       80,636          272            .
2015       30,592          794            .       89,795          937            .
2016       53,389          283            .       98,277        4,475            .
2017       38,278            .            .       51,489        3,921            .
```

(Continued)

```
                                        druggr

       TZDxDPP4    DPP4xSGLT2    InsxGLP1     fastIns       intIns      longIns

All            69           34          949      903,942    1,985,315    1,120,783
Date
1995            .            .            .       20,240       45,899            .
1996            .            .            .       21,779       51,880            .
1997            .            .            .       23,266       55,421            *
1998            .            .            .       25,897       61,848            *
1999            .            .            .       27,767       68,147            *
2000            .            .            .       28,140       71,326            5
2001            .            .            .       30,282       80,327            .
2002            .            .            .       32,445       90,277            .
2003            .            .            .       33,232      100,890            .
2004            .            .            .       35,361      110,421        1,082
2005            .            .            .       38,201      114,485        6,460
2006            .            .            .       40,639      117,892       10,788
2007            .            .            .       43,728      119,922       14,098
2008            .            .            .       46,131      115,391       29,668
2009            .            .            .       48,781      105,192       57,097
2010            .            .            .       49,646       99,622       74,583
2011            .            .            .       49,042       93,930       90,485
2012            .            .            .       51,083       91,204      107,918
2013            .            .            .       52,557       92,183      120,825
2014           14            .            .       55,105       92,755      139,137
2015           11            .            .       58,240       90,264      162,097
2016           26            .            .       61,273       81,286      196,948
2017           18           34          949       31,107       34,753      109,589
```

(Continued)

```
        druggr

        mixIns

All     1,795,061
Date
1995       19,099
1996       22,131
1997       24,288
1998       30,356
1999       37,187
2000       40,445
```

```
 2001       47,645
 2002       55,223
 2003       64,718
 2004       80,023
 2005       94,725
 2006      111,025
 2007      128,684
 2008      136,126
 2009      133,849
 2010      125,914
 2011      117,373
 2012      110,717
 2013      105,560
 2014      100,730
 2015       93,939
 2016       81,166
 2017       34,138


Dispensations on T2 from the RPMS                           19:40 Tuesday, May 8, 2018   3


 Metformin
   A10BA02  metformin                                10,743,209
 SU
   A10BB01  glibenclamid                              1,257,899
   A10BB03  tolbutamid                                  417,734
   A10BB04  glibornurid                                      98
   A10BB07  glipizid                                    656,429
   A10BB09  gliclazid                                   564,254
   A10BB12  glimepirid                                2,892,080
   A10BX02  repaglinid                                  222,391
   A10BX03  nateglinid                                       95
 TZD
   A10BG02  rosiglitazon                                 41,362
   A10BG03  pioglitazon                                  20,760
 DPP4
   A10BH01  sitagliptin                                 405,232
   A10BH02  vildagliptin                                 76,189
   A10BH03  saxagliptin                                  38,701
   A10BH04  alogliptin                                    6,665
   A10BH05  linagliptin                                  78,228
 GLP1
   A10BJ01  exenatid                                     43,375
   A10BJ02  liraglutid                                  996,743
   A10BJ03  lixisenatid                                   2,662
   A10BJ05  dulaglutid                                    8,191
 SGLT2
   A10BK01  dapagliflozin                                94,670
   A10BK02  canagliflozin                                 5,478
   A10BK03  empagliflozin                                44,418
 Acarbose
   A10BF01  acarbose                                    109,318
 MetxTZD
   A10BD03  metformin og rosiglitazon                   115,942
 MetxDPP4
   A10BD07  metformin og sitagliptin                    267,209
   A10BD08  metformin og vildagliptin                   270,674
   A10BD10  metformin og saxagliptin                        274
   A10BD11  metformin og linagliptin                      1,882
   A10BD13  metformin og alogliptin                       7,367
 MetxSGLT2
```

```
   A10BD15  metformin og dapagliflozin                    4,283
   A10BD16  metformin og canagliflozin                      225
   A10BD20  metformin og empagliflozin                    5,097
 SUxTZD
   A10BD04  glimepirid og rosiglitazon                      271
 TZDxDPP4
   A10BD09  pioglitazon og alogliptin                        69
 DPP4xSGLT2
   A10BD21  saxagliptin og dapagliflozin                     34
 InsxGLP1
   A10AE56  insulin degludec og liraglutid                  949
 fastIns
   A10AB01  insulin (human)                             461,700
   A10AB04  insulin lispro                               22,989
   A10AB05  insulin aspart                              408,159
   A10AB06  insulin glulisin                             11,094
 intIns
   A10AC01  insulin (human)                           1,985,315
 longIns
   A10AE01  insulin (human)                                   8
   A10AE04  insulin glargin                             633,768
   A10AE05  insulin detemir                             434,416
   A10AE06  insulin degludec                             52,591
 mixIns
   A10AD01  insulin (human)                             650,168
   A10AD04  insulin lispro                               14,676
   A10AD05  insulin aspart                            1,130,076
   A10AD06  insulin degludec og insulin aspart              141

Dispensed *drugs* to T2 ptt. from the RPMS                  19:40 Tuesday, May 8, 2018   4


                                                druggr

          All       Metformin        SU          TZD          DPP4         GLP1

           N            N            N            N            N            N

 All   26,878,885   12,416,162    6,011,251      178,404    1,152,524    1,050,971
 Date
 1995      364,856       68,573      209,175            .            .            .
 1996      420,944       82,128      236,688            .            .            .
 1997      454,555       91,503      250,638            .            .            .
 1998      504,996      104,375      271,182            .            .            .
 1999      563,147      127,803      290,980            .            .            .
 2000      608,447      164,539      293,860          115            .            .
 2001      679,074      205,400      303,689        2,734            .            .
 2002      748,965      252,127      307,795        3,725            .            .
 2003      834,072      303,459      321,128        4,287            .            .
 2004      946,563      371,651      334,014        8,456            .            .
 2005    1,049,322      434,995      339,883       15,506            .            .
 2006    1,166,936      515,474      341,096       25,348            .            .
 2007    1,281,549      591,151      340,337       33,682        5,375          371
 2008    1,415,921      682,601      336,491       31,201       29,323        5,169
 2009    1,520,867      765,734      315,331       27,935       49,592       14,312
 2010    1,650,756      855,889      291,803       20,337       71,639       58,850
 2011    1,784,402      957,544      265,320        1,557       98,042      108,984
 2012    1,891,885    1,041,070      231,891        1,192      117,018      137,962
 2013    1,931,904    1,064,173      200,590          950      136,864      150,395
 2014    1,962,088    1,069,866      175,371          539      159,659      151,692
 2015    1,980,788    1,047,445      155,239          366      180,398      160,477
```

```
 2016    2,073,959    1,085,395      137,500          302      199,450      172,492
 2017    1,042,889      533,267       61,250          172      105,164       90,267

(Continued)


                                         druggr

         SGLT2       Acarbose     InsxGLP1     fastIns       intIns      longIns

           N            N            N            N            N            N

 All       154,205      109,318          949      903,942    1,985,315    1,120,783
 Date
 1995            .        1,870            .       20,240       45,899            .
 1996            .        6,338            .       21,779       51,880            .
 1997            .        9,438            .       23,266       55,421            *
 1998            .       11,337            .       25,897       61,848            *
 1999            .       11,262            .       27,767       68,147            *
 2000            .       10,017            .       28,140       71,326            5
 2001            .        8,997            .       30,282       80,327            .
 2002            .        7,373            .       32,445       90,277            .
 2003            .        6,358            .       33,232      100,890            .
 2004            .        5,555            .       35,361      110,421        1,082
 2005            .        5,067            .       38,201      114,485        6,460
 2006            .        4,674            .       40,639      117,892       10,788
 2007            .        4,201            .       43,728      119,922       14,098
 2008            .        3,820            .       46,131      115,391       29,668
 2009            .        3,044            .       48,781      105,192       57,097
 2010            .        2,473            .       49,646       99,622       74,583
 2011            .        2,125            .       49,042       93,930       90,485
 2012           20        1,810            .       51,083       91,204      107,918
 2013        6,241        1,566            .       52,557       92,183      120,825
 2014       16,318          916            .       55,105       92,755      139,137
 2015       31,529          794            .       58,240       90,264      162,097
 2016       57,864          283            .       61,273       81,286      196,948
 2017       42,233            .          949       31,107       34,753      109,589

(Continued)


         druggr

         mixIns

           N

 All     1,795,061
 Date
 1995       19,099
 1996       22,131
 1997       24,288
 1998       30,356
 1999       37,187
 2000       40,445
 2001       47,645
 2002       55,223
 2003       64,718
```

```
 2004       80,023
 2005       94,725
 2006      111,025
 2007      128,684
 2008      136,126
 2009      133,849
 2010      125,914
 2011      117,373
 2012      110,717
 2013      105,560
 2014      100,730
 2015       93,939
 2016       81,166
 2017       34,138


                                                               19:40 Tuesday, May 8, 2018   5

The CONTENTS Procedure

Data Set Name        DAFDAT.PRMPS                  Observations          383033
Member Type          DATA                          Variables             30
Engine               V9                            Indexes               0
Created              08/05/2018 19:40:12           Observation Length    232
Last Modified        08/05/2018 19:40:12           Deleted Observations  0
Protection                                         Compressed            NO
Data Set Type                                      Sorted                NO
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                       Engine/Host Dependent Information

Data Set Page Size          65536
Number of Data Set Pages    1359
First Data Page             *
Max Obs per Page            282
Obs in First Data Page      265
Number of Data Set Repairs  0
ExtendObsCounter            YES
Filename                    E:\workdata\705093\BxC\daffodil\DATA\prmps.sas7bdat
Release Created             9.0401M3
Host Created                X64_SRV12


              Alphabetic List of Variables and Attributes

 #    Variable     Type    Len    Format       Informat    Label

28    DMtp         Char      *                             Type of DM
14    danyAca      Num       8
 9    danyDPP4     Num       8
10    danyGLP1     Num       8
15    danyMeg      Num       8
 *    danyMet      Num       8
12    danySGLT2    Num       8
 5    danySU       Num       8
 7    danyTZD      Num       8
26    doBth        Num       8    DDMMYY10.
29    doDM         Num       8    DDMMYY10.
27    doDth        Num       8    DDMMYY10.
```

```
22    doIns        Num      8    DDMMYY10.
24    doIns2       Num      4    YYMMDDN8.
21    doOAD        Num      8    DDMMYY10.
23    doOAD2       Num      4    YYMMDDN8.
20    doRMPS       Num      8
16    dofIns       Num      8
17    doiIns       Num      8
19    dolIns       Num      8
18    domIns       Num      8
13    donlAca      Num      8
 8    donlDPP4     Num      8
 *    donlMet      Num      8
11    donlSGLT2    Num      8
 4    donlSU       Num      8
 6    donlTZD      Num      8
30    inCr         Char     4
 *    pnr          Char    12    $12.        $10.        Personnummer
25    sex          Num      8

                                                 19:40 Tuesday, May 8, 2018   6

The CONTENTS Procedure

Data Set Name        DAFDAT.DISP                 Observations          26205558
Member Type          DATA                        Variables             9
Engine               V9                          Indexes               0
Created              08/05/2018 19:48:40         Observation Length    72
Last Modified        08/05/2018 19:48:40         Deleted Observations  0
Protection                                       Compressed            NO
Data Set Type                                    Sorted                NO
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                      Engine/Host Dependent Information

Data Set Page Size          65536
Number of Data Set Pages    28861
First Data Page             *
Max Obs per Page            908
Obs in First Data Page      880
Number of Data Set Repairs  0
ExtendObsCounter            YES
Filename                    E:\workdata\705093\BxC\daffodil\DATA\disp.sas7bdat
Release Created             9.0401M3
Host Created                X64_SRV12


                      Alphabetic List of Variables and Attributes

#    Variable    Type    Len    Format       Informat    Label

6    ATC         Char      8    $8.          $16.        ATC-kode detaljeret (s)
8    PACKSIZE    Num       8    13.3         13.3        Numerisk pakningsstrrelse (s)
7    Volume      Num       8    13.3         13.3        Mype
4    apk         Num       8    BEST12.                  Antal pakninger
9    doDM        Num       8    DDMMYY10.
5    doso        Char      7    $7.                      Doseringskode
1    druggr      Char      7
3    eksd        Num       4    YYMMDDN8.                Ekspeditionsdato
2    pnr         Char     12    $12.         $10.        Personnummer
```

```
                                                         19:40 Tuesday, May 8, 2018   7

The CONTENTS Procedure

Data Set Name        DAFDAT.XDISP                 Observations          26878885
Member Type          DATA                         Variables             9
Engine               V9                           Indexes               0
Created              08/05/2018 19:48:50          Observation Length    72
Last Modified        08/05/2018 19:48:50          Deleted Observations  0
Protection                                        Compressed            NO
Data Set Type                                     Sorted                NO
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                       Engine/Host Dependent Information

Data Set Page Size          65536
Number of Data Set Pages    29603
First Data Page             *
Max Obs per Page            908
Obs in First Data Page      880
Number of Data Set Repairs  0
ExtendObsCounter            YES
Filename                    E:\workdata\705093\BxC\daffodil\DATA\xdisp.sas7bdat
Release Created             9.0401M3
Host Created                X64_SRV12


                      Alphabetic List of Variables and Attributes

#    Variable    Type    Len    Format       Informat    Label

6    ATC         Char      8    $8.          $16.        ATC-kode detaljeret (s)
8    PACKSIZE    Num       8    13.3         13.3        Numerisk pakningsstrrelse (s)
7    Volume      Num       8    13.3         13.3        Mype
4    apk         Num       8    BEST12.                  Antal pakninger
9    doDM        Num       8    DDMMYY10.
5    doso        Char      7    $7.                      Doseringskode
1    druggr      Char      7
3    eksd        Num       4    YYMMDDN8.                Ekspeditionsdato
2    pnr         Char     12    $12.         $10.        Personnummer
```

4.6 07-newuse

Extracts the new user dates of various drugs and defines the index dates (`doIx`) and index drugs (`Ixdr`) for each episode. There may be several episodes for each person, even episodes that start the same day, if more than one drug is first dispensed the same day.

Adds counts of pre and post index HF events and date of the first of the post-index ones. Also adds indicators of use of drugs during the last year before index.

```
1                              "Program: 07-newuse.sas"     16:43 Wednesday, May 9, 2018
```

```
NOTE: AUTOEXEC processing completed.

1          * Enumerate the new user epidsodes after 2012 with date and drug,
2            based on the dispensation data ;
3
4          * maximal allowed gap allowed before we call it a stop (days) ;
5          %let mgap = 180 ;
6          * windows of evaluation from index date and back ;
7          %let mwin = 365.25   ; * medication ;
8          %let hwin = 365.25   ; * hospitalization ;
9          %let cwin = 365.25*5 ; * cancer diagnosis ;
10         * date of SGLT2 intro on market ;
11         %let s2i = '01dec2012'd ;
12
13         * note we use the dataset with single drugs,
14           so some dispensations yield 2 different episodes ;
15         proc sort  data = dafdat.xdisp ( where = ( eksd lt &end. ) )
16                     out = sxdisp ;
17           by pnr druggr eksd ;
18         run ;

NOTE: There were 25835996 observations read from the data set DAFDAT.XDISP.
      WHERE eksd<'01JAN2017'D;
NOTE: The data set WORK.SXDISP has 25835996 observations and 9 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           25.78 seconds
      cpu time            13.07 seconds



19
20         * dataset with starting dates for episodes ;
21         * newepi has one record per episode ;
22         * newrec has a record per dispensation in episodes ;
23         data newepi
24              newrec ;
25           set sxdisp ( keep = pnr druggr atc eksd doDM ) ;
26           by pnr druggr ;
27           if first.pnr then epiN = 0 ;
28           retain doIx Ixdr Ixatc ;
29           if ( first.druggr ) then do ; Ixdr  = put( druggr, $druggr. ) ;
30                                         Ixatc = atc    ; end ;
31           if ( (  first.druggr ) or
32                ( ^first.druggr and dif( eksd ) gt &mwin. ) ) and
33              ( eksd gt &s2i. )
34              then do ;
35              doIx = eksd ;
36              epiN + 1 ;
37              output newepi ;
38              end ;
39           if epiN gt 0 then output newrec ;
40         run ;

NOTE: There were 25835996 observations read from the data set WORK.SXDISP.
NOTE: The data set WORK.NEWEPI has 244715 observations and 9 variables.
NOTE: The data set WORK.NEWREC has 4450151 observations and 9 variables.
NOTE: DATA statement used (Total process time):
      real time           5.96 seconds
      cpu time            3.81 seconds
```

```
41
42         * Now find the last dispensation in each episode ;
43         data epiX ( keep = pnr druggr eksd epiN
44                  rename = ( eksd = lastpr ) ) ;
45           set newrec ;
46           by pnr druggr epiN ;
47           if last.epiN ;
48         run ;

NOTE: There were 4450151 observations read from the data set WORK.NEWREC.
NOTE: The data set WORK.EPIX has 307602 observations and 4 variables.
NOTE: DATA statement used (Total process time):
      real time           0.78 seconds
      cpu time            0.56 seconds


49
50         * Merge last dispensation in each episode with the episodes and
51           compute date of termination (if before end of study) ;
52         data newu ;
53           merge newepi ( in = ok )
54                 epiX ;
55           by pnr druggr epiN ;
56           if ok ;
57           doTm = lastpr + &mgap. ;
58           if doTm gt &end. then doTm = . ;
59         run ;

NOTE: There were 244715 observations read from the data set WORK.NEWEPI.
NOTE: There were 307602 observations read from the data set WORK.EPIX.
NOTE: The data set WORK.NEWU has 244715 observations and 11 variables.
NOTE: DATA statement used (Total process time):
      real time           0.14 seconds
      cpu time            0.12 seconds


60
61         * epiN is not chronological so make it;
62         proc sort  data = newu ; by pnr doIx Ixdr ; run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: The data set WORK.NEWU has 244715 observations and 11 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.07 seconds
      cpu time            0.14 seconds


63         data newu ;
64           set newu ;
65           by pnr ;
66           if first.pnr then epN = 0 ;
67           epN+1 ;
68           epiN = epN ;
69           drop epN ;
70         run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: The data set WORK.NEWU has 244715 observations and 11 variables.
NOTE: DATA statement used (Total process time):
      real time           0.09 seconds
      cpu time            0.07 seconds
```

```

           * newu now has one record per new-use episode
             - some persons have more episodes, some overlapping,
             - and even with identical index dates ;
           title1 'All new start episodes (some persons with > 1) in T2 after dec 2012' ;
           proc tabulate  data = newu  missing  noseps ;
             class Ixdr doIx doTm epiN;
             table all Ixdr,
                 ( all doIx doTm) * f = comma7.
                 / rts = 15  condense ;
             table all epiN,
                 ( all Ixdr ) * f=comma7.
                   / rts = 8  indent = 2 ;
             format doIx doTm yyqs6.
                      Ixdr $druggr. ;
           run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: The PROCEDURE TABULATE printed pages 1-3.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.10 seconds
      cpu time            0.31 seconds


           title1 ;

           * Sort all diabetes dispensations by pnr and date ;
           proc sort  data = dafdat.disp  out = disp ;
              by pnr eksd ;
           run ;

NOTE: There were 26205558 observations read from the data set DAFDAT.DISP.
NOTE: The data set WORK.DISP has 26205558 observations and 9 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           23.18 seconds
      cpu time            11.06 seconds



           * Restrict NPR records to persons in data ;
           proc sort  data = newu (keep=pnr)  out = pers  nodupkey ; by pnr ; run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: 88533 observations with duplicate key values were deleted.
NOTE: The data set WORK.PERS has 156182 observations and 1 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.06 seconds
      cpu time            0.09 seconds


           data phosp ;
             merge dafdat.hosp pers ( in = ok ) ;
             by pnr ;
             if ok ;
           run ;

NOTE: There were 34324010 observations read from the data set DAFDAT.HOSP.
NOTE: There were 156182 observations read from the data set WORK.PERS.
NOTE: The data set WORK.PHOSP has 1889909 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           26.14 seconds
```

```
      cpu time            4.73 seconds


101
102           * Find date and type of first line dispensation (FL) for each person ;
103           data FL ( keep = pnr doFL FLdr FLatc ) ;
104             set disp ;
105             by pnr eksd ;
106             if first.pnr then do ;
107                doFL    = eksd ;
108                  FLdr  = druggr ;
109                  FLatc = atc ;
110                output ;
111                end  ;
112             format doFl ddmmyy10. ;
113           run ;

NOTE: There were 26205558 observations read from the data set WORK.DISP.
NOTE: The data set WORK.FL has 383033 observations and 4 variables.
NOTE: DATA statement used (Total process time):
      real time           5.17 seconds
      cpu time            3.74 seconds


114
115           * Things to merge onto the >episodes<, which are classified by pnr,
116             doIx and Ixdr. The characteristics we append to the episodes comes
117             from datasets with multiple records per pnr. Hence we must merge with
118             subsets of the episodes datasets where only one intancen of each pnr
119             is present ;
120
121           * datasets to collect covariate information across episodes within persons ;
122           data hosp  ; * hospitalizations and cancer in the last 5 years ;
123            run ;

NOTE: The data set WORK.HOSP has 1 observations and 0 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds


124           data ldrug ; * DM drugs in last year before doIx ;
125            run ;

NOTE: The data set WORK.LDRUG has 1 observations and 0 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds


126           data lmed  ; * Other drugs in last year before doIx ;
127            run ;

NOTE: The data set WORK.LMED has 1 observations and 0 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds


128
129           options nomprint ;
130
```

```
%macro colcov ;

* This macro COLlects COVariates for the episodes ;

%do ne = 1 %to 11 ;

************** start of looping with &ne. ******************** ;

data hosp&ne. ( keep = pnr epiN doIx maxH frail doCancer ) ;
  merge newu ( in = nu
            where = (epiN eq &ne.) )
        phosp ;
  by pnr ;
  retain maxH doCancer ;
  label maxH = 'Longest hospital stay in last year before doIx'
       frail = 'More than 3 consecutive hospital days last yr' ;
  if nu ;
  if first.pnr then do ;
     maxH = 0 ;
     doCancer = . ;
     end ;
  * The latest cancer during the last cwin days before doIx ;
  if (doIx - &cwin.) < d_inddto < doIx and compl eq 'Cancer'
     then doCancer = max( doCancer, d_inddto ) ;
  * Maximum bed-days in the last hwin days before doIx ;
  if (doIx - &hwin.) < d_inddto < doIx
     then maxH = max( maxH, v_sengdage ) ;
  if last.pnr then do ;
     frail = ( maxH ge 4 ) ;
     output ;
     end ;
run ;

data hosp ; set hosp hosp&ne. ; run ;

* derive other DM dispensations in the last year before doIx ;
data ldrug&ne. ;
  merge newu ( in = nu
            where = (epiN eq &ne.) )
        dafdat.disp ( where = (eksd ge (&s2i.-366)) ) ;
  by pnr ;
  if nu ;
  if ( ( doIx - &mwin. ) < eksd <= doIx ) and ( druggr ne Ixdr ) ;
  drgr = put( druggr, $druggr. ) ;
run ;

proc sort data = ldrug&ne. ;
  by pnr drgr eksd ;
run ;

* last dispense before index in the last year ;
data ldrug&ne. ;
  set ldrug&ne. ;
  by pnr drgr eksd ;
  if last.drgr ;
  format eksd ddmmyy10. ;
run ;

* transpose to be able to merge to analysis dataset ;
proc transpose  data = ldrug&ne.
                 out = ldrug&ne. ( drop = _LABEL_ _NAME_ )
              prefix = dol ;
```

```
  by pnr epiN ;
  var eksd ;
  id drgr ;
run ;

data ldrug ; set ldrug ldrug&ne. ; run ;

* other types of dispensations taken out during last year before doIx ;
data lmed&ne. ;
  merge newu ( in = nu
             where = (epiN eq &ne.) )
        dafdat.lmed ;
  by pnr ;
  if nu ;
  if ( ( doIx - &mwin. ) < eksd < doIx )  ;
run ;

proc sort data = lmed&ne. ;
  by pnr medgr eksd ;
run ;

* last dispense before index in the last year ;
data lmed&ne. ;
  set lmed&ne. ;
  by pnr medgr eksd ;
  if last.medgr ;
  format eksd ddmmyy10. ;
run ;

* turn it on side to merge to analysis dataset ;
proc transpose  data = lmed&ne.
                 out = lmed&ne. ( drop = _LABEL_ _NAME_ )
              prefix = dol ;
  by pnr epiN ;
  var eksd ;
  id medgr ;
run ;

data lmed ; set lmed lmed&ne. ; run ;

%end ;

%mend colcov ;

%colcov ;

NOTE: There were 156182 observations read from the data set WORK.NEWU.
      WHERE epiN=1;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP1 has 156182 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.46 seconds
      cpu time            0.35 seconds



NOTE: There were 1 observations read from the data set WORK.HOSP.
NOTE: There were 156182 observations read from the data set WORK.HOSP1.
NOTE: The data set WORK.HOSP has 156183 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.03 seconds
      cpu time            0.01 seconds
```

```
NOTE: There were 156182 observations read from the data set WORK.NEWU.
      WHERE epiN=1;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG1 has 924554 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           20.59 seconds
      cpu time            3.48 seconds



NOTE: There were 924554 observations read from the data set WORK.LDRUG1.
NOTE: The data set WORK.LDRUG1 has 924554 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.40 seconds
      cpu time            0.50 seconds



NOTE: There were 924554 observations read from the data set WORK.LDRUG1.
NOTE: The data set WORK.LDRUG1 has 251732 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.32 seconds
      cpu time            0.14 seconds



NOTE: There were 251732 observations read from the data set WORK.LDRUG1.
NOTE: The data set WORK.LDRUG1 has 152371 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.37 seconds
      cpu time            0.29 seconds



NOTE: There were 1 observations read from the data set WORK.LDRUG.
NOTE: There were 152371 observations read from the data set WORK.LDRUG1.
NOTE: The data set WORK.LDRUG has 152372 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.03 seconds



NOTE: There were 156182 observations read from the data set WORK.NEWU.
      WHERE epiN=1;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED1 has 1824109 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           14.70 seconds
      cpu time            3.15 seconds



NOTE: There were 1824109 observations read from the data set WORK.LMED1.
NOTE: The data set WORK.LMED1 has 1824109 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.62 seconds
      cpu time            0.92 seconds
```

```
NOTE: There were 1824109 observations read from the data set WORK.LMED1.
NOTE: The data set WORK.LMED1 has 416530 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.56 seconds
      cpu time            0.35 seconds



NOTE: There were 416530 observations read from the data set WORK.LMED1.
NOTE: The data set WORK.LMED1 has 124862 observations and 22 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.45 seconds
      cpu time            0.37 seconds



NOTE: There were 1 observations read from the data set WORK.LMED.
NOTE: There were 124862 observations read from the data set WORK.LMED1.
NOTE: The data set WORK.LMED has 124863 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.03 seconds



NOTE: There were 57025 observations read from the data set WORK.NEWU.
      WHERE epiN=2;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP2 has 57025 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.42 seconds
      cpu time            0.26 seconds



NOTE: There were 156183 observations read from the data set WORK.HOSP.
NOTE: There were 57025 observations read from the data set WORK.HOSP2.
NOTE: The data set WORK.HOSP has 213208 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 57025 observations read from the data set WORK.NEWU.
      WHERE epiN=2;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG2 has 513113 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           22.59 seconds
      cpu time            3.23 seconds



NOTE: There were 513113 observations read from the data set WORK.LDRUG2.
NOTE: The data set WORK.LDRUG2 has 513113 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.15 seconds
```

```
      cpu time            0.34 seconds



NOTE: There were 513113 observations read from the data set WORK.LDRUG2.
NOTE: The data set WORK.LDRUG2 has 130759 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.13 seconds
      cpu time            0.14 seconds



NOTE: There were 130759 observations read from the data set WORK.LDRUG2.
NOTE: The data set WORK.LDRUG2 has 56686 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.15 seconds
      cpu time            0.15 seconds



NOTE: There were 152372 observations read from the data set WORK.LDRUG.
NOTE: There were 56686 observations read from the data set WORK.LDRUG2.
NOTE: The data set WORK.LDRUG has 209058 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.03 seconds
      cpu time            0.03 seconds



NOTE: There were 57025 observations read from the data set WORK.NEWU.
      WHERE epiN=2;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED2 has 705486 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           13.29 seconds
      cpu time            2.96 seconds



NOTE: There were 705486 observations read from the data set WORK.LMED2.
NOTE: The data set WORK.LMED2 has 705486 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.17 seconds
      cpu time            0.37 seconds



NOTE: There were 705486 observations read from the data set WORK.LMED2.
NOTE: The data set WORK.LMED2 has 163287 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.17 seconds
      cpu time            0.17 seconds



NOTE: There were 163287 observations read from the data set WORK.LMED2.
NOTE: The data set WORK.LMED2 has 48093 observations and 22 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.15 seconds
      cpu time            0.15 seconds
```

```
NOTE: There were 124863 observations read from the data set WORK.LMED.
NOTE: There were 48093 observations read from the data set WORK.LMED2.
NOTE: The data set WORK.LMED has 172956 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 20996 observations read from the data set WORK.NEWU.
      WHERE epiN=3;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP3 has 20996 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.31 seconds
      cpu time            0.31 seconds



NOTE: There were 213208 observations read from the data set WORK.HOSP.
NOTE: There were 20996 observations read from the data set WORK.HOSP3.
NOTE: The data set WORK.HOSP has 234204 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 20996 observations read from the data set WORK.NEWU.
      WHERE epiN=3;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG3 has 233601 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           20.28 seconds
      cpu time            3.20 seconds



NOTE: There were 233601 observations read from the data set WORK.LDRUG3.
NOTE: The data set WORK.LDRUG3 has 233601 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.07 seconds
      cpu time            0.17 seconds



NOTE: There were 233601 observations read from the data set WORK.LDRUG3.
NOTE: The data set WORK.LDRUG3 has 58769 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.07 seconds



NOTE: There were 58769 observations read from the data set WORK.LDRUG3.
NOTE: The data set WORK.LDRUG3 has 20838 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.06 seconds
      cpu time            0.06 seconds
```

```
NOTE: There were 209058 observations read from the data set WORK.LDRUG.
NOTE: There were 20838 observations read from the data set WORK.LDRUG3.
NOTE: The data set WORK.LDRUG has 229896 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 20996 observations read from the data set WORK.NEWU.
      WHERE epiN=3;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED3 has 261298 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           13.29 seconds
      cpu time            2.98 seconds



NOTE: There were 261298 observations read from the data set WORK.LMED3.
NOTE: The data set WORK.LMED3 has 261298 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.07 seconds
      cpu time            0.14 seconds



NOTE: There were 261298 observations read from the data set WORK.LMED3.
NOTE: The data set WORK.LMED3 has 61549 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.06 seconds



NOTE: There were 61549 observations read from the data set WORK.LMED3.
NOTE: The data set WORK.LMED3 has 18097 observations and 22 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.06 seconds
      cpu time            0.06 seconds



NOTE: There were 172956 observations read from the data set WORK.LMED.
NOTE: There were 18097 observations read from the data set WORK.LMED3.
NOTE: The data set WORK.LMED has 191053 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 7284 observations read from the data set WORK.NEWU.
      WHERE epiN=4;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP4 has 7284 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.31 seconds
      cpu time            0.31 seconds
```

```
NOTE: There were 234204 observations read from the data set WORK.HOSP.
NOTE: There were 7284 observations read from the data set WORK.HOSP4.
NOTE: The data set WORK.HOSP has 241488 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.03 seconds
      cpu time            0.03 seconds



NOTE: There were 7284 observations read from the data set WORK.NEWU.
      WHERE epiN=4;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG4 has 92725 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           18.45 seconds
      cpu time            3.18 seconds



NOTE: There were 92725 observations read from the data set WORK.LDRUG4.
NOTE: The data set WORK.LDRUG4 has 92725 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.06 seconds
      cpu time            0.03 seconds



NOTE: There were 92725 observations read from the data set WORK.LDRUG4.
NOTE: The data set WORK.LDRUG4 has 22943 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 22943 observations read from the data set WORK.LDRUG4.
NOTE: The data set WORK.LDRUG4 has 7250 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.03 seconds
      cpu time            0.03 seconds



NOTE: There were 229896 observations read from the data set WORK.LDRUG.
NOTE: There were 7250 observations read from the data set WORK.LDRUG4.
NOTE: The data set WORK.LDRUG has 237146 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.03 seconds



NOTE: There were 7284 observations read from the data set WORK.NEWU.
      WHERE epiN=4;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED4 has 89172 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           12.68 seconds
      cpu time            2.87 seconds
```

```
NOTE: There were 89172 observations read from the data set WORK.LMED4.
NOTE: The data set WORK.LMED4 has 89172 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.03 seconds
      cpu time            0.03 seconds



NOTE: There were 89172 observations read from the data set WORK.LMED4.
NOTE: The data set WORK.LMED4 has 21153 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.03 seconds
      cpu time            0.03 seconds



NOTE: There were 21153 observations read from the data set WORK.LMED4.
NOTE: The data set WORK.LMED4 has 6254 observations and 22 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 191053 observations read from the data set WORK.LMED.
NOTE: There were 6254 observations read from the data set WORK.LMED4.
NOTE: The data set WORK.LMED has 197307 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.04 seconds



NOTE: There were 2267 observations read from the data set WORK.NEWU.
      WHERE epiN=5;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP5 has 2267 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.38 seconds
      cpu time            0.23 seconds



NOTE: There were 241488 observations read from the data set WORK.HOSP.
NOTE: There were 2267 observations read from the data set WORK.HOSP5.
NOTE: The data set WORK.HOSP has 243755 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.04 seconds



NOTE: There were 2267 observations read from the data set WORK.NEWU.
      WHERE epiN=5;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG5 has 30908 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           19.32 seconds
```

```
      cpu time            3.18 seconds



NOTE: There were 30908 observations read from the data set WORK.LDRUG5.
NOTE: The data set WORK.LDRUG5 has 30908 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.00 seconds



NOTE: There were 30908 observations read from the data set WORK.LDRUG5.
NOTE: The data set WORK.LDRUG5 has 7778 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 7778 observations read from the data set WORK.LDRUG5.
NOTE: The data set WORK.LDRUG5 has 2253 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 237146 observations read from the data set WORK.LDRUG.
NOTE: There were 2253 observations read from the data set WORK.LDRUG5.
NOTE: The data set WORK.LDRUG has 239399 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.07 seconds



NOTE: There were 2267 observations read from the data set WORK.NEWU.
      WHERE epiN=5;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED5 has 26004 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           9.92 seconds
      cpu time            2.95 seconds



NOTE: There were 26004 observations read from the data set WORK.LMED5.
NOTE: The data set WORK.LMED5 has 26004 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 26004 observations read from the data set WORK.LMED5.
NOTE: The data set WORK.LMED5 has 6289 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds
```

```
NOTE: There were 6289 observations read from the data set WORK.LMED5.
NOTE: The data set WORK.LMED5 has 1933 observations and 22 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 197307 observations read from the data set WORK.LMED.
NOTE: There were 1933 observations read from the data set WORK.LMED5.
NOTE: The data set WORK.LMED has 199240 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 671 observations read from the data set WORK.NEWU.
      WHERE epiN=6;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP6 has 671 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.37 seconds
      cpu time            0.31 seconds



NOTE: There were 243755 observations read from the data set WORK.HOSP.
NOTE: There were 671 observations read from the data set WORK.HOSP6.
NOTE: The data set WORK.HOSP has 244426 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.04 seconds



NOTE: There were 671 observations read from the data set WORK.NEWU.
      WHERE epiN=6;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG6 has 9086 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.84 seconds
      cpu time            3.36 seconds



NOTE: There were 9086 observations read from the data set WORK.LDRUG6.
NOTE: The data set WORK.LDRUG6 has 9086 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 9086 observations read from the data set WORK.LDRUG6.
NOTE: The data set WORK.LDRUG6 has 2384 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds
```

```
NOTE: There were 2384 observations read from the data set WORK.LDRUG6.
NOTE: The data set WORK.LDRUG6 has 666 observations and 16 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 239399 observations read from the data set WORK.LDRUG.
NOTE: There were 666 observations read from the data set WORK.LDRUG6.
NOTE: The data set WORK.LDRUG has 240065 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.04 seconds



NOTE: There were 671 observations read from the data set WORK.NEWU.
      WHERE epiN=6;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED6 has 6251 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           3.01 seconds
      cpu time            3.00 seconds



NOTE: There were 6251 observations read from the data set WORK.LMED6.
NOTE: The data set WORK.LMED6 has 6251 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 6251 observations read from the data set WORK.LMED6.
NOTE: The data set WORK.LMED6 has 1668 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 1668 observations read from the data set WORK.LMED6.
NOTE: The data set WORK.LMED6 has 539 observations and 21 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 199240 observations read from the data set WORK.LMED.
NOTE: There were 539 observations read from the data set WORK.LMED6.
NOTE: The data set WORK.LMED has 199779 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.03 seconds
```

```
NOTE: There were 207 observations read from the data set WORK.NEWU.
      WHERE epiN=7;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP7 has 207 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.37 seconds
      cpu time            0.25 seconds



NOTE: There were 244426 observations read from the data set WORK.HOSP.
NOTE: There were 207 observations read from the data set WORK.HOSP7.
NOTE: The data set WORK.HOSP has 244633 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.00 seconds



NOTE: There were 207 observations read from the data set WORK.NEWU.
      WHERE epiN=7;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG7 has 2840 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.31 seconds
      cpu time            3.31 seconds



NOTE: There were 2840 observations read from the data set WORK.LDRUG7.
NOTE: The data set WORK.LDRUG7 has 2840 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 2840 observations read from the data set WORK.LDRUG7.
NOTE: The data set WORK.LDRUG7 has 749 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 749 observations read from the data set WORK.LDRUG7.
NOTE: The data set WORK.LDRUG7 has 207 observations and 15 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 240065 observations read from the data set WORK.LDRUG.
NOTE: There were 207 observations read from the data set WORK.LDRUG7.
NOTE: The data set WORK.LDRUG has 240272 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.03 seconds
```

```
NOTE: There were 207 observations read from the data set WORK.NEWU.
      WHERE epiN=7;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED7 has 1649 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           2.98 seconds
      cpu time            2.98 seconds



NOTE: There were 1649 observations read from the data set WORK.LMED7.
NOTE: The data set WORK.LMED7 has 1649 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 1649 observations read from the data set WORK.LMED7.
NOTE: The data set WORK.LMED7 has 478 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 478 observations read from the data set WORK.LMED7.
NOTE: The data set WORK.LMED7 has 161 observations and 19 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 199779 observations read from the data set WORK.LMED.
NOTE: There were 161 observations read from the data set WORK.LMED7.
NOTE: The data set WORK.LMED has 199940 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.03 seconds



NOTE: There were 64 observations read from the data set WORK.NEWU.
      WHERE epiN=8;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP8 has 64 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.37 seconds
      cpu time            0.20 seconds



NOTE: There were 244633 observations read from the data set WORK.HOSP.
NOTE: There were 64 observations read from the data set WORK.HOSP8.
NOTE: The data set WORK.HOSP has 244697 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.06 seconds
```

```
NOTE: There were 64 observations read from the data set WORK.NEWU.
      WHERE epiN=8;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG8 has 845 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.31 seconds
      cpu time            3.31 seconds



NOTE: There were 845 observations read from the data set WORK.LDRUG8.
NOTE: The data set WORK.LDRUG8 has 845 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 845 observations read from the data set WORK.LDRUG8.
NOTE: The data set WORK.LDRUG8 has 241 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 241 observations read from the data set WORK.LDRUG8.
NOTE: The data set WORK.LDRUG8 has 64 observations and 14 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 240272 observations read from the data set WORK.LDRUG.
NOTE: There were 64 observations read from the data set WORK.LDRUG8.
NOTE: The data set WORK.LDRUG has 240336 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.04 seconds



NOTE: There were 64 observations read from the data set WORK.NEWU.
      WHERE epiN=8;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED8 has 457 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           2.95 seconds
      cpu time            2.93 seconds



NOTE: There were 457 observations read from the data set WORK.LMED8.
NOTE: The data set WORK.LMED8 has 457 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds
```

```
NOTE: There were 457 observations read from the data set WORK.LMED8.
NOTE: The data set WORK.LMED8 has 131 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 131 observations read from the data set WORK.LMED8.
NOTE: The data set WORK.LMED8 has 48 observations and 17 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 199940 observations read from the data set WORK.LMED.
NOTE: There were 48 observations read from the data set WORK.LMED8.
NOTE: The data set WORK.LMED has 199988 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.03 seconds



NOTE: There were 15 observations read from the data set WORK.NEWU.
      WHERE epiN=9;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP9 has 15 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.37 seconds
      cpu time            0.26 seconds



NOTE: There were 244697 observations read from the data set WORK.HOSP.
NOTE: There were 15 observations read from the data set WORK.HOSP9.
NOTE: The data set WORK.HOSP has 244712 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.03 seconds



NOTE: There were 15 observations read from the data set WORK.NEWU.
      WHERE epiN=9;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG9 has 221 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.32 seconds
      cpu time            3.28 seconds



NOTE: There were 221 observations read from the data set WORK.LDRUG9.
NOTE: The data set WORK.LDRUG9 has 221 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds
```

```
NOTE: There were 221 observations read from the data set WORK.LDRUG9.
NOTE: The data set WORK.LDRUG9 has 65 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 65 observations read from the data set WORK.LDRUG9.
NOTE: The data set WORK.LDRUG9 has 15 observations and 13 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 240336 observations read from the data set WORK.LDRUG.
NOTE: There were 15 observations read from the data set WORK.LDRUG9.
NOTE: The data set WORK.LDRUG has 240351 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.06 seconds



NOTE: There were 15 observations read from the data set WORK.NEWU.
      WHERE epiN=9;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED9 has 81 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           2.93 seconds
      cpu time            2.93 seconds



NOTE: There were 81 observations read from the data set WORK.LMED9.
NOTE: The data set WORK.LMED9 has 81 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 81 observations read from the data set WORK.LMED9.
NOTE: The data set WORK.LMED9 has 33 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 33 observations read from the data set WORK.LMED9.
NOTE: The data set WORK.LMED9 has 12 observations and 14 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 199988 observations read from the data set WORK.LMED.
```

```
NOTE: There were 12 observations read from the data set WORK.LMED9.
NOTE: The data set WORK.LMED has 200000 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.06 seconds



NOTE: There were 3 observations read from the data set WORK.NEWU.
      WHERE epiN=10;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP10 has 3 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.29 seconds
      cpu time            0.28 seconds



NOTE: There were 244712 observations read from the data set WORK.HOSP.
NOTE: There were 3 observations read from the data set WORK.HOSP10.
NOTE: The data set WORK.HOSP has 244715 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.04 seconds
      cpu time            0.04 seconds



NOTE: There were 3 observations read from the data set WORK.NEWU.
      WHERE epiN=10;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG10 has 24 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.18 seconds
      cpu time            3.15 seconds



NOTE: There were 24 observations read from the data set WORK.LDRUG10.
NOTE: The data set WORK.LDRUG10 has 24 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 24 observations read from the data set WORK.LDRUG10.
NOTE: The data set WORK.LDRUG10 has 11 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 11 observations read from the data set WORK.LDRUG10.
NOTE: The data set WORK.LDRUG10 has 3 observations and 9 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds
```

```
NOTE: There were 240351 observations read from the data set WORK.LDRUG.
NOTE: There were 3 observations read from the data set WORK.LDRUG10.
NOTE: The data set WORK.LDRUG has 240354 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.04 seconds



NOTE: There were 3 observations read from the data set WORK.NEWU.
      WHERE epiN=10;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED10 has 3 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           2.70 seconds
      cpu time            2.70 seconds



NOTE: There were 3 observations read from the data set WORK.LMED10.
NOTE: The data set WORK.LMED10 has 3 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 3 observations read from the data set WORK.LMED10.
NOTE: The data set WORK.LMED10 has 2 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 2 observations read from the data set WORK.LMED10.
NOTE: The data set WORK.LMED10 has 2 observations and 4 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 200000 observations read from the data set WORK.LMED.
NOTE: There were 2 observations read from the data set WORK.LMED10.
NOTE: The data set WORK.LMED has 200002 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.04 seconds



NOTE: There were 1 observations read from the data set WORK.NEWU.
      WHERE epiN=11;
NOTE: There were 1889909 observations read from the data set WORK.PHOSP.
NOTE: The data set WORK.HOSP11 has 1 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.34 seconds
      cpu time            0.29 seconds
```

```
NOTE: There were 244715 observations read from the data set WORK.HOSP.
NOTE: There were 1 observations read from the data set WORK.HOSP11.
NOTE: The data set WORK.HOSP has 244716 observations and 6 variables.
NOTE: DATA statement used (Total process time):
      real time           0.06 seconds
      cpu time            0.04 seconds



NOTE: There were 1 observations read from the data set WORK.NEWU.
      WHERE epiN=11;
NOTE: There were 10576531 observations read from the data set DAFDAT.DISP.
      WHERE eksd>='01DEC2011'D;
NOTE: The data set WORK.LDRUG11 has 11 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           3.20 seconds
      cpu time            3.20 seconds



NOTE: There were 11 observations read from the data set WORK.LDRUG11.
NOTE: The data set WORK.LDRUG11 has 11 observations and 16 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 11 observations read from the data set WORK.LDRUG11.
NOTE: The data set WORK.LDRUG11 has 5 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 5 observations read from the data set WORK.LDRUG11.
NOTE: The data set WORK.LDRUG11 has 1 observations and 7 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 240354 observations read from the data set WORK.LDRUG.
NOTE: There were 1 observations read from the data set WORK.LDRUG11.
NOTE: The data set WORK.LDRUG has 240355 observations and 16 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.06 seconds



NOTE: There were 1 observations read from the data set WORK.NEWU.
      WHERE epiN=11;
NOTE: There were 25061393 observations read from the data set DAFDAT.LMED.
NOTE: The data set WORK.LMED11 has 5 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           2.71 seconds
      cpu time            2.67 seconds
```

```
NOTE: There were 5 observations read from the data set WORK.LMED11.
NOTE: The data set WORK.LMED11 has 5 observations and 12 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 5 observations read from the data set WORK.LMED11.
NOTE: The data set WORK.LMED11 has 4 observations and 12 variables.
NOTE: DATA statement used (Total process time):
      real time           0.01 seconds
      cpu time            0.01 seconds



NOTE: There were 4 observations read from the data set WORK.LMED11.
NOTE: The data set WORK.LMED11 has 1 observations and 6 variables.
NOTE: PROCEDURE TRANSPOSE used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds



NOTE: There were 200002 observations read from the data set WORK.LMED.
NOTE: There were 1 observations read from the data set WORK.LMED11.
NOTE: The data set WORK.LMED has 200003 observations and 22 variables.
NOTE: DATA statement used (Total process time):
      real time           0.07 seconds
      cpu time            0.06 seconds


238
239          * Cause of death ;
240          data cod  ( keep = pnr deCVDD coD ) ;
241            set grund.dodsaasg2016 ;
242            format deCVDD  ddmmyy10. ;
243          * label coD = "Cause of (CVD) death"
244                deCVDD = "Date of CVD-death" ;
245            if ( substr( C_DODTILGRUNDL_ACME, 1, 1 ) eq "I" and
246                 substr( C_DODTILGRUNDL_ACME, 1, 3 ) ne "I10" ) ;
247            deCVDD = D_DODSDATO ;
248            coD = C_DODTILGRUNDL_ACME ;
249            if deCVDD > '01DEC2012'd ;
250          run ;

NOTE: There were 811233 observations read from the data set GRUND.DODSAASG2016.
NOTE: The data set WORK.COD has 39750 observations and 3 variables.
NOTE: DATA statement used (Total process time):
      real time           0.76 seconds
      cpu time            0.07 seconds


251
252          proc sort  data = cod  nodupkey ; by pnr ; run ;

NOTE: There were 39750 observations read from the data set WORK.COD.
NOTE: 0 observations with duplicate key values were deleted.
NOTE: The data set WORK.COD has 39750 observations and 3 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
```

```
      cpu time            0.01 seconds


253
254        title 'Causes of death counted as CVD' ;
255        proc tabulate  data = cod  missing  noseps ;
256          class coD deCVDD ;
257          table all coD,
258              ( all deCVDD ) * f=comma7.
259                / rts = 6 ;
260          format deCVDD year4.
261                 coD $ICD10_L1L1_KT. ;
262          keylabel n = ' ' ;
263        run ;

NOTE: There were 39750 observations read from the data set WORK.COD.
NOTE: The PROCEDURE TABULATE printed page 4.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.50 seconds
      cpu time            0.03 seconds


264        title ;
265
266        * Merge in type and date of firstline treatment, date and cause of death,
267          dates of first complications and populaion information ;
268        data newu ;
269          merge newu ( in = nu )
270                FL
271                cod
272                dafdat.wcompl
273                DMdat.pop ;
274          by pnr ;
275          if nu ;
276        run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: There were 383033 observations read from the data set WORK.FL.
NOTE: There were 39750 observations read from the data set WORK.COD.
NOTE: There were 1997992 observations read from the data set DAFDAT.WCOMPL.
NOTE: There were 7411436 observations read from the data set DMDAT.POP.
NOTE: The data set WORK.NEWU has 244715 observations and 48 variables.
NOTE: DATA statement used (Total process time):
      real time           9.62 seconds
      cpu time            3.56 seconds


277
278        * Then merge with the datasets classified by epiN too ;
279        proc sort  data = newu ; by epiN pnr ; run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: The data set WORK.NEWU has 244715 observations and 48 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.32 seconds
      cpu time            0.28 seconds


280        data newu ;
281          merge newu ( in = nu )
282                lmed
283                ldrug
```

```
284                   hosp ;
285             by epiN pnr ;
286             if nu ;
287             label doIx = 'Index date'
288                   doTm = 'Index drug termination date'
289                   doFL = 'Date of first line treatment'
290                   FLdr = 'First line drug'
291                   FLatc= 'First line drug (atc)'
292                   Ixdr = 'Index drug'
293                   Ixatc= 'Index drug (atc)'
294                   epiN = 'Drug episode no since 2012-12-01' ;
295           run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: There were 200003 observations read from the data set WORK.LMED.
NOTE: There were 240355 observations read from the data set WORK.LDRUG.
NOTE: There were 244716 observations read from the data set WORK.HOSP.
NOTE: The data set WORK.NEWU has 244715 observations and 84 variables.
NOTE: DATA statement used (Total process time):
      real time           0.53 seconds
      cpu time            0.28 seconds


296
297           * Adding complications AFTER index date ;
298           * As before this needs to be in a loop over the episode numbers ;
299           * Macro for defining >first< complications after doIx ;
300           %macro getcomp( nam, cl ) ;
301             retain de&nam. ;
302             format de&nam. ddmmyy10. ;
303             if first.pnr then de&nam. = . ;
304             if doCompl > doIx and
305                de&nam. le .z  and
306                compl in ( &cl. ) then de&nam. = doCompl ;
307           %mend ;
308
309           data compl ; run ;

NOTE: The data set WORK.COMPL has 1 observations and 0 variables.
NOTE: DATA statement used (Total process time):
      real time           0.00 seconds
      cpu time            0.00 seconds


310
311           %macro colcomp ;
312           **** Loop over episode numbers *********** ;
313           %do ne = 1 %to 11 ;
314
315           data compl&ne. ( drop = doCompl ) ;
316             merge newu ( in = nu
317                        where = (epiN eq &ne.) )
318                   dafdat.compl ;
319             by pnr ;
320             if nu ;
321             %getcomp( HF  , "HF" )
322             %getcomp( MACE, %str("MI","HmStr","IscStr") )
323             %getcomp( MI  , "MI" )
324             %getcomp( Str , %str("HmStr","IscStr") )
325             %getcomp( IscStr, "IscStr" )
326             %getcomp( AF  , "AtrFib" )
327             %getcomp( HH  , "Hypo" )
```

```
328           %getcomp( DKD , "DKD" )
329           if last.pnr then output ;
330         run ;
331
332         data compl ; set compl compl&ne. ; run ;
333
334         %end ;
335         **** End of loop over episode numbers *********** ;
336         %mend colcomp ;
337
338         %colcomp ;

NOTE: There were 156182 observations read from the data set WORK.NEWU.
      WHERE epiN=1;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL1 has 156182 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           8.63 seconds
      cpu time            2.10 seconds



NOTE: There were 1 observations read from the data set WORK.COMPL.
NOTE: There were 156182 observations read from the data set WORK.COMPL1.
NOTE: The data set WORK.COMPL has 156183 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.21 seconds
      cpu time            0.10 seconds



NOTE: There were 57025 observations read from the data set WORK.NEWU.
      WHERE epiN=2;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL2 has 57025 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           2.12 seconds
      cpu time            2.04 seconds



NOTE: There were 156183 observations read from the data set WORK.COMPL.
NOTE: There were 57025 observations read from the data set WORK.COMPL2.
NOTE: The data set WORK.COMPL has 213208 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.35 seconds
      cpu time            0.12 seconds



NOTE: There were 20996 observations read from the data set WORK.NEWU.
      WHERE epiN=3;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL3 has 20996 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           2.00 seconds
      cpu time            1.87 seconds



NOTE: There were 213208 observations read from the data set WORK.COMPL.
NOTE: There were 20996 observations read from the data set WORK.COMPL3.
```

```
NOTE: The data set WORK.COMPL has 234204 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.39 seconds
      cpu time            0.14 seconds



NOTE: There were 7284 observations read from the data set WORK.NEWU.
      WHERE epiN=4;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL4 has 7284 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.96 seconds
      cpu time            1.89 seconds



NOTE: There were 234204 observations read from the data set WORK.COMPL.
NOTE: There were 7284 observations read from the data set WORK.COMPL4.
NOTE: The data set WORK.COMPL has 241488 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.40 seconds
      cpu time            0.14 seconds



NOTE: There were 2267 observations read from the data set WORK.NEWU.
      WHERE epiN=5;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL5 has 2267 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.93 seconds
      cpu time            1.78 seconds



NOTE: There were 241488 observations read from the data set WORK.COMPL.
NOTE: There were 2267 observations read from the data set WORK.COMPL5.
NOTE: The data set WORK.COMPL has 243755 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.40 seconds
      cpu time            0.17 seconds



NOTE: There were 671 observations read from the data set WORK.NEWU.
      WHERE epiN=6;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL6 has 671 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.92 seconds
      cpu time            1.84 seconds



NOTE: There were 243755 observations read from the data set WORK.COMPL.
NOTE: There were 671 observations read from the data set WORK.COMPL6.
NOTE: The data set WORK.COMPL has 244426 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.42 seconds
      cpu time            0.11 seconds
```

```
NOTE: There were 207 observations read from the data set WORK.NEWU.
      WHERE epiN=7;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL7 has 207 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.90 seconds
      cpu time            1.78 seconds



NOTE: There were 244426 observations read from the data set WORK.COMPL.
NOTE: There were 207 observations read from the data set WORK.COMPL7.
NOTE: The data set WORK.COMPL has 244633 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.42 seconds
      cpu time            0.18 seconds



NOTE: There were 64 observations read from the data set WORK.NEWU.
      WHERE epiN=8;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL8 has 64 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.89 seconds
      cpu time            1.81 seconds



NOTE: There were 244633 observations read from the data set WORK.COMPL.
NOTE: There were 64 observations read from the data set WORK.COMPL8.
NOTE: The data set WORK.COMPL has 244697 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.43 seconds
      cpu time            0.09 seconds



NOTE: There were 15 observations read from the data set WORK.NEWU.
      WHERE epiN=9;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL9 has 15 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.87 seconds
      cpu time            1.76 seconds



NOTE: There were 244697 observations read from the data set WORK.COMPL.
NOTE: There were 15 observations read from the data set WORK.COMPL9.
NOTE: The data set WORK.COMPL has 244712 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.42 seconds
      cpu time            0.11 seconds



NOTE: There were 3 observations read from the data set WORK.NEWU.
      WHERE epiN=10;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
```

```
NOTE: The data set WORK.COMPL10 has 3 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.79 seconds
      cpu time            1.68 seconds



NOTE: There were 244712 observations read from the data set WORK.COMPL.
NOTE: There were 3 observations read from the data set WORK.COMPL10.
NOTE: The data set WORK.COMPL has 244715 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.40 seconds
      cpu time            0.09 seconds



NOTE: There were 1 observations read from the data set WORK.NEWU.
      WHERE epiN=11;
NOTE: There were 11204191 observations read from the data set DAFDAT.COMPL.
NOTE: The data set WORK.COMPL11 has 1 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           1.76 seconds
      cpu time            1.65 seconds



NOTE: There were 244715 observations read from the data set WORK.COMPL.
NOTE: There were 1 observations read from the data set WORK.COMPL11.
NOTE: The data set WORK.COMPL has 244716 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.42 seconds
      cpu time            0.17 seconds


339
340          data dafdat.episodes ;
341            merge newu ( in = nu )
342                  compl ;
343            by epiN pnr ;
344            if nu ;
345            format doFL doIx doTm doBth doDM doDth ddmmyy10. ;
346          run ;

NOTE: There were 244715 observations read from the data set WORK.NEWU.
NOTE: There were 244716 observations read from the data set WORK.COMPL.
NOTE: The data set DAFDAT.EPISODES has 244715 observations and 98 variables.
NOTE: DATA statement used (Total process time):
      real time           0.89 seconds
      cpu time            0.29 seconds


347
348          title1 'New episodes (1,2,3) after December 2012' ;
349          proc tabulate  data = dafdat.episodes (where = (epiN le 3) )  missing  noseps ;
350            class doIx deCVDD deHF deMACE deMI deStr deAF deHH epiN ;
351            table epiN = "Episode no:", all
352                  deCVDD deHF deMACE deMI deStr deAF deHH,
353                ( all doIx ) * f=comma8.
354                  / rts = 11 condense ;
355            format deCVDD deHF deMACE deMI deStr deAF deHH doIx year4.
356                   Ixatc $atc_L1L1_kt. ;
357          run ;
```

```
NOTE: There were 234203 observations read from the data set DAFDAT.EPISODES.
      WHERE epiN<=3;
NOTE: The PROCEDURE TABULATE printed page 5.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           1.12 seconds
      cpu time            0.20 seconds


358
359          title1 'All new episodes after December 2012' ;
360          proc tabulate  data = dafdat.episodes  missing  noseps ;
361            class doIx deCVDD deHF deMACE deMI deStr deAF deHH epiN ;
362            table all
363                  deCVDD deHF deMACE deMI deStr deAF deHH,
364                ( all doIx ) * f=comma8.
365                  / rts = 11 condense ;
366            format deCVDD deHF deMACE deMI deStr deAF deHH doIx year4.
367                   Ixatc $atc_L1L1_kt. ;
368          run ;

NOTE: There were 244715 observations read from the data set DAFDAT.EPISODES.
NOTE: The PROCEDURE TABULATE printed page 6.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.10 seconds
      cpu time            0.18 seconds


369
370          proc tabulate  data = dafdat.episodes  missing  noseps ;
371            class doIx Ixdr Ixatc epiN ;
372            table Ixdr * (all Ixatc),
373                ( all doIx ) * f=comma7.
374                  / rts = 40  indent=2 ;
375            table Ixdr * (all Ixatc),
376                ( all epiN ) * f=comma7.
377                  / rts = 40  indent=2 ;
378            format doIx year4.
379                   Ixatc $atc_L1L1_kt. ;
380            label Ixdr= Ixatc= ;
381          run ;

NOTE: There were 244715 observations read from the data set DAFDAT.EPISODES.
NOTE: The PROCEDURE TABULATE printed pages 7-9.
NOTE: PROCEDURE TABULATE used (Total process time):
      real time           0.10 seconds
      cpu time            0.20 seconds


382
383          proc sort      data = dafdat.episodes ; by pnr epiN ; run ;

NOTE: There were 244715 observations read from the data set DAFDAT.EPISODES.
NOTE: The data set DAFDAT.EPISODES has 244715 observations and 98 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           1.10 seconds
      cpu time            0.48 seconds


384          proc contents  data = dafdat.episodes  varnum ; run ;

NOTE: PROCEDURE CONTENTS used (Total process time):
```

```
      real time           0.00 seconds
      cpu time            0.00 seconds

NOTE: The PROCEDURE CONTENTS printed page 10.

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414
NOTE: The SAS System used:
      real time           5:48.44
      cpu time            2:22.87
```

4.6.1 07-newuse.lst

```
All new start episodes (some persons with > 1) in T2 after dec 2012                      1
                                                              16:43 Wednesday, May 9, 2018


                                                    doIx

                 All   2012/4  2013/1  2013/2  2013/3  2013/4  2014/1  2014/2  2014/3

                  N       N       N       N       N       N       N       N       N

 All           244,715   4,489  14,766  14,323  12,172  13,800  14,864  13,624  12,338
 Ixdr
 Acarbose          179       9      24      16      11       9      13      12       9
 DPP4           39,306     673   2,248   2,172   1,875   2,444   2,579   2,333   1,989
 GLP1           17,370     383   1,275   1,034     788     821     956     818     823
 Metformin      90,029   1,936   5,996   5,575   4,733   5,147   5,494   5,050   4,600
 SGLT2          17,678      20     302     554     485     588     616     744     672
 SU             19,099     412   1,427   1,354   1,137   1,242   1,348   1,201   1,061
 TZD               156       4      13      12      11      12      20      10       8
 fastIns        20,145     342   1,081   1,129   1,018   1,159   1,205   1,145   1,074
 intIns         11,859     262     919     914     807     870     913     754     688
 longIns        23,244     299     959   1,088     914   1,093   1,260   1,155   1,086
 mixIns          5,650     149     522     475     393     415     460     402     328

(Continued)



                                                doIx

               2014/4  2015/1  2015/2  2015/3  2015/4  2016/1  2016/2  2016/3  2016/4

                  N       N       N       N       N       N       N       N       N

 All            14,490  15,767  15,707  13,987  16,163  17,297  18,563  15,141  17,224
 Ixdr
 Acarbose           18      11      13       9       9       9       7       .       .
 DPP4            2,344   2,609   2,724   2,330   2,485   2,694   2,920   2,269   2,618
 GLP1              952   1,047   1,199   1,038   1,143   1,149   1,353   1,194   1,397
 Metformin       5,309   5,668   5,694   5,177   5,852   6,254   6,611   5,264   5,669
 SGLT2           1,006   1,131   1,119     892   1,619   1,878   2,122   1,730   2,200
 SU              1,119   1,244   1,202   1,100   1,111   1,080   1,175     868   1,018
 TZD                 5       8       7       4      15       8       5       5       9
 fastIns         1,321   1,353   1,241   1,208   1,341   1,362   1,352   1,292   1,522
 intIns            754     859     707     606     647     619     600     475     465
 longIns         1,299   1,453   1,472   1,347   1,662   1,991   2,176   1,861   2,129
 mixIns            363     384     329     276     279     253     242     183     197
```

```
(Continued)


                                                doTm

                  .    2013/2  2013/3  2013/4  2014/1  2014/2  2014/3  2014/4  2015/1

                  N       N       N       N       N       N       N       N       N

 All           156,920     801   3,138   3,820   3,942   4,671   5,482   5,359   5,381
 Ixdr
 Acarbose            .       *      11       7       8      13      10      12       8
 DPP4           25,382     104     432     531     551     709     889     849     800
 GLP1           12,190      41     214     233     250     315     301     283     307
 Metformin      63,905     251     925   1,139   1,181   1,317   1,629   1,572   1,643
 SGLT2          12,581       4      61     136     162     221     216     244     263
 SU              9,998      85     373     447     438     490     607     574     614
 TZD                43       *       8       5       6      10      13      13      11
 fastIns         6,891     183     619     696     649     775     854     891     805
 intIns          5,449      49     240     294     334     409     456     420     412
 longIns        17,774      49     142     181     206     249     264     294     317
 mixIns          2,707      31     113     151     157     163     243     207     201

(Continued)


                                            doTm

               2015/2  2015/3  2015/4  2016/1  2016/2  2016/3  2016/4  2017/1

                  N       N       N       N       N       N       N       N

 All             5,970   6,904   7,136   6,950   7,346   8,923  11,794     178
 Ixdr
 Acarbose           10      11      24       5      14      12      31       .
 DPP4              908   1,182   1,236   1,173   1,243   1,455   1,833      29
 GLP1              324     335     385     420     471     597     689      15
 Metformin       1,726   1,958   2,154   2,058   2,041   2,633   3,830      67
 SGLT2             348     432     468     452     505     684     892       9
 SU                627     744     709     711     765     826   1,077      14
 TZD                 6       4       6       6       7       9       8       .
 fastIns           998   1,064   1,019     952   1,060   1,215   1,454      20
 intIns            451     522     451     480     509     622     751      10
 longIns           383     421     452     451     506     624     920      11
 mixIns            189     231     232     242     225     246     309       *

All new start episodes (some persons with > 1) in T2 after dec 2012                     2
                                                              16:43 Wednesday, May 9, 2018


                                                 Ixdr

                Acarbo-                 Metfor-
          All     se     DPP4    GLP1     min    SGLT2    SU      TZD   fastIns intIns

           N       N       N       N       N       N       N       N       N       N
```

```
 All     244,715      179  39,306  17,370  90,029  17,678  19,099      156  20,145  11,859
 *       156,182      135  24,604   8,786  79,030   6,909  10,298       67   9,628   5,351
 *        57,025       33  11,378   4,993   7,764   6,165   6,622       52   5,902   4,264
 *        20,996        7   2,463   2,380   2,123   3,018   1,621       22   2,851   1,564
 4         7,284        *     616     858     748   1,091     385        9   1,191     505
 5         2,267        *     179     254     253     336     117        *     403     125
 6           671        .      44      77      74     109      40        *     114      35
 7           207        .      17      18      25      36      10        .      38      13
 8            64        .       *       *      10      10       4        .      15       *
 9            15        .       *       *       *       *       *        .       *       .
 10            *        .       .       .       .       *       .        .       .       .
 11            *        .       .       .       .       .       .        .       *       .

(Continued)

All new start episodes (some persons with > 1) in T2 after dec 2012                    3
                                                          16:43 Wednesday, May 9, 2018


             Ixdr

        longIns mixIns

           N       N

 All     23,244   5,650
 *        8,700   2,674
 *        8,114   1,738
 *        4,119     828
 4        1,593     285
 5          513      83
 6          147      28
 7           39      11
 8           16       *
 9            *       .
 10           *       *
 11           .       .

Causes of death counted as CVD                            16:43 Wednesday, May 9, 2018   4


                                 deCVDD

        All    2012    2013    2014    2015    2016

 All   39,750     794   8,948   9,463  10,360  10,185
 coD
 I009       *       .       .       *       .       .
 I018       *       .       .       *       .       .
 I019      10       .       *       *       *       *
 I029       *       .       .       .       .       *
 I050       *       .       *       *       .       .
 I051       *       .       *       *       .       .
 I052       *       .       .       .       *       .
 I059       *       .       *       .       .       .
 I060       7       .       4       *       *       *
 I061       6       *       .       *       .       *
 I062     206       *      38      56      53      58
 I069       *       .       .       .       *       .
```

I082	*	.	.	.	*	.
I088	10	.	*	*	5	*
I089	4	.	*	*	.	*
I091	*	.	*	.	.	*
I092	*	.	*	.	.	.
I110	426	10	94	103	105	114
I119	68	*	20	17	15	13
I120	193	*	43	42	55	51
I129	*	.	*	.	.	*
I130	287	5	50	51	79	102
I131	34	.	5	7	10	12
I132	609	5	109	136	168	191
I139	33	.	6	7	6	14
I200	10	.	4	.	4	*
I201	*	.	.	*	*	.
I208	4	.	*	*	.	*
I209	76	*	16	25	21	13
I210	135	*	28	31	21	54
I211	56	*	16	9	14	14
I212	55	4	16	16	7	12
I213	351	9	79	81	82	100
I214	315	12	80	75	76	72
I219	4,081	99	1,061	1,014	1,019	888
I240	*	*	*	.	.	.
I241	*	.	.	.	.	*
I248	178	5	24	42	56	51
I249	1,236	28	228	242	366	372
I250	562	12	162	148	133	107
I251	1,786	32	431	440	447	436
I253	*	.	.	.	*	*
I255	382	6	81	82	111	102
I256	8	*	*	*	*	*
I258	377	6	86	83	105	97
I259	2,346	41	513	590	581	621
I260	70	.	18	18	21	13
I269	529	16	121	122	144	126
I270	69	.	18	14	18	19
I271	*	.	*	.	.	*
I272	16	.	*	*	4	9
I278	11	.	*	5	*	*
I279	94	*	18	29	22	22
I289	4	.	.	*	*	*
I300	7	.	.	*	*	*
I301	*	.	.	*	*	.
I309	*	.	.	*	.	.
I311	11	.	7	*	.	*
I312	4	.	*	*	*	.
I313	*	.	.	*	*	.
I318	*	.	*	.	.	.
I319	5	.	*	.	*	*
I330	91	*	28	20	20	22
I339	111	*	27	27	27	28
I340	148	6	29	36	40	37
I341	12	*	*	*	5	*
I342	11	.	*	*	5	*
I348	*	.	*	.	*	.
I349	18	*	4	5	4	4
I350	1,132	19	229	271	322	291
I351	112	*	30	28	27	25
I352	112	4	22	24	28	34
I358	*	.	.	*	.	*
I359	106	*	31	22	24	26

```
I361       8       .       4       *       *       *
I368       *       .       .       .       .       *
I369       *       .       *       .       .       .
I371       *       .       .       .       .       *
I38       11       .       *       *       *       *
I389     131       *      31      31      33      34
I400       7       .       *       .       4       *
I409      40       *      13       8      10       8
I420     195       4      32      56      54      49
I421      20       .       5       8       4       *
I422      20       .       5       7       6       *
I424       5       .       .       4       .       *
I425       5       .       .       *       .       *
I426      22       .       6       5       4       7
I427       *       .       .       .       *       *
I428      14       .       5       *       5       *
I429     179       *      36      41      53      47
I440      27       .       5       *       5      14
I441      21       .       4       5       6       6
I442     175       *      42      39      36      55
I443      26       *       8       5       7       5
I447       *       .       .       *       .       *
I452       *       .       *       .       .       *
I453       5       .       *       *       .       *
I455      21       .       7       *       6       5
I458       *       .       .       *       .       *
I459      10       .       4       *       *       *
I460     402       9      91      89      94     119
I461     221       *      26      62      63      69
I470       *       .       *       *       .       .
I471       9       .       *       *       5       *
I472      25       *      10       *       6       5
I479      12       .       *       4       *       *
I48        *       *       .       .       .       .
I489   2,578      50     584     562     656     726
I490      94       *      28      19      22      23
I494       *       .       *       .       .       .
I495      73       5      17      10      20      21
I498      16       .       *       6       5       *
I499     120       *      29      28      30      31
I500     136       6      34      39      25      32
I501     531      10     119     129     135     138
I509   2,388      53     512     551     626     646
I510       *       .       .       *       .       .
I511       *       .       .       .       *       .
I513       *       .       *       .       .       .
I514      19       *       *       9       *       4
I515       6       *       *       *       .       *
I516      63       *      12      18      24       7
I517      20       *       5       5       *       7
I518     120       *      20      34      32      31
I519     379      12      71      74     134      88
I600      23       *       5       8       *       7
I601      51       5       6      16      14      10
I602      48       .      13      18       7      10
I603      12       .       4       *       *       *
I604      28       .       9      11       *       6
I605       8       .       .       *       *       *
I606     112       .      21      26      26      39
I607      52       *       9      13      14      15
I608      58       .      18      12      19       9
I609     239       7      55      65      52      60
```

I610	86	*	23	23	25	14
I611	37	*	11	*	11	10
I612	362	4	88	78	104	88
I613	85	.	18	20	26	21
I614	60	*	14	13	10	22
I615	56	*	10	15	9	20
I616	67	*	11	13	18	23
I618	167	*	26	40	48	52
I619	1,372	26	294	319	386	347
I620	199	4	42	52	46	55
I621	*	.	*	*	*	.
I629	28	*	5	*	4	16
I630	21	.	4	6	8	*
I631	19	*	*	9	4	*
I632	25	.	*	8	7	7
I633	110	*	19	31	33	24
I634	67	*	13	12	19	22
I635	31	*	6	12	6	6
I636	4	.	*	*	.	*
I638	69	.	15	20	17	17
I639	1,311	23	304	333	356	295
I64	261	6	48	.	105	102
I649	6,469	113	1,438	1,596	1,701	1,621
I671	16	.	*	4	7	*
I672	86	*	29	20	19	15
I673	5	.	*	*	*	.
I674	*	.	.	.	.	*
I675	*	.	.	.	*	*
I676	4	.	.	*	*	*
I677	*	.	.	*	.	*
I678	10	.	*	4	*	*
I679	67	*	6	26	23	11
I693	*	.	.	.	.	*
I694	5	.	.	.	.	5
I700	16	.	*	5	6	4
I701	4	.	*	*	*	.
I702	395	7	84	98	102	104
I708	16	.	4	4	4	4
I709	560	13	130	142	129	146
I710	385	9	91	102	80	103
I711	56	*	16	15	12	12
I712	21	.	11	*	6	*
I713	632	7	164	152	166	143
I714	122	*	24	37	29	30
I715	331	10	76	73	79	93
I716	58	*	14	8	17	16
I718	56	*	20	14	13	7
I719	72	*	19	16	18	18
I720	5	.	*	*	*	.
I722	*	.	.	*	.	.
I723	11	.	*	*	*	4
I724	*	.	*	.	.	*
I728	20	.	*	4	9	4
I729	10	.	*	*	*	5
I738	*	.	*	*	*	.
I739	48	*	9	11	10	16
I740	14	.	*	5	6	*
I741	8	.	.	*	*	4
I743	37	.	11	8	8	10
I744	4	.	*	*	*	*
I745	8	.	4	*	*	*
I748	58	*	14	13	17	12

```
 I749      69       .      21      14      26       8
 I772       9       .       *       .       4       *
 I775       4       .       *       *       .       .
 I778      16       .       *       *       5       5
 I779       4       .       *       *       *       *
 I780       *       .       *       *       .       .
 I800       *       .       *       *       .       .
 I801       *       .       *       .       *       .
 I802       9       .       *       5       *       .
 I803      18       .       5       4       *       6
 I808       *       .       .       .       *       .
 I809       *       .       .       *       .       *
 I819      18       .       7       4       5       *
 I820       *       *       *       .       *       .
 I822       *       .       *       .       *       *
 I828      22       *       4       7       5       5
 I829      30       .       9       5      10       6
 I830       5       .       .       *       *       *
 I839       *       .       .       *       *       .
 I850      18       .       5       *       *       7
 I864       4       .       *       *       .       *
 I868       *       .       .       .       .       *
 I871       *       .       .       *       .       .
 I872       6       .       .       *       *       *
 I890       *       .       .       *       .       .
 I898       *       .       .       .       *       .
 I950      19       *       *       *      10       4
 I951       *       .       .       .       .       *
 I952       *       .       *       .       *       .
 I958       *       .       .       *       *       .
 I959      10       .       *       *       4       *
 I999      24       .       *       4       8      10

New episodes (1,2,3) after December 2012                  16:43 Wednesday, May 9, 2018   5

Episode no: *

                                     Index date

             All      2012     2013     2014     2015     2016

              N        N        N        N        N        N

 All        156,182    4,286   45,714   37,193   35,139   33,850
 deCVDD
 .          153,541    4,172   44,513   36,459   34,741   33,656
 2012             5        4        *        .        .        .
 2013           270       40      230        .        .        .
 2014           533       21      324      188        .        .
 2015           822       29      324      294      175        .
 2016         1,011       20      322      252      223      194
 deHF
 .          152,053    4,116   43,934   36,027   34,445   33,531
 2012             5        5        .        .        .        .
 2013           540       62      478        .        .        .
 2014           971       45      545      381        .        .
 2015         1,206       30      419      440      317        .
 2016         1,407       28      338      345      377      319
 deMACE
 .          150,979    4,051   43,358   35,779   34,289   33,502
 2012             *        *        .        .        .        .
```

```
 2013           545       82      463        .        .        .
 2014         1,191       52      743      396        .        .
 2015         1,577       51      588      575      363        .
 2016         1,888       48      562      443      487      348
 deMI
 .          153,766    4,173   44,590   36,528   34,772   33,703
 2013           258       37      221        .        .        .
 2014           551       28      341      182        .        .
 2015           742       28      287      267      160        .
 2016           865       20      275      216      207      147
 deStr
 .          153,302    4,160   44,429   36,418   34,647   33,648
 2012             *        *        .        .        .        .
 2013           303       47      256        .        .        .
 2014           658       25      414      219        .        .
 2015           868       23      315      324      206        .
 2016         1,049       29      300      232      286      202
 deAF
 .          151,090    4,059   43,561   35,781   34,243   33,446
 2012             5        5        .        .        .        .
 2013           597       77      520        .        .        .
 2014         1,147       62      648      437        .        .
 2015         1,528       41      513      533      441        .
 2016         1,815       42      472      442      455      404
 deHH
 .          154,230    4,208   44,759   36,657   34,854   33,752
 2012             *        *        .        .        .        .
 2013           277       35      242        .        .        .
 2014           462       17      282      163        .        .
 2015           582        9      234      204      135        .
 2016           629       15      197      169      150       98



Episode no: *

                                     Index date

             All      2012     2013     2014     2015     2016

              N        N        N        N        N        N

 All          57,025      188    7,884   13,309   16,699   18,945
 deCVDD
 .           56,178      177    7,666   13,005   16,478   18,852
 2012             *        *        .        .        .        .
 2013            57        *       54        .        .        .
 2014           139        *       59       77        .        .
 2015           245        *       46      112       86        .
 2016           404        *       59      115      135       93
 deHF
 .           55,600      181    7,514   12,839   16,308   18,758
 2012             *        *        .        .        .        .
 2013            99        *       97        .        .        .
 2014           274        .      119      155        .        .
 2015           454        *       87      167      198        .
 2016           596        *       67      148      193      187
 deMACE
 .           55,393      178    7,446   12,731   16,273   18,765
 2013           101        *       98        .        .        .
```

```
 2014           298        *      128      167        .        .
 2015           503        *      103      223      175        .
 2016           730        *      109      188      251      180
 deMI
 .           56,289      182    7,680   13,044   16,518   18,865
 2013            49        *       48        .        .        .
 2014           125        *       59       64        .        .
 2015           227        *       45      107       73        .
 2016           335        *       52       94      108       80
 deStr
 .           56,111      184    7,645   12,989   16,449   18,844
 2013            54        *       52        .        .        .
 2014           176        *       70      105        .        .
 2015           284        .       60      121      103        .
 2016           400        *       57       94      147      101
 deAF
 .           55,564      184    7,542   12,826   16,262   18,750
 2013            75        .       75        .        .        .
 2014           250        *      109      140        .        .
 2015           460        *       81      181      197        .
 2016           676        *       77      162      240      195
 deHH
 .           56,173      180    7,639   13,009   16,489   18,856
 2013            64        5       59        .        .        .
 2014           168        *       73       92        .        .
 2015           269        .       55      117       97        .
 2016           351        .       58       91      113       89




Episode no: *

                                      Index date

             All      2012     2013     2014     2015     2016

              N        N        N        N        N        N

 All         20,996       15    1,268    3,682    6,682    9,349
 deCVDD
 .           20,735       14    1,231    3,611    6,586    9,293
 2013            13        *       12        .        .        .
 2014            30        .       11       19        .        .
 2015            52        .        5       21       26        .
 2016           166        .        9       31       70       56
 deHF
 .           20,533       15    1,218    3,556    6,495    9,249
 2013            12        .       12        .        .        .
 2014            63        .       21       42        .        .
 2015           144        .       12       44       88        .
 2016           244        .        5       40       99      100
 deMACE
 .           20,533       15    1,204    3,535    6,529    9,250
 2013            12        .       12        .        .        .
 2014            61        .       18       43        .        .
 2015           130        .       13       61       56        .
 2016           260        .       21       43       97       99
 deMI
 .           20,785       15    1,237    3,614    6,606    9,313
 2013             5        .        5        .        .        .
```

```
 2014            30         .         9        21         .         .
 2015            57         .         6        28        23         .
 2016           119         .        11        19        53        36
 deStr
 .           20,742        15     1,235     3,603     6,603     9,286
 2013             7         .         7         .         .         .
 2014            31         .         9        22         .         .
 2015            74         .         7        33        34         .
 2016           142         .        10        24        45        63
 deAF
 .           20,535        15     1,212     3,551     6,518     9,239
 2013             8         .         8         .         .         .
 2014            53         .        19        34         .         .
 2015           146         .        16        52        78         .
 2016           254         .        13        45        86       110
 deHH
 .           20,694        13     1,225     3,587     6,582     9,287
 2013            18         *        17         .         .         .
 2014            39         *        11        27         .         .
 2015            80         .         4        33        43         .
 2016           165         .        11        35        57        62


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                                     Index date

             All      2012     2013     2014     2015     2016

              N        N        N        N        N        N

 All        244,715     4,489    55,061    55,316    61,624    68,225
 deCVDD
 .          240,879     4,363    53,596    54,188    60,880    67,852
 2012             7         6         *         .         .         .
 2013           342        44       298         .         .         .
 2014           709        24       396       289         .         .
 2015         1,142        30       378       434       300         .
 2016         1,636        22       392       405       444       373
 deHF
 .          238,512     4,312    52,852    53,527    60,263    67,558
 2012             7         7         .         .         .         .
 2013           653        64       589         .         .         .
 2014         1,319        45       688       586         .         .
 2015         1,852        32       521       663       636         .
 2016         2,372        29       411       540       725       667
 deMACE
 .          237,249     4,244    52,192    53,146    60,130    67,537
 2012             *         *         .         .         .         .
 2013           660        85       575         .         .         .
 2014         1,562        55       892       615         .         .
 2015         2,238        53       705       867       613         .
 2016         3,004        50       697       688       881       688
 deMI
 .          241,266     4,370    53,696    54,300    60,967    67,933
 2013           313        38       275         .         .         .
 2014           715        30       412       273         .         .
 2015         1,037        30       338       405       264         .
 2016         1,384        21       340       338       393       292
 deStr
 .          240,585     4,359    53,499    54,129    60,771    67,827
```

```
 2012             *        *        .        .        .        .
 2013           365       49      316        .        .        .
 2014           868       26      493      349        .        .
 2015         1,243       23      383      483      354        .
 2016         1,652       30      370      355      499      398
 deAF
 .          237,526    4,258   52,503   53,258   60,056   67,451
 2012             5        5        .        .        .        .
 2013           680       77      603        .        .        .
 2014         1,454       63      778      613        .        .
 2015         2,178       42      614      779      743        .
 2016         2,872       44      563      666      825      774
 deHH
 .          241,488    4,401   53,815   54,362   60,978   67,932
 2012             *        *        .        .        .        .
 2013           360       41      319        .        .        .
 2014           672       21      367      284        .        .
 2015           954        9      293      361      291        .
 2016         1,239       15      267      309      355      293


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                                                              Index date

                                         All     2012    2013    2014    2015    2016

                                           N       N       N       N       N       N

 Acarbose
   All                                      179       9      60      52      42      16
   A10BF01  acarbose                        179       9      60      52      42      16
 DPP4
   All                                   39,306     673   8,739   9,245  10,148  10,501
   A10BD07  metformin og sitagliptin      7,521     106   1,518   1,749   1,988   2,160
   A10BD08  metformin og vildagliptin     6,861     157   1,892   1,633   1,547   1,632
   A10BD09  pioglitazon og alogliptin         5       .       .       *       *       .
   A10BD10  metformin og saxagliptin         16       .       *       6       4       *
   A10BD11  metformin og linagliptin        104       *      20      21      28      34
   A10BD13  metformin og alogliptin         343       .       .      82     158     103
   A10BH01  sitagliptin                  14,764     265   3,237   3,436   3,797   4,029
   A10BH02  vildagliptin                  2,931      58     769     820     694     590
   A10BH03  saxagliptin                     908      35     300     210     207     156
   A10BH04  alogliptin                      727       .       *     172     312     240
   A10BH05  linagliptin                   5,126      51     997   1,113   1,411   1,554
 GLP1
   All                                   17,370     383   3,918   3,549   4,427   5,093
   A10BJ01  exenatid                        502      14     122     111     156      99
   A10BJ02  liraglutid                   16,499     369   3,781   3,388   4,239   4,722
   A10BJ03  lixisenatid                      79       .      15      50       9       5
   A10BJ05  dulaglutid                      290       .       .       .      23     267
 Metformin
   All                                   90,029   1,936  21,451  20,453  22,391  23,798
   A10BA02  metformin                    89,248   1,923  21,267  20,280  22,176  23,602
   A10BD03  metformin og rosiglitazon        61       *      17      14      18      11
   A10BD07  metformin og sitagliptin        379       5      89      70     114     101
   A10BD08  metformin og vildagliptin       294       7      77      81      68      61
   A10BD10  metformin og saxagliptin          6       .       *       *       *       *
   A10BD11  metformin og linagliptin          4       .       .       *       *       *
   A10BD13  metformin og alogliptin          10       .       .       *       6       *
   A10BD15  metformin og dapagliflozin       12       .       .       *       *       7
```

```
   A10BD16  metformin og canagliflozin        *       .       .       .       *       .
   A10BD20  metformin og empagliflozin       14       .       .       .       *      11
 SGLT2
   All                                   17,678      20   1,929   3,038   4,761   7,930
   A10BD15  metformin og dapagliflozin      407       .       .      84     102     221
   A10BD16  metformin og canagliflozin       13       .       .       .       7       6
   A10BD20  metformin og empagliflozin      487       .       .       .      54     433
   A10BK01  dapagliflozin                10,684      20   1,929   2,659   3,069   3,007
   A10BK02  canagliflozin                   465       .       .      99     232     134
   A10BK03  empagliflozin                 5,622       .       .     196   1,297   4,129
 SU
   All                                   19,099     412   5,160   4,729   4,657   4,141
   A10BB01  glibenclamid                  1,088      23     337     277     262     189
   A10BB03  tolbutamid                      327       7     103      79      80      58
   A10BB07  glipizid                        821      19     238     209     187     168
   A10BB09  gliclazid                     1,916      42     501     522     442     409
   A10BB12  glimepirid                   14,571     315   3,875   3,550   3,589   3,242
   A10BX02  repaglinid                      375       6     106      91      97      75
   A10BX03  nateglinid                        *       .       .       *       .       .
 TZD
   All                                      156       4      48      43      34      27
   A10BD03  metformin og rosiglitazon        10       .       5       *       *       *
   A10BD09  pioglitazon og alogliptin        10       .       .       *       *       6
   A10BG02  rosiglitazon                     15       *       4       4       4       *
   A10BG03  pioglitazon                     121       *      39      35      26      18
 fastIns
   All                                   20,145     342   4,387   4,745   5,143   5,528
   A10AB01  insulin (human)               7,146     126   1,630   1,736   1,837   1,817
   A10AB04  insulin lispro                   67       *      11      17      16      22
   A10AB05  insulin aspart               12,599     211   2,669   2,916   3,196   3,607
   A10AB06  insulin glulisin                333       4      77      76      94      82
 intIns
   All                                   11,859     262   3,510   3,109   2,819   2,159
   A10AC01  insulin (human)              11,859     262   3,510   3,109   2,819   2,159
 longIns
   All                                   23,244     299   4,054   4,800   5,934   8,157
   A10AE04  insulin glargin              15,610     168   2,554   3,321   4,549   5,018
   A10AE05  insulin detemir               5,575     131   1,484   1,463   1,370   1,127
   A10AE06  insulin degludec              2,059       .      16      16      15   2,012
 mixIns
   All                                    5,650     149   1,805   1,553   1,268     875
   A10AD01  insulin (human)                 643      15     225     170     127     106
   A10AD04  insulin lispro                   22       .       6       5       8       *
   A10AD05  insulin aspart                4,980     134   1,574   1,378   1,131     763
   A10AD06  insulin degludec og insulin
   aspart                                     5       .       .       .       *       *


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                                                   Drug episode no since 2012-12-01

                                          All      *       *       *       4       5

                                           N       N       N       N       N       N


 Acarbose
   All                                      179     135      33       7       *       *
   A10BF01  acarbose                        179     135      33       7       *       *
 DPP4
   All                                   39,306  24,604  11,378   2,463     616     179
```

```
  A10BD07  metformin og sitagliptin      7,521   4,760   2,244     389      96      24
  A10BD08  metformin og vildagliptin     6,861   4,619   1,774     346      76      36
  A10BD09  pioglitazon og alogliptin         5       *       *       .       .       *
  A10BD10  metformin og saxagliptin         16      11       4       *       .       .
  A10BD11  metformin og linagliptin        104      61      38       5       .       .
  A10BD13  metformin og alogliptin         343     177     135      24       6       .
  A10BH01  sitagliptin                  14,764   8,872   4,461   1,062     262      74
  A10BH02  vildagliptin                  2,931   1,848     863     161      46      10
  A10BH03  saxagliptin                     908     578     241      71      12       4
  A10BH04  alogliptin                      727     341     257      90      29       7
  A10BH05  linagliptin                   5,126   3,335   1,359     314      89      23
GLP1
  All                                   17,370   8,786   4,993   2,380     858     254
  A10BJ01  exenatid                        502     236     134      74      34      16
  A10BJ02  liraglutid                   16,499   8,461   4,730   2,210     786     223
  A10BJ03  lixisenatid                      79      39      23      12       4       *
  A10BJ05  dulaglutid                      290      50     106      84      34      14
Metformin
  All                                   90,029  79,030   7,764   2,123     748     253
  A10BA02  metformin                    89,248  78,908   7,182   2,081     724     245
  A10BD03  metformin og rosiglitazon        61      32      18       7       *       *
  A10BD07  metformin og sitagliptin        379      33     310      16      15       4
  A10BD08  metformin og vildagliptin       294      33     235      17       6       *
  A10BD10  metformin og saxagliptin          6       .       5       .       *       .
  A10BD11  metformin og linagliptin          4       .       4       .       .       .
  A10BD13  metformin og alogliptin          10       .       8       *       .       .
  A10BD15  metformin og dapagliflozin       12      10       *       .       .       *
  A10BD16  metformin og canagliflozin        *       *       .       .       .       .
  A10BD20  metformin og empagliflozin       14      13       *       .       .       .
SGLT2
  All                                   17,678   6,909   6,165   3,018   1,091     336
  A10BD15  metformin og dapagliflozin      407     160     165      62      12       4
  A10BD16  metformin og canagliflozin       13       4       8       .       *       .
  A10BD20  metformin og empagliflozin      487     151     192      92      36      14
  A10BK01  dapagliflozin                10,684   4,762   3,565   1,593     515     164
  A10BK02  canagliflozin                   465     175     185      70      19      12
  A10BK03  empagliflozin                 5,622   1,657   2,050   1,201     508     142
SU
  All                                   19,099  10,298   6,622   1,621     385     117
  A10BB01  glibenclamid                  1,088     631     357      70      17       7
  A10BB03  tolbutamid                      327     207      81      29       9       *
  A10BB07  glipizid                        821     489     260      53      14       *
  A10BB09  gliclazid                     1,916     993     675     176      47      15
  A10BB12  glimepirid                   14,571   7,779   5,124   1,255     287      89
  A10BX02  repaglinid                      375     198     125      38      11       *
  A10BX03  nateglinid                        *       *       .       .       .       .
TZD
  All                                      156      67      52      22       9       *
  A10BD03  metformin og rosiglitazon        10       4       6       .       .       .
  A10BD09  pioglitazon og alogliptin        10       .       *       5       *       *
  A10BG02  rosiglitazon                     15       5       7       *       .       .
  A10BG03  pioglitazon                     121      58      38      14       7       *
fastIns
  All                                   20,145   9,628   5,902   2,851   1,191     403
  A10AB01  insulin (human)               7,146   3,675   2,051     929     332     115
  A10AB04  insulin lispro                   67      37      12      13       *       *
  A10AB05  insulin aspart               12,599   5,790   3,736   1,856     822     277
  A10AB06  insulin glulisin                333     126     103      53      36       8
intIns
  All                                   11,859   5,351   4,264   1,564     505     125
  A10AC01  insulin (human)              11,859   5,351   4,264   1,564     505     125
longIns
```

```
   All                                      23,244   8,700   8,114   4,119   1,593     513
   A10AE04  insulin glargin                 15,610   5,583   5,524   2,884   1,119     359
   A10AE05  insulin detemir                  5,575   2,512   1,941     759     248      76
   A10AE06  insulin degludec                 2,059     605     649     476     226      78
 mixIns
   All                                       5,650   2,674   1,738     828     285      83
   A10AD01  insulin (human)                    643     334     175      78      39       9
   A10AD04  insulin lispro                      22      12       5       *       *       .
   A10AD05  insulin aspart                   4,980   2,328   1,557     745     242      74
   A10AD06  insulin degludec og insulin
   aspart                                        5       .       *       *       *       .


(Continued)

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                                               Drug episode no since 2012-12-01

                                            6       7       8       9      10      11

                                            N       N       N       N       N       N

 Acarbose
   All                                          .       .       .       .       .       .
   A10BF01  acarbose                            .       .       .       .       .       .
 DPP4
   All                                         44      17       *       *       .       .
   A10BD07  metformin og sitagliptin            5       *       .       .       .       .
   A10BD08  metformin og vildagliptin           6       *       .       *       .       .
   A10BD09  pioglitazon og alogliptin           .       .       .       .       .       .
   A10BD10  metformin og saxagliptin            .       .       .       .       .       .
   A10BD11  metformin og linagliptin            .       .       .       .       .       .
   A10BD13  metformin og alogliptin             *       .       .       .       .       .
   A10BH01  sitagliptin                        22       8       *       *       .       .
   A10BH02  vildagliptin                        *       *       .       .       .       .
   A10BH03  saxagliptin                         *       .       .       .       .       .
   A10BH04  alogliptin                          *       .       *       .       .       .
   A10BH05  linagliptin                         4       *       .       .       .       .
 GLP1
   All                                         77      18       *       *       .       .
   A10BJ01  exenatid                            8       .       .       .       .       .
   A10BJ02  liraglutid                         67      18       *       *       .       .
   A10BJ03  lixisenatid                         .       .       .       .       .       .
   A10BJ05  dulaglutid                          *       .       .       .       .       .
 Metformin
   All                                         74      25      10       *       .       .
   A10BA02  metformin                          71      25      10       *       .       .
   A10BD03  metformin og rosiglitazon           *       .       .       .       .       .
   A10BD07  metformin og sitagliptin            *       .       .       .       .       .
   A10BD08  metformin og vildagliptin           *       .       .       .       .       .
   A10BD10  metformin og saxagliptin            .       .       .       .       .       .
   A10BD11  metformin og linagliptin            .       .       .       .       .       .
   A10BD13  metformin og alogliptin             .       .       .       .       .       .
   A10BD15  metformin og dapagliflozin          .       .       .       .       .       .
   A10BD16  metformin og canagliflozin          .       .       .       .       .       .
   A10BD20  metformin og empagliflozin          .       .       .       .       .       .
 SGLT2
   All                                        109      36      10       *       *       .
   A10BD15  metformin og dapagliflozin          *       *       .       .       .       .
   A10BD16  metformin og canagliflozin          .       .       .       .       .       .
```

```
   A10BD20  metformin og empagliflozin        *       *       .       .       .       .
   A10BK01  dapagliflozin                    57      20       6       *       .       .
   A10BK02  canagliflozin                     *       .       *       .       *       .
   A10BK03  empagliflozin                    46      14       *       *       .       .
 SU
   All                                       40      10       4       *       .       .
   A10BB01  glibenclamid                      *       *       *       .       .       .
   A10BB03  tolbutamid                        .       .       .       .       .       .
   A10BB07  glipizid                          *       .       *       .       .       .
   A10BB09  gliclazid                         8       *       .       *       .       .
   A10BB12  glimepirid                       28       7       *       *       .       .
   A10BX02  repaglinid                        .       .       *       .       .       .
   A10BX03  nateglinid                        .       .       .       .       .       .
 TZD
   All                                        *       .       .       .       .       .
   A10BD03  metformin og rosiglitazon         .       .       .       .       .       .
   A10BD09  pioglitazon og alogliptin         *       .       .       .       .       .
   A10BG02  rosiglitazon                      .       .       .       .       .       .
   A10BG03  pioglitazon                       *       .       .       .       .       .
 fastIns
   All                                      114      38      15       *       .       *
   A10AB01  insulin (human)                  30      10       4       .       .       .
   A10AB04  insulin lispro                    *       .       .       .       .       .
   A10AB05  insulin aspart                   80      24      11       *       .       *
   A10AB06  insulin glulisin                  *       4       .       .       .       .
 intIns
   All                                       35      13       *       .       .       .
   A10AC01  insulin (human)                  35      13       *       .       .       .
 longIns
   All                                      147      39      16       *       *       .
   A10AE04  insulin glargin                  99      29      11       *       *       .
   A10AE05  insulin detemir                  29       5       4       *       .       .
   A10AE06  insulin degludec                 19       5       *       .       .       .
 mixIns
   All                                       28      11       *       .       *       .
   A10AD01  insulin (human)                   5       *       *       .       .       .
   A10AD04  insulin lispro                    .       .       .       .       .       .
   A10AD05  insulin aspart                   23       9       *       .       *       .
   A10AD06  insulin degludec og insulin
   aspart                                     .       .       .       .       .       .


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The CONTENTS Procedure

Data Set Name        DAFDAT.EPISODES               Observations          244715
Member Type          DATA                          Variables             98
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Protection                                         Compressed            NO
Data Set Type                                      Sorted                YES
Label
Data Representation  WINDOWS_64
Encoding             wlatin1  Western (Windows)


                        Engine/Host Dependent Information

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Number of Data Set Pages    2424
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Obs in First Data Page      83
Number of Data Set Repairs  0
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Release Created             9.0401M3
Host Created                X64_SRV12


                                Variables in Creation Order

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 * eksd         Num    4 YYMMDDN8.          Ekspeditionsdato
 4 ATC          Char   8 $8.       $16.     ATC-kode detaljeret (s)
 5 doDM         Num    8 DDMMYY10.
 6 epiN         Num    8                    Drug episode no since 2012-12-01
 7 doIx         Num    8 DDMMYY10.          Index date
 8 Ixdr         Char  10                    Index drug
 9 Ixatc        Char   8                    Index drug (atc)
10 lastpr       Num    4 YYMMDDN8.          Ekspeditionsdato
11 doTm         Num    8 DDMMYY10.          Index drug termination date
12 doFL         Num    8 DDMMYY10.          Date of first line treatment
13 FLdr         Char   7                    First line drug
14 FLatc        Char   8                    First line drug (atc)
15 deCVDD       Num    8 DDMMYY10.
16 coD          Char   4
17 doTIA        Num    8 DATE9.
18 doAngina     Num    8 DATE9.
19 doBleed      Num    8 DATE9.
20 doCOPD       Num    8 DATE9.
21 doPAD        Num    8 DATE9.
22 doHF         Num    8 DATE9.
23 doCancer     Num    8 DATE9.
24 doDMcompl    Num    8 DATE9.
25 doNeuro      Num    8 DATE9.
26 doDKD        Num    8 DATE9.
27 doDiaEye     Num    8 DATE9.
28 doHypo       Num    8 DATE9.
29 doAtrFib     Num    8 DATE9.
30 doMI         Num    8 DATE9.
31 doUnstAng    Num    8 DATE9.
32 doHmStr      Num    8 DATE9.
33 doDiaFoot    Num    8 DATE9.
34 doOther      Num    8 DATE9.
35 doPeriAng    Num    8 DATE9.
36 doIscStr     Num    8 DATE9.
37 doAmp        Num    8 DATE9.
38 doCKD        Num    8 DATE9.
39 doPCIsten    Num    8 DATE9.
40 doCABG       Num    8 DATE9.
41 doKeto       Num    8 DATE9.
42 doDial       Num    8 DATE9.
43 doBari       Num    8 DATE9.
44 sex          Num    8
45 doBth        Num    8 DDMMYY10.
46 whBth        Char   *
47 doDth        Num    8 DDMMYY10.
48 dSrc         Char   5
```

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49 dolACE       Num    4 DDMMYY10.
50 dolSta       Num    4 DDMMYY10.
51 dolBBl       Num    4 DDMMYY10.
52 dolARB       Num    4 DDMMYY10.
53 dolAlA       Num    4 DDMMYY10.
54 dolDHP       Num    4 DDMMYY10.
55 dolWtL       Num    4 DDMMYY10.
56 dolRPA       Num    4 DDMMYY10.
57 dolWrf       Num    4 DDMMYY10.
58 dolAsp       Num    4 DDMMYY10.
59 dolHCD       Num    4 DDMMYY10.
60 dolTHZ       Num    4 DDMMYY10.
61 dolCcs       Num    4 DDMMYY10.
62 dolDXI       Num    4 DDMMYY10.
63 dolDgo       Num    4 DDMMYY10.
64 dolAPl       Num    4 DDMMYY10.
65 dolAmi       Num    4 DDMMYY10.
66 dolDTI       Num    4 DDMMYY10.
67 dolNHP       Num    4 DDMMYY10.
68 dolFla       Num    4 DDMMYY10.
69 dolMetformin Num    4 DDMMYY10.
70 dolGLP1      Num    4 DDMMYY10.
71 dolMetxSGLT2 Num    4 DDMMYY10.
72 dolMetxDPP4  Num    4 DDMMYY10.
73 dolSGLT2     Num    4 DDMMYY10.
74 dollongIns   Num    4 DDMMYY10.
75 dolmixIns    Num    4 DDMMYY10.
76 dolDPP4      Num    4 DDMMYY10.
77 dolSU        Num    4 DDMMYY10.
78 dolintIns    Num    4 DDMMYY10.
79 dolfastIns   Num    4 DDMMYY10.
80 dolTZD       Num    4 DDMMYY10.
81 dolAcarbose  Num    4 DDMMYY10.
82 dolTZDxDPP4  Num    4 DDMMYY10.
83 maxH         Num    8                    Longest hospital stay in last year before doIx
84 frail        Num    8                    More than * consecutive hospital days last yr
85 recnum       Char  20 $20.               LPR-identnummer
86 C_ADIAG      Char   6 $6.       $6.      C_ADIAG
87 compl        Char   7
88 C_OPR        Char  10 $10.      $10.     C_OPR
89 D_INDDTO     Num    8 DATE9.    DATE9.   D_INDDTO
90 V_SENGDAGE   Num    8 6.        6.       V_SENGDAGE
91 deHF         Num    8 DDMMYY10.
92 deMACE       Num    8 DDMMYY10.
93 deMI         Num    8 DDMMYY10.
94 deStr        Num    8 DDMMYY10.
95 deIscStr     Num    8 DDMMYY10.
96 deAF         Num    8 DDMMYY10.
97 deHH         Num    8 DDMMYY10.
98 deDKD        Num    8 DDMMYY10.


   Sort Information

Sortedby       pnr epiN
Validated      YES
Character Set  ANSI
```