Time dependent covariates in Lexis objects

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Start time: 2024-07-18, 15:26:06

Chapter 1

Overview and rationale

This note describes the functions `addCov.Lexis`, designed to add values of clinical measurements, and `addDrug.Lexis` designed to add drug exposure to time-split `Lexis` objects.

If time-dependent variables are binary, such as for example "occurrence of CVD diagnosis" it may be relevant to define a new state as, say, `CVD`; this is the business of the funtions `cutLexis` and its cousins. The purposes of the two functions discussed here are to append quantitative variables that in principle can take any value.

Both functions are so-called S3 methods for `Lexis` objects, so in code you can omit the ".Lexis". Note that neither `cutLexis`, `splitLexis` or `splitMulti` are S3 methods (there is no "." in the names).

1.1   addCov.Lexis

...provides the ability to amend a `Lexis` object with clinical measurements taken at different times, and propagate the values as LOCF (Last Observation Carried Forward) to all subsequent records. This means that time-splitting of a `Lexis` object *after* adding clinical measurements will be meaningful, because both `splitLexis` and `splitMulti` will carry variables forward across the split records. The follow-up in the resulting `Lexis` object will be cut at dates of clinical measurement.

`addCov.Lexis` will also propagate missing values supplied as measurements. Therefore, if you want to have LOCF *across* supplied times of measurement you must explicitly apply `tidyr::fill` to the resulting `Lexis` object, after a suitable `group_by`.

1.2   addDrug.Lexis

As opposed to this, `addDrug.Lexis` will first use drug information at each date of recorded drug purchase, and subsequently `compute` cumulative exposure measures at the times in the resulting `Lexis` object. This is essentially by linear interpolation, so it will not be meaningful to further split an object resulting from `addDrug.Lexis`—LOCF is not meaningful for continuously time-varying covariates such as cumulative exposure.

If persons have very frequent drug purchases, the intervals may become very small and the sheer number of records may present an impediment to analysis. Therefore the function `coarse.Lexis` is provided to collapse adjacent follow-up records. Note that

`coarse.Lexis` is *not* an S3 method.

Chapter 2

addCov.Lexis

2.1 Rationale

The function has arisen out of a need to attach values measured at clinical visits to a Lexis object representing follow-up for events constituting a multistate model. Hence the data frame with measurements at clinical visits will be called `clin` for mnemonic reasons.

2.2 Example

For illustration we devise a small bogus cohort of 3 people, where we convert the character dates into numerical variables (fractional years) using `cal.yr`. Note that we are using a character variable as `id`:

```
> xcoh <- structure(list(id = c("A", "B", "C"),
+                     birth = c("1952-07-14", "1954-04-01", "1987-06-10"),
+                     entry = c("1965-08-04", "1972-09-08", "1991-12-23"),
+                      exit = c("1997-06-27", "1995-05-23", "1998-07-24"),
+                      fail = c(1, 0, 1) ),
+                  .Names = c("id", "birth", "entry", "exit", "fail"),
+               row.names = c("1", "2", "3"),
+                   class = "data.frame" )
> xcoh$dob <- cal.yr(xcoh$birth)
> xcoh$doe <- cal.yr(xcoh$entry)
> xcoh$dox <- cal.yr(xcoh$exit )
> xcoh
  id      birth      entry       exit fail      dob      doe      dox
1  A 1952-07-14 1965-08-04 1997-06-27    1 1952.533 1965.589 1997.485
2  B 1954-04-01 1972-09-08 1995-05-23    0 1954.246 1972.686 1995.388
3  C 1987-06-10 1991-12-23 1998-07-24    1 1987.437 1991.974 1998.559
```

2.2.1 A `Lexis` object

Define this as a `Lexis` object with timescales calendar time (`per`, period) and age (`age`):

```
> Lcoh <- Lexis(entry = list(per = doe),
+                exit = list(per = dox,
+                            age = dox - dob),
+                  id = id,
```

```
+            exit.status = factor(fail, 0:1, c("Alive","Dead")),
+                  data = xcoh)
NOTE: entry.status has been set to "Alive" for all.
> str(Lcoh)
Classes 'Lexis' and 'data.frame':        3 obs. of  14 variables:
 $ per    : 'cal.yr' num  1966 1973 1992
 $ age    : 'cal.yr' num  13.06 18.44 4.54
 $ lex.dur: 'cal.yr' num  31.9 22.7 6.58
 $ lex.Cst: Factor w/ 2 levels "Alive","Dead": 1 1 1
 $ lex.Xst: Factor w/ 2 levels "Alive","Dead": 2 1 2
 $ lex.id : chr  "A" "B" "C"
 $ id     : chr  "A" "B" "C"
 $ birth  : chr  "1952-07-14" "1954-04-01" "1987-06-10"
 $ entry  : chr  "1965-08-04" "1972-09-08" "1991-12-23"
 $ exit   : chr  "1997-06-27" "1995-05-23" "1998-07-24"
 $ fail   : num  1 0 1
 $ dob    : 'cal.yr' num  1953 1954 1987
 $ doe    : 'cal.yr' num  1966 1973 1992
 $ dox    : 'cal.yr' num  1997 1995 1999
 - attr(*, "time.scales")= chr [1:2] "per" "age"
 - attr(*, "time.since")= chr [1:2] "" ""
 - attr(*, "breaks")=List of 2
  ..$ per: NULL
  ..$ age: NULL
> (Lx <- Lcoh[,1:6])
 lex.id      per    age lex.dur lex.Cst lex.Xst
      A 1965.59 13.06   31.90   Alive    Dead
      B 1972.69 18.44   22.70   Alive   Alive
      C 1991.97  4.54    6.58   Alive    Dead
```

Factor or character `lex.id`?

Note that when the `id` argument to `Lexis` is a character variable then the `lex.id` will be a factor. Which, if each person has a lot of records may save time, but if you subset may be a waste of space. Moreover merging (*i.e.* joining in the language of `tidyverse`) may present problems with different levels. `merge` from the `base` R, will coerce to factor with union of levels as levels, where as the `_join` functions from `dplyr` will coerce to character.

Thus the most reasonable strategy thus seems to keep `lex.id` as a character variable.

```
> Lx$lex.id <- as.character(Lx$lex.id)
> str(Lx)
Classes 'Lexis' and 'data.frame':        3 obs. of  6 variables:
 $ per    : 'cal.yr' num  1966 1973 1992
 $ age    : 'cal.yr' num  13.06 18.44 4.54
 $ lex.dur: 'cal.yr' num  31.9 22.7 6.58
 $ lex.Cst: Factor w/ 2 levels "Alive","Dead": 1 1 1
 $ lex.Xst: Factor w/ 2 levels "Alive","Dead": 2 1 2
 $ lex.id : chr  "A" "B" "C"
 - attr(*, "time.scales")= chr [1:2] "per" "age"
 - attr(*, "time.since")= chr [1:2] "" ""
 - attr(*, "breaks")=List of 2
  ..$ per: NULL
  ..$ age: NULL
```

```
> Lx
 lex.id      per   age lex.dur lex.Cst lex.Xst
      A 1965.59 13.06   31.90   Alive    Dead
      B 1972.69 18.44   22.70   Alive   Alive
      C 1991.97  4.54    6.58   Alive    Dead
```

Clinical measurements

Then we generate data frame with clinical examination data, that is date of examination in `per`, some (bogus) clinical measurements and also names of the examination rounds:

```
> clin <- data.frame(lex.id = c("A", "A", "C", "B", "C"),
+                     per = cal.yr(c("1977-3-17",
+                                    "1973-7-29",
+                                    "1996-3-1",
+                                    "1990-7-14",
+                                    "1989-1-31")),
+                     bp = c(120, 140, 160, 157, 145),
+                     chol = c(NA, 5, 8, 9, 6),
+                     xnam = c("X2", "X1", "X1", "X2", "X0"),
+          stringsAsFactors = FALSE)
> str(clin)
'data.frame':       5 obs. of  5 variables:
 $ lex.id: chr  "A" "A" "C" "B" ...
 $ per   : 'cal.yr' num  1977 1974 1996 1991 1989
 $ bp    : num  120 140 160 157 145
 $ chol  : num  NA 5 8 9 6
 $ xnam  : chr  "X2" "X1" "X1" "X2" ...
> clin
  lex.id       per  bp chol xnam
1      A 1977.206 120   NA   X2
2      A 1973.573 140    5   X1
3      C 1996.163 160    8   X1
4      B 1990.531 157    9   X2
5      C 1989.083 145    6   X0
```

We set up this data frame with an `id` variable called `lex.id` and a date of examination, `per`, that has the same name as one of the time scales in the Lexis object `Lx`. Note that we have chosen a measurement for person `C` from 1989—before the person's entry to the study, and have an `NA` for `chol` for person `A`.

2.2.2   Adding clinical data

There is a slightly different behaviour according to whether the variable with the name of the examination is given or not, and whether the name of the (incomplete) time scale is given or not:

```
> (Cx <- addCov.Lexis(Lx, clin))
 lex.id      per   age   tfc lex.dur lex.Cst lex.Xst exnam  bp chol xnam
      A 1965.59 13.06    NA    7.98   Alive   Alive  <NA>  NA   NA <NA>
      A 1973.57 21.04  0.00    3.63   Alive   Alive   ex1 140    5   X1
      A 1977.21 24.67  0.00   20.28   Alive    Dead   ex2 120   NA   X2
      B 1972.69 18.44    NA   17.85   Alive   Alive  <NA>  NA   NA <NA>
```

```
      B 1990.53 36.28 0.00     4.86    Alive    Alive    ex1 157    9    X2
      C 1991.97  4.54 2.89     4.19    Alive    Alive    ex1 145    6    X0
      C 1996.16  8.73 0.00     2.40    Alive     Dead    ex2 160    8    X1
```

Note that the clinical measurement preceding the entry of person C is included, and that
the `tfc` (time from clinical measurement) is correctly rendered, we a non-zero value at date
of entry.

   We also see that a variable `exnam` is constructed with consecutive numbering of
examinations within each person, while the variable `xnam` is just carried over as any other.

   If we explicitly give the name of the variable holding the examination names we do not
get a constructed `exnam`. We can also define the name of the (incomplete) timescale to hold
the time since measurement, in this case as `tfCl`:

```
> (Dx <- addCov.Lexis(Lx, clin, exnam = "xnam", tfc = "tfCl"))
 lex.id      per    age tfCl lex.dur lex.Cst lex.Xst xnam  bp chol
      A 1965.59 13.06   NA    7.98    Alive    Alive <NA>  NA   NA
      A 1973.57 21.04 0.00    3.63    Alive    Alive   X1 140    5
      A 1977.21 24.67 0.00   20.28    Alive     Dead   X2 120   NA
      B 1972.69 18.44   NA   17.85    Alive    Alive <NA>  NA   NA
      B 1990.53 36.28 0.00    4.86    Alive    Alive   X2 157    9
      C 1991.97  4.54 2.89    4.19    Alive    Alive   X0 145    6
      C 1996.16  8.73 0.00    2.40    Alive     Dead   X1 160    8
> summary(Dx, t=T)

Transitions:
     To
From    Alive Dead  Records:  Events: Risk time:  Persons:
  Alive     5    2         7        2      61.18         3


Timescales:
 per  age tfCl
  ""   ""  "X"
```

2.3   Exchanging split and add

As noted in the beginning of this note, `addCov.Lexis` uses LOCF, and so it is
commutative with `splitLexis`:

```
> # split BEFORE add
> Lb <- addCov.Lexis(splitLexis(Lx,
+                      time.scale = "age",
+                       breaks = seq(0, 80, 5)),
+                 clin,
+                 exnam = "xnam" )
> Lb
 lex.id      per    age   tfc lex.dur lex.Cst lex.Xst xnam  bp chol
      A 1965.59 13.06    NA    1.94    Alive    Alive <NA>  NA   NA
      A 1967.53 15.00    NA    5.00    Alive    Alive <NA>  NA   NA
      A 1972.53 20.00    NA    1.04    Alive    Alive <NA>  NA   NA
      A 1973.57 21.04  0.00    3.63    Alive    Alive   X1 140    5
      A 1977.21 24.67  0.00    0.33    Alive    Alive   X2 120   NA
      A 1977.53 25.00  0.33    5.00    Alive    Alive   X2 120   NA
      A 1982.53 30.00  5.33    5.00    Alive    Alive   X2 120   NA
```

```
            A 1987.53 35.00 10.33    5.00   Alive    Alive   X2 120   NA
            A 1992.53 40.00 15.33    4.95   Alive    Dead    X2 120   NA
            B 1972.69 18.44    NA    1.56   Alive    Alive <NA>  NA    NA
            B 1974.25 20.00    NA    5.00   Alive    Alive <NA>  NA    NA
            B 1979.25 25.00    NA    5.00   Alive    Alive <NA>  NA    NA
            B 1984.25 30.00    NA    5.00   Alive    Alive <NA>  NA    NA
            B 1989.25 35.00    NA    1.28   Alive    Alive <NA>  NA    NA
            B 1990.53 36.28  0.00    3.72   Alive    Alive   X2 157    9
            B 1994.25 40.00  3.72    1.14   Alive    Alive   X2 157    9
            C 1991.97  4.54  2.89    0.46   Alive    Alive   X0 145    6
            C 1992.44  5.00  3.35    3.73   Alive    Alive   X0 145    6
            C 1996.16  8.73  0.00    1.27   Alive    Alive   X1 160    8
            C 1997.44 10.00  1.27    1.12   Alive    Dead    X1 160    8
> #
> # split AFTER add
> La <- splitLexis(addCov.Lexis(Lx,
+                          clin,
+                       exnam = "xnam" ),
+               time.scale = "age",
+                  breaks = seq(0, 80, 5))
> La
 lex.id      per    age    tfc lex.dur lex.Cst lex.Xst  xnam  bp chol
        A 1965.59 13.06    NA    1.94   Alive    Alive <NA>  NA    NA
        A 1967.53 15.00    NA    5.00   Alive    Alive <NA>  NA    NA
        A 1972.53 20.00    NA    1.04   Alive    Alive <NA>  NA    NA
        A 1973.57 21.04  0.00    3.63   Alive    Alive   X1 140    5
        A 1977.21 24.67  0.00    0.33   Alive    Alive   X2 120   NA
        A 1977.53 25.00  0.33    5.00   Alive    Alive   X2 120   NA
        A 1982.53 30.00  5.33    5.00   Alive    Alive   X2 120   NA
        A 1987.53 35.00 10.33    5.00   Alive    Alive   X2 120   NA
        A 1992.53 40.00 15.33    4.95   Alive    Dead    X2 120   NA
        B 1972.69 18.44    NA    1.56   Alive    Alive <NA>  NA    NA
        B 1974.25 20.00    NA    5.00   Alive    Alive <NA>  NA    NA
        B 1979.25 25.00    NA    5.00   Alive    Alive <NA>  NA    NA
        B 1984.25 30.00    NA    5.00   Alive    Alive <NA>  NA    NA
        B 1989.25 35.00    NA    1.28   Alive    Alive <NA>  NA    NA
        B 1990.53 36.28  0.00    3.72   Alive    Alive   X2 157    9
        B 1994.25 40.00  3.72    1.14   Alive    Alive   X2 157    9
        C 1991.97  4.54  2.89    0.46   Alive    Alive   X0 145    6
        C 1992.44  5.00  3.35    3.73   Alive    Alive   X0 145    6
        C 1996.16  8.73  0.00    1.27   Alive    Alive   X1 160    8
        C 1997.44 10.00  1.27    1.12   Alive    Dead    X1 160    8
```

We see that the results are identical, bar the sequence of variables and attributes.

We can more explicitly verify that the resulting data frames are the same:

```
> La$tfc == Lb$tfc
 [1]   NA   NA   NA TRUE TRUE TRUE TRUE TRUE TRUE   NA   NA   NA   NA   NA TRUE TRUE TRUE
[18] TRUE TRUE TRUE
> La$age == Lb$age
 [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
[18] TRUE TRUE TRUE
> La$per == Lb$per
 [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
[18] TRUE TRUE TRUE
```

The same goes for `splitMulti`:

```
> ## split BEFORE add
> Mb <- addCov.Lexis(splitMulti(Lx, age = seq(0, 80, 5)),
+                     clin,
+                     exnam = "xnam" )
> ##
> ## split AFTER add
> Ma <- splitMulti(addCov.Lexis(Lx,
+                               clin,
+                               exnam = "xnam" ),
+                  age = seq(0, 80, 5))
> La$tfc == Mb$tfc
 [1]   NA   NA   NA TRUE TRUE TRUE TRUE TRUE TRUE   NA   NA   NA   NA   NA TRUE TRUE TRUE
[18] TRUE TRUE TRUE
> Ma$tfc == Mb$tfc

 [1]   NA   NA   NA TRUE TRUE TRUE TRUE TRUE TRUE   NA   NA   NA   NA   NA TRUE TRUE TRUE
[18] TRUE TRUE TRUE
```

In summary, because both `addCov.Lexis` and `splitLexis`/`splitMulti` use LOCF for covariates the order of splitting and adding does not matter.

This is certainly not the case with addDrug.Lexis as we shall see.

2.4   Filling the `NAs`

As mentioned in the beginning, clinical measurements given as `NA` in the `clin` data frame are carried forward. If you want to have these replaced by 'older' clinical measurements you can do that explicitly by `dplyr::fill` with a construction like:

```
> cov <- c("bp", "chol")
> Lx <- La
> Lx <- group_by(Lx, lex.id) %>%
+         fill(all_of(cov)) %>%
+      ungroup()
> class(Lx)
[1] "tbl_df"      "tbl"         "data.frame"
```

We see that the `Lexis` attributes are lost by using the `group_by` function, so we fish out the covariates from the `tibble` and stick them back into the `Lexis` object:

```
> Lx <- La
> Lx[,cov] <- as.data.frame(group_by(Lx, lex.id)
+                           %>% fill(all_of(cov)))[,cov]
> class(Lx)
[1] "Lexis"       "data.frame"
> La

 lex.id      per    age    tfc lex.dur lex.Cst lex.Xst xnam  bp chol
      A 1965.59 13.06     NA    1.94   Alive   Alive <NA>  NA   NA
      A 1967.53 15.00     NA    5.00   Alive   Alive <NA>  NA   NA
      A 1972.53 20.00     NA    1.04   Alive   Alive <NA>  NA   NA
      A 1973.57 21.04   0.00    3.63   Alive   Alive   X1 140    5
      A 1977.21 24.67   0.00    0.33   Alive   Alive   X2 120   NA
      A 1977.53 25.00   0.33    5.00   Alive   Alive   X2 120   NA
```

```
        A 1982.53 30.00   5.33    5.00    Alive    Alive    X2 120    NA
        A 1987.53 35.00  10.33    5.00    Alive    Alive    X2 120    NA
        A 1992.53 40.00  15.33    4.95    Alive     Dead    X2 120    NA
        B 1972.69 18.44     NA    1.56    Alive    Alive <NA>  NA    NA
        B 1974.25 20.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1979.25 25.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1984.25 30.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1989.25 35.00     NA    1.28    Alive    Alive <NA>  NA    NA
        B 1990.53 36.28   0.00    3.72    Alive    Alive    X2 157     9
        B 1994.25 40.00   3.72    1.14    Alive    Alive    X2 157     9
        C 1991.97  4.54   2.89    0.46    Alive    Alive    X0 145     6
        C 1992.44  5.00   3.35    3.73    Alive    Alive    X0 145     6
        C 1996.16  8.73   0.00    1.27    Alive    Alive    X1 160     8
        C 1997.44 10.00   1.27    1.12    Alive     Dead    X1 160     8
> Lx
 lex.id      per     age    tfc lex.dur lex.Cst lex.Xst xnam   bp chol
        A 1965.59 13.06     NA    1.94    Alive    Alive <NA>  NA    NA
        A 1967.53 15.00     NA    5.00    Alive    Alive <NA>  NA    NA
        A 1972.53 20.00     NA    1.04    Alive    Alive <NA>  NA    NA
        A 1973.57 21.04   0.00    3.63    Alive    Alive    X1 140     5
        A 1977.21 24.67   0.00    0.33    Alive    Alive    X2 120     5
        A 1977.53 25.00   0.33    5.00    Alive    Alive    X2 120     5
        A 1982.53 30.00   5.33    5.00    Alive    Alive    X2 120     5
        A 1987.53 35.00  10.33    5.00    Alive    Alive    X2 120     5
        A 1992.53 40.00  15.33    4.95    Alive     Dead    X2 120     5
        B 1972.69 18.44     NA    1.56    Alive    Alive <NA>  NA    NA
        B 1974.25 20.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1979.25 25.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1984.25 30.00     NA    5.00    Alive    Alive <NA>  NA    NA
        B 1989.25 35.00     NA    1.28    Alive    Alive <NA>  NA    NA
        B 1990.53 36.28   0.00    3.72    Alive    Alive    X2 157     9
        B 1994.25 40.00   3.72    1.14    Alive    Alive    X2 157     9
        C 1991.97  4.54   2.89    0.46    Alive    Alive    X0 145     6
        C 1992.44  5.00   3.35    3.73    Alive    Alive    X0 145     6
        C 1996.16  8.73   0.00    1.27    Alive    Alive    X1 160     8
        C 1997.44 10.00   1.27    1.12    Alive     Dead    X1 160     8
```

The slightly convoluted code where the covariate columns are explicitly selected, owes to the fact that the `dplyr` functions will strip the data frames of the `Lexis` attributes. So we needed to use `fill` to just generate the covariates and not touch the `Lexis` object itself.

This should of course be built into `addCov.Lexis` as a separate argument, but is not yet.

Note that the `tfc`, time from clinical measurement, is now not a valid time scale variable any more; the 5 in `chol` is measured at 1973.7 but `tfc` is reset to 0 at 1977.21, even if only `bp` but not `chol` is measured at that time. If you want that remedied you will have to use `addCov.Lexis` twice, one with a `clin` data frame with only `bp` and another with a data frame with only `chol`, each generating a differently named variable holding the time from clinical measurement.

This is a problem that comes from the structure of the supplied *data* not from the program features; in the example we had basically measurements of different clinical variables at different times, and so necessarily also a need for different times since last measurement.

Chapter 3

`addDrug.Lexis`

The general purpose of the function is to amend a `Lexis` object with drug exposure data. The data base with information on a specific drug is assumed to be a data frame with one entry per drug purchase (or prescription), containing the date and the amount purchased and optionally the prescribed dosage (that is how much is supposed to be taken per time). We assume that we have such a data base for each drug of interest, which also includes an id variable, `lex.id`, that matches the `lex.id` variable in the `Lexis` object.

For each type of drug the function derives 4 variables:

`ex` : logical, is the person currently `ex`posed
`tf` : numeric, `t`ime since `f`irst purchase
`ct` : numeric, `c`umulative `t`ime on the drug
`cd` : numeric, `c`umulative `d`ose of the drug

These names are pre- or suf-fixed by the drug name, so that exposures to different drugs can be distinguished; see the examples.

The resulting `Lexis` object has extra records corresponding to cuts at each drug purchase and at each expiry date of a purchase. For each purchase the coverage period is derived (different methods for this are available), and if the end of this (the expiry date) is earlier than the next purchase of the person, the person is considered off the drug from the expiry date, and a cut in the follow-up is generated with `ex` set to `FALSE`.

3.1 The help example

The following is a slight modification of the code from the example section of the help page for `addDrug.Lexis`

First we generate follow-up of 2 persons, and split the follow-up in intervals of length 0.6 years along the calendar time scale, `per`:

```
> fu <- data.frame(doe = c(2006, 2008),
+                  dox = c(2015, 2018),
+                  dob = c(1950, 1951),
+                  xst = factor(c("A","D")))
> Lx <- Lexis(entry = list(per = doe,
+                          age = doe- dob),
+              exit = list(per = dox),
+       exit.status = xst,
+              data = fu)
```

```
NOTE: entry.status has been set to "A" for all.
> Lx <- subset(Lx, select = -c(doe, dob, dox, xst))
> Sx <- splitLexis(Lx, "per", breaks = seq(1990, 2020, 0.6))
> summary(Sx)

Transitions:
     To
From  A D  Records:  Events: Risk time:  Persons:
   A 32 1        33        1        19         2

> str(Sx)

Classes 'Lexis' and 'data.frame':       33 obs. of  6 variables:
 $ lex.id : int  1 1 1 1 1 1 1 1 1 1 ...
 $ per    : num   2006 2006 2007 2007 2008 ...
 $ age    : num   56 56.2 56.8 57.4 58 ...
 $ lex.dur: num   0.2 0.6 0.6 0.6 0.6 ...
 $ lex.Cst: Factor w/ 2 levels "A","D": 1 1 1 1 1 1 1 1 1 1 ...
 $ lex.Xst: Factor w/ 2 levels "A","D": 1 1 1 1 1 1 1 1 1 1 ...
 - attr(*, "breaks")=List of 2
  ..$ per: num [1:51] 1990 1991 1991 1992 1992 ...
  ..$ age: NULL
 - attr(*, "time.scales")= chr [1:2] "per" "age"
 - attr(*, "time.since")= chr [1:2] "" ""
```

Note that as opposed to the previous example, the time scales are not of class `cal.yr`, they are just numerical.

Then we generate example drug purchases for these two persons, one data frame for each of the drugs `F` and `G`. Note that we generate `lex.id`$\in (1,2)$ referring to the values of `lex.id` in the lexis object `Sx`.

```
> set.seed(1952)
> rf <- data.frame(per = c(2005 + runif(12, 0, 10)),
+                   amt = sample(2:4, 12, replace = TRUE),
+               lex.id = sample(1:2, 12, replace = TRUE)) %>%
+       arrange(lex.id, per)
> rg <- data.frame(per = c(2009 + runif(10, 0, 10)),
+                   amt = sample(round(2:4/3,1), 10, replace = TRUE),
+               lex.id = sample(1:2, 10, replace = TRUE)) %>%
+       arrange(lex.id, per)
```

We do not need to sort the drug purchase data frames (it is done internally by `addDrug.Lexis`), but it makes it easier to grasp the structure. Note that we generated the drug purchase files with the required variable names.

The way purchase data is supplied to the function is in a `list` where each element is a data frame of purchase records for one type of drug. The list must be named, because the names are used as prefixes of the generated exposure variables. We can show the resulting data in a list:

```
> pdat <- list(F = rf, G = rg)
> pdat
$F
        per amt lex.id
1  2013.964   4      1
2  2014.251   4      1
3  2014.509   3      1
4  2014.990   2      1
```

```
5   2005.311   2       2
6   2007.595   3       2
7   2011.710   4       2
8   2011.812   3       2
9   2012.865   2       2
10  2013.331   2       2
11  2013.417   2       2
12  2013.932   2       2

$G
        per amt lex.id
1   2009.630 1.3      1
2   2012.987 1.3      1
3   2013.018 1.3      1
4   2016.954 0.7      1
5   2017.924 1.0      1
6   2009.089 1.3      2
7   2011.599 0.7      2
8   2014.566 1.0      2
9   2016.912 0.7      2
10  2017.004 1.0      2

> Lx

 lex.id  per age lex.dur lex.Cst lex.Xst
      1 2006  56       9       A       A
      2 2008  57      10       A       D
```

Note that we have generated data so that there are drug purchases of drug F that is *before* start of follow-up for person 2.

We can then expand the time-split Lexis object, Sx with the drug information. addDrug.Lexis not only adds 8 *variables* (4 from each drug), it also adds *records* representing cuts at the purchase dates and possible expiry dates.

```
> summary(Sx) ; names(Sx)
Transitions:
     To
From  A D  Records:  Events: Risk time:  Persons:
   A 32 1        33        1        19         2

[1] "lex.id"  "per"     "age"     "lex.dur" "lex.Cst" "lex.Xst"

> ex1 <- addDrug.Lexis(Sx, pdat, method = "ext") # default

NOTE: timescale taken as 'per'
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).

> summary(ex1) ; names(ex1)

Transitions:
     To
From  A D  Records:  Events: Risk time:  Persons:
   A 64 1        65        1        19         2

 [1] "lex.id"  "per"     "age"     "lex.dur" "lex.Cst" "lex.Xst" "F.ex"    "F.tf"
 [9] "F.ct"    "F.cd"    "G.ex"    "G.tf"    "G.ct"    "G.cd"

> print(ex1, nd = 2)
```

lex.id	per	age	lex.dur	lex.Cst	lex.Xst	F.ex	F.tf	F.ct	F.cd	G.ex	G.tf	G.ct	G.cd
1	2006.00	56.00	0.20	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2006.20	56.20	0.60	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2006.80	56.80	0.60	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2007.40	57.40	0.60	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2008.00	58.00	0.60	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2008.60	58.60	0.60	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2009.20	59.20	0.43	A	A	FALSE	0.00	0.00	0.00	FALSE	0.00	0.00	0.00
1	2009.63	59.63	0.17	A	A	FALSE	0.00	0.00	0.00	TRUE	0.00	0.00	0.00
1	2009.80	59.80	0.60	A	A	FALSE	0.00	0.00	0.00	TRUE	0.17	0.17	0.07
1	2010.40	60.40	0.60	A	A	FALSE	0.00	0.00	0.00	TRUE	0.77	0.77	0.30
1	2011.00	61.00	0.60	A	A	FALSE	0.00	0.00	0.00	TRUE	1.37	1.37	0.53
1	2011.60	61.60	0.60	A	A	FALSE	0.00	0.00	0.00	TRUE	1.97	1.97	0.76
1	2012.20	62.20	0.60	A	A	FALSE	0.00	0.00	0.00	TRUE	2.57	2.57	1.00
1	2012.80	62.80	0.19	A	A	FALSE	0.00	0.00	0.00	TRUE	3.17	3.17	1.23
1	2012.99	62.99	0.03	A	A	FALSE	0.00	0.00	0.00	TRUE	3.36	3.36	1.30
1	2013.02	63.02	0.03	A	A	FALSE	0.00	0.00	0.00	TRUE	3.39	3.39	2.60
1	2013.05	63.05	0.35	A	A	FALSE	0.00	0.00	0.00	FALSE	3.42	3.42	3.90
1	2013.40	63.40	0.56	A	A	FALSE	0.00	0.00	0.00	FALSE	3.77	3.42	3.90
1	2013.96	63.96	0.00	A	A	TRUE	0.00	0.00	0.00	FALSE	4.33	3.42	3.90
1	2013.96	63.96	0.04	A	A	TRUE	0.00	0.00	0.00	FALSE	4.33	3.42	3.90
1	2014.00	64.00	0.25	A	A	TRUE	0.04	0.04	0.50	FALSE	4.37	3.42	3.90
1	2014.25	64.25	0.00	A	A	TRUE	0.29	0.29	4.00	FALSE	4.62	3.42	3.90
1	2014.25	64.25	0.26	A	A	TRUE	0.29	0.29	4.00	FALSE	4.62	3.42	3.90
1	2014.51	64.51	0.00	A	A	TRUE	0.54	0.54	8.00	FALSE	4.88	3.42	3.90
1	2014.51	64.51	0.09	A	A	TRUE	0.54	0.54	8.00	FALSE	4.88	3.42	3.90
1	2014.60	64.60	0.10	A	A	TRUE	0.64	0.64	9.41	FALSE	4.97	3.42	3.90
1	2014.70	64.70	0.00	A	A	FALSE	0.74	0.74	11.00	FALSE	5.07	3.42	3.90
1	2014.70	64.70	0.29	A	A	FALSE	0.74	0.74	11.00	FALSE	5.07	3.42	3.90
1	2014.99	64.99	0.01	A	A	TRUE	1.03	0.74	11.00	FALSE	5.36	3.42	3.90
2	2008.00	57.00	0.60	A	A	TRUE	0.00	0.40	0.35	FALSE	0.00	0.00	0.00
2	2008.60	57.60	0.49	A	A	TRUE	0.60	1.00	0.88	FALSE	0.00	0.00	0.00
2	2009.09	58.09	0.11	A	A	TRUE	1.09	1.49	1.31	TRUE	0.00	0.00	0.00
2	2009.20	58.20	0.60	A	A	TRUE	1.20	1.60	1.40	TRUE	0.11	0.11	0.06
2	2009.80	58.80	0.60	A	A	TRUE	1.80	2.20	1.93	TRUE	0.71	0.71	0.37
2	2010.40	59.40	0.60	A	A	TRUE	2.40	2.80	2.46	TRUE	1.31	1.31	0.68
2	2011.00	60.00	0.02	A	A	TRUE	3.00	3.40	2.98	TRUE	1.91	1.91	0.99
2	2011.02	60.02	0.00	A	A	FALSE	3.02	3.43	3.00	TRUE	1.93	1.93	1.00
2	2011.02	60.02	0.58	A	A	FALSE	3.02	3.43	3.00	TRUE	1.93	1.93	1.00
2	2011.60	60.60	0.00	A	A	FALSE	3.60	3.43	3.00	TRUE	2.51	2.51	1.30
2	2011.60	60.60	0.11	A	A	FALSE	3.60	3.43	3.00	TRUE	2.51	2.51	1.30
2	2011.71	60.71	0.00	A	A	TRUE	3.71	3.43	3.00	TRUE	2.62	2.62	1.36
2	2011.71	60.71	0.10	A	A	TRUE	3.71	3.43	3.00	TRUE	2.62	2.62	1.36
2	2011.81	60.81	0.08	A	A	TRUE	3.81	3.53	7.00	TRUE	2.72	2.72	1.41
2	2011.89	60.89	0.31	A	A	FALSE	3.89	3.61	10.00	TRUE	2.80	2.80	1.45
2	2012.20	61.20	0.60	A	A	FALSE	4.20	3.61	10.00	TRUE	3.11	3.11	1.61
2	2012.80	61.80	0.07	A	A	FALSE	4.80	3.61	10.00	TRUE	3.71	3.71	1.92
2	2012.87	61.87	0.09	A	A	TRUE	4.87	3.61	10.00	TRUE	3.78	3.78	1.96
2	2012.95	61.95	0.38	A	A	TRUE	4.95	3.69	10.37	FALSE	3.86	3.86	2.00
2	2013.33	62.33	0.07	A	A	TRUE	5.33	4.07	12.00	FALSE	4.24	3.86	2.00
2	2013.40	62.40	0.02	A	A	TRUE	5.40	4.14	13.61	FALSE	4.31	3.86	2.00
2	2013.42	62.42	0.09	A	A	TRUE	5.42	4.16	14.00	FALSE	4.33	3.86	2.00
2	2013.50	62.50	0.43	A	A	FALSE	5.50	4.24	16.00	FALSE	4.41	3.86	2.00
2	2013.93	62.93	0.07	A	A	TRUE	5.93	4.24	16.00	FALSE	4.84	3.86	2.00
2	2014.00	63.00	0.45	A	A	TRUE	6.00	4.31	16.27	FALSE	4.91	3.86	2.00
2	2014.45	63.45	0.12	A	A	FALSE	6.45	4.76	18.00	FALSE	5.36	3.86	2.00
2	2014.57	63.57	0.03	A	A	FALSE	6.57	4.76	18.00	TRUE	5.48	3.86	2.00

```
    2 2014.60 63.60     0.60        A        A FALSE 6.60 4.76 18.00   TRUE 5.51 3.90 2.01
    2 2015.20 64.20     0.60        A        A FALSE 7.20 4.76 18.00   TRUE 6.11 4.50 2.27
    2 2015.80 64.80     0.60        A        A FALSE 7.80 4.76 18.00   TRUE 6.71 5.10 2.53
    2 2016.40 65.40     0.51        A        A FALSE 8.40 4.76 18.00   TRUE 7.31 5.70 2.78
    2 2016.91 65.91     0.09        A        A FALSE 8.91 4.76 18.00   TRUE 7.82 6.21 3.00
    2 2017.00 66.00     0.00        A        A FALSE 9.00 4.76 18.00   TRUE 7.91 6.30 3.67
    2 2017.00 66.00     0.13        A        A FALSE 9.00 4.76 18.00   TRUE 7.91 6.30 3.70
    2 2017.14 66.14     0.46        A        A FALSE 9.14 4.76 18.00 FALSE 8.05 6.43 4.70
    2 2017.60 66.60     0.40        A        D FALSE 9.60 4.76 18.00 FALSE 8.51 6.43 4.70
```

```
> ex2 <- addDrug.Lexis(Sx, pdat, method = "ext", grace = 0.5)

NOTE: timescale taken as 'per'
Values of grace has been recycled across 2 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).

> summary(ex2)

Transitions:
     To
From  A D  Records:  Events: Risk time:  Persons:
   A 62 1        63        1        19         2

> print(ex2, nd = 2)

 lex.id      per     age lex.dur lex.Cst lex.Xst  F.ex F.tf F.ct   F.cd   G.ex G.tf G.ct G.cd
      1 2006.00 56.00     0.20        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.20 56.20     0.60        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.80 56.80     0.60        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2007.40 57.40     0.60        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.00 58.00     0.60        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.60 58.60     0.60        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.20 59.20     0.43        A        A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.63 59.63     0.17        A        A FALSE 0.00 0.00   0.00  TRUE 0.00 0.00 0.00
      1 2009.80 59.80     0.60        A        A FALSE 0.00 0.00   0.00  TRUE 0.17 0.17 0.07
      1 2010.40 60.40     0.60        A        A FALSE 0.00 0.00   0.00  TRUE 0.77 0.77 0.30
      1 2011.00 61.00     0.60        A        A FALSE 0.00 0.00   0.00  TRUE 1.37 1.37 0.53
      1 2011.60 61.60     0.60        A        A FALSE 0.00 0.00   0.00  TRUE 1.97 1.97 0.76
      1 2012.20 62.20     0.60        A        A FALSE 0.00 0.00   0.00  TRUE 2.57 2.57 1.00
      1 2012.80 62.80     0.19        A        A FALSE 0.00 0.00   0.00  TRUE 3.17 3.17 1.23
      1 2012.99 62.99     0.03        A        A FALSE 0.00 0.00   0.00  TRUE 3.36 3.36 1.30
      1 2013.02 63.02     0.38        A        A FALSE 0.00 0.00   0.00  TRUE 3.39 3.39 2.60
      1 2013.40 63.40     0.15        A        A FALSE 0.00 0.00   0.00  TRUE 3.77 3.77 3.53
      1 2013.55 63.55     0.41        A        A FALSE 0.00 0.00   0.00 FALSE 3.92 3.92 3.90
      1 2013.96 63.96     0.00        A        A  TRUE 0.00 0.00   0.00 FALSE 4.33 3.92 3.90
      1 2013.96 63.96     0.04        A        A  TRUE 0.00 0.00   0.00 FALSE 4.33 3.92 3.90
      1 2014.00 64.00     0.25        A        A  TRUE 0.04 0.04   0.50 FALSE 4.37 3.92 3.90
      1 2014.25 64.25     0.00        A        A  TRUE 0.29 0.29   4.00 FALSE 4.62 3.92 3.90
      1 2014.25 64.25     0.26        A        A  TRUE 0.29 0.29   4.00 FALSE 4.62 3.92 3.90
      1 2014.51 64.51     0.00        A        A  TRUE 0.54 0.54   8.00 FALSE 4.88 3.92 3.90
      1 2014.51 64.51     0.09        A        A  TRUE 0.54 0.54   8.00 FALSE 4.88 3.92 3.90
      1 2014.60 64.60     0.39        A        A  TRUE 0.64 0.64   8.57 FALSE 4.97 3.92 3.90
      1 2014.99 64.99     0.00        A        A  TRUE 1.03 1.03  11.00 FALSE 5.36 3.92 3.90
      1 2014.99 64.99     0.01        A        A  TRUE 1.03 1.03  11.00 FALSE 5.36 3.92 3.90
      2 2008.00 57.00     0.60        A        A  TRUE 0.00 0.40   0.31 FALSE 0.00 0.00 0.00
      2 2008.60 57.60     0.49        A        A  TRUE 0.60 1.00   0.77 FALSE 0.00 0.00 0.00
      2 2009.09 58.09     0.11        A        A  TRUE 1.09 1.49   1.14  TRUE 0.00 0.00 0.00
      2 2009.20 58.20     0.60        A        A  TRUE 1.20 1.60   1.23  TRUE 0.11 0.11 0.06
      2 2009.80 58.80     0.60        A        A  TRUE 1.80 2.20   1.68  TRUE 0.71 0.71 0.37
      2 2010.40 59.40     0.60        A        A  TRUE 2.40 2.80   2.14  TRUE 1.31 1.31 0.68
```

```
        2 2011.00 60.00     0.52        A       A  TRUE 3.00 3.40   2.60  TRUE 1.91 1.91 0.99
        2 2011.52 60.52     0.00        A       A FALSE 3.52 3.93   3.00  TRUE 2.43 2.43 1.26
        2 2011.52 60.52     0.08        A       A FALSE 3.52 3.93   3.00  TRUE 2.43 2.43 1.26
        2 2011.60 60.60     0.00        A       A FALSE 3.60 3.93   3.00  TRUE 2.51 2.51 1.30
        2 2011.60 60.60     0.11        A       A FALSE 3.60 3.93   3.00  TRUE 2.51 2.51 1.30
        2 2011.71 60.71     0.00        A       A  TRUE 3.71 3.93   3.00  TRUE 2.62 2.62 1.34
        2 2011.71 60.71     0.10        A       A  TRUE 3.71 3.93   3.00  TRUE 2.62 2.62 1.34
        2 2011.81 60.81     0.39        A       A  TRUE 3.81 4.03   7.00  TRUE 2.72 2.72 1.38
        2 2012.20 61.20     0.19        A       A  TRUE 4.20 4.42   9.02  TRUE 3.11 3.11 1.53
        2 2012.39 61.39     0.41        A       A FALSE 4.39 4.61  10.00  TRUE 3.30 3.30 1.60
        2 2012.80 61.80     0.07        A       A FALSE 4.80 4.61  10.00  TRUE 3.71 3.71 1.75
        2 2012.87 61.87     0.47        A       A  TRUE 4.87 4.61  10.00  TRUE 3.78 3.78 1.78
        2 2013.33 62.33     0.07        A       A  TRUE 5.33 5.07  12.00  TRUE 4.24 4.24 1.95
        2 2013.40 62.40     0.02        A       A  TRUE 5.40 5.14  13.61  TRUE 4.31 4.31 1.98
        2 2013.42 62.42     0.03        A       A  TRUE 5.42 5.16  14.00  TRUE 4.33 4.33 1.99
        2 2013.45 62.45     0.48        A       A  TRUE 5.45 5.19  14.13 FALSE 4.36 4.36 2.00
        2 2013.93 62.93     0.07        A       A  TRUE 5.93 5.67  16.00 FALSE 4.84 4.36 2.00
        2 2014.00 63.00     0.57        A       A  TRUE 6.00 5.74  16.13 FALSE 4.91 4.36 2.00
        2 2014.57 63.57     0.03        A       A  TRUE 6.57 6.31  17.25  TRUE 5.48 4.36 2.00
        2 2014.60 63.60     0.35        A       A  TRUE 6.60 6.34  17.32  TRUE 5.51 4.40 2.01
        2 2014.95 63.95     0.25        A       A FALSE 6.95 6.69  18.00  TRUE 5.86 4.74 2.16
        2 2015.20 64.20     0.60        A       A FALSE 7.20 6.69  18.00  TRUE 6.11 5.00 2.27
        2 2015.80 64.80     0.60        A       A FALSE 7.80 6.69  18.00  TRUE 6.71 5.60 2.53
        2 2016.40 65.40     0.51        A       A FALSE 8.40 6.69  18.00  TRUE 7.31 6.20 2.78
        2 2016.91 65.91     0.09        A       A FALSE 8.91 6.69  18.00  TRUE 7.82 6.71 3.00
        2 2017.00 66.00     0.00        A       A FALSE 9.00 6.69  18.00  TRUE 7.91 6.80 3.67
        2 2017.00 66.00     0.60        A       A FALSE 9.00 6.69  18.00  TRUE 7.91 6.80 3.70
        2 2017.60 66.60     0.04        A       A FALSE 9.60 6.69  18.00  TRUE 8.51 7.40 4.64
        2 2017.64 66.64     0.36        A       D FALSE 9.64 6.69  18.00 FALSE 8.55 7.43 4.70
> dos <- addDrug.Lexis(Sx, pdat, method = "dos", dpt = 6)

NOTE: timescale taken as 'per'
NOTE: end of exposure based on purchase and dosage (dpt).

> summary(dos)

Transitions:
     To
From  A D  Records:  Events: Risk time:  Persons:
   A 66 1        67        1        19         2

> print(dos, nd = 2)

 lex.id      per     age lex.dur lex.Cst lex.Xst   F.ex F.tf F.ct   F.cd   G.ex G.tf G.ct G.cd
      1 2006.00 56.00    0.20        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.20 56.20    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.80 56.80    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2007.40 57.40    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.00 58.00    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.60 58.60    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.20 59.20    0.43        A       A FALSE 0.00 0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.63 59.63    0.17        A       A FALSE 0.00 0.00   0.00  TRUE 0.00 0.00 0.00
      1 2009.80 59.80    0.05        A       A FALSE 0.00 0.00   0.00  TRUE 0.17 0.17 1.02
      1 2009.85 59.85    0.55        A       A FALSE 0.00 0.00   0.00 FALSE 0.22 0.22 1.30
      1 2010.40 60.40    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 0.77 0.22 1.30
      1 2011.00 61.00    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 1.37 0.22 1.30
      1 2011.60 61.60    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 1.97 0.22 1.30
      1 2012.20 62.20    0.60        A       A FALSE 0.00 0.00   0.00 FALSE 2.57 0.22 1.30
      1 2012.80 62.80    0.19        A       A FALSE 0.00 0.00   0.00 FALSE 3.17 0.22 1.30
      1 2012.99 62.99    0.03        A       A FALSE 0.00 0.00   0.00  TRUE 3.36 0.22 1.30
```

```
      1 2013.02 63.02    0.22        A        A FALSE 0.00 0.00   0.00  TRUE 3.39 0.25 2.60
      1 2013.23 63.23    0.17        A        A FALSE 0.00 0.00   0.00 FALSE 3.60 0.46 3.90
      1 2013.40 63.40    0.56        A        A FALSE 0.00 0.00   0.00 FALSE 3.77 0.46 3.90
      1 2013.96 63.96    0.00        A        A  TRUE 0.00 0.00   0.00 FALSE 4.33 0.46 3.90
      1 2013.96 63.96    0.04        A        A  TRUE 0.00 0.00   0.00 FALSE 4.33 0.46 3.90
      1 2014.00 64.00    0.25        A        A  TRUE 0.04 0.04   0.50 FALSE 4.37 0.46 3.90
      1 2014.25 64.25    0.00        A        A  TRUE 0.29 0.29   4.00 FALSE 4.62 0.46 3.90
      1 2014.25 64.25    0.26        A        A  TRUE 0.29 0.29   4.00 FALSE 4.62 0.46 3.90
      1 2014.51 64.51    0.00        A        A  TRUE 0.54 0.54   8.00 FALSE 4.88 0.46 3.90
      1 2014.51 64.51    0.09        A        A  TRUE 0.54 0.54   8.00 FALSE 4.88 0.46 3.90
      1 2014.60 64.60    0.39        A        A  TRUE 0.64 0.64   8.57 FALSE 4.97 0.46 3.90
      1 2014.99 64.99    0.00        A        A  TRUE 1.03 1.03  11.00 FALSE 5.36 0.46 3.90
      1 2014.99 64.99    0.01        A        A  TRUE 1.03 1.03  11.00 FALSE 5.36 0.46 3.90
      2 2008.00 57.00    0.10        A        A  TRUE 0.00 0.40   2.43 FALSE 0.00 0.00 0.00
      2 2008.10 57.10    0.00        A        A FALSE 0.10 0.50   3.00 FALSE 0.00 0.00 0.00
      2 2008.10 57.10    0.50        A        A FALSE 0.10 0.50   3.00 FALSE 0.00 0.00 0.00
      2 2008.60 57.60    0.49        A        A FALSE 0.60 0.50   3.00 FALSE 0.00 0.00 0.00
      2 2009.09 58.09    0.11        A        A FALSE 1.09 0.50   3.00  TRUE 0.00 0.00 0.00
      2 2009.20 58.20    0.11        A        A FALSE 1.20 0.50   3.00  TRUE 0.11 0.11 0.67
      2 2009.31 58.31    0.49        A        A FALSE 1.31 0.50   3.00 FALSE 0.22 0.22 1.30
      2 2009.80 58.80    0.60        A        A FALSE 1.80 0.50   3.00 FALSE 0.71 0.22 1.30
      2 2010.40 59.40    0.60        A        A FALSE 2.40 0.50   3.00 FALSE 1.31 0.22 1.30
      2 2011.00 60.00    0.60        A        A FALSE 3.00 0.50   3.00 FALSE 1.91 0.22 1.30
      2 2011.60 60.60    0.00        A        A FALSE 3.60 0.50   3.00  TRUE 2.51 0.22 1.30
      2 2011.60 60.60    0.11        A        A FALSE 3.60 0.50   3.00  TRUE 2.51 0.22 1.30
      2 2011.71 60.71    0.01        A        A  TRUE 3.71 0.50   3.00  TRUE 2.62 0.33 1.97
      2 2011.72 60.72    0.10        A        A  TRUE 3.72 0.51   3.22 FALSE 2.63 0.33 2.00
      2 2011.81 60.81    0.39        A        A  TRUE 3.81 0.60   7.00 FALSE 2.72 0.33 2.00
      2 2012.20 61.20    0.11        A        A  TRUE 4.20 0.99   9.33 FALSE 3.11 0.33 2.00
      2 2012.31 61.31    0.49        A        A FALSE 4.31 1.10  10.00 FALSE 3.22 0.33 2.00
      2 2012.80 61.80    0.07        A        A FALSE 4.80 1.10  10.00 FALSE 3.71 0.33 2.00
      2 2012.87 61.87    0.33        A        A  TRUE 4.87 1.10  10.00 FALSE 3.78 0.33 2.00
      2 2013.20 62.20    0.13        A        A FALSE 5.20 1.44  12.00 FALSE 4.11 0.33 2.00
      2 2013.33 62.33    0.07        A        A  TRUE 5.33 1.44  12.00 FALSE 4.24 0.33 2.00
      2 2013.40 62.40    0.02        A        A  TRUE 5.40 1.50  13.61 FALSE 4.31 0.33 2.00
      2 2013.42 62.42    0.33        A        A  TRUE 5.42 1.52  14.00 FALSE 4.33 0.33 2.00
      2 2013.75 62.75    0.18        A        A FALSE 5.75 1.85  16.00 FALSE 4.66 0.33 2.00
      2 2013.93 62.93    0.07        A        A  TRUE 5.93 1.85  16.00 FALSE 4.84 0.33 2.00
      2 2014.00 63.00    0.27        A        A  TRUE 6.00 1.92  16.41 FALSE 4.91 0.33 2.00
      2 2014.27 63.27    0.30        A        A FALSE 6.27 2.19  18.00 FALSE 5.18 0.33 2.00
      2 2014.57 63.57    0.03        A        A FALSE 6.57 2.19  18.00  TRUE 5.48 0.33 2.00
      2 2014.60 63.60    0.13        A        A FALSE 6.60 2.19  18.00  TRUE 5.51 0.37 2.20
      2 2014.73 63.73    0.47        A        A FALSE 6.73 2.19  18.00 FALSE 5.64 0.50 3.00
      2 2015.20 64.20    0.60        A        A FALSE 7.20 2.19  18.00 FALSE 6.11 0.50 3.00
      2 2015.80 64.80    0.60        A        A FALSE 7.80 2.19  18.00 FALSE 6.71 0.50 3.00
      2 2016.40 65.40    0.51        A        A FALSE 8.40 2.19  18.00 FALSE 7.31 0.50 3.00
      2 2016.91 65.91    0.09        A        A FALSE 8.91 2.19  18.00  TRUE 7.82 0.50 3.00
      2 2017.00 66.00    0.00        A        A FALSE 9.00 2.19  18.00  TRUE 7.91 0.59 3.67
      2 2017.00 66.00    0.17        A        A FALSE 9.00 2.19  18.00  TRUE 7.91 0.59 3.70
      2 2017.17 66.17    0.43        A        A FALSE 9.17 2.19  18.00 FALSE 8.08 0.76 4.70
      2 2017.60 66.60    0.40        A        D FALSE 9.60 2.19  18.00 FALSE 8.51 0.76 4.70

> fix <- addDrug.Lexis(Sx, pdat, method = "fix", maxt = 1)

NOTE: timescale taken as 'per'
Values of maxt has been recycled across 2 drugs
NOTE: end of exposure based on fixed coverage time of 1 .

> summary(fix)
```

```
Transitions:
     To
From  A  D  Records:  Events: Risk time:  Persons:
   A 63  1        64        1        19         2
> print(fix, nd = 2)

 lex.id     per     age lex.dur lex.Cst lex.Xst   F.ex F.tf  F.ct   F.cd   G.ex G.tf G.ct G.cd
      1 2006.00 56.00    0.20       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.20 56.20    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2006.80 56.80    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2007.40 57.40    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.00 58.00    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2008.60 58.60    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.20 59.20    0.43       A       A FALSE 0.00  0.00   0.00 FALSE 0.00 0.00 0.00
      1 2009.63 59.63    0.17       A       A FALSE 0.00  0.00   0.00  TRUE 0.00 0.00 0.00
      1 2009.80 59.80    0.60       A       A FALSE 0.00  0.00   0.00  TRUE 0.17 0.17 0.22
      1 2010.40 60.40    0.23       A       A FALSE 0.00  0.00   0.00  TRUE 0.77 0.77 1.00
      1 2010.63 60.63    0.37       A       A FALSE 0.00  0.00   0.00 FALSE 1.00 1.00 1.30
      1 2011.00 61.00    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 1.37 1.00 1.30
      1 2011.60 61.60    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 1.97 1.00 1.30
      1 2012.20 62.20    0.60       A       A FALSE 0.00  0.00   0.00 FALSE 2.57 1.00 1.30
      1 2012.80 62.80    0.19       A       A FALSE 0.00  0.00   0.00 FALSE 3.17 1.00 1.30
      1 2012.99 62.99    0.03       A       A FALSE 0.00  0.00   0.00  TRUE 3.36 1.00 1.30
      1 2013.02 63.02    0.38       A       A FALSE 0.00  0.00   0.00  TRUE 3.39 1.03 2.60
      1 2013.40 63.40    0.56       A       A FALSE 0.00  0.00   0.00  TRUE 3.77 1.41 3.10
      1 2013.96 63.96    0.00       A       A  TRUE 0.00  0.00   0.00  TRUE 4.33 1.98 3.83
      1 2013.96 63.96    0.04       A       A  TRUE 0.00  0.00   0.00  TRUE 4.33 1.98 3.83
      1 2014.00 64.00    0.02       A       A  TRUE 0.04  0.04   0.50  TRUE 4.37 2.01 3.88
      1 2014.02 64.02    0.23       A       A  TRUE 0.05  0.05   0.75 FALSE 4.39 2.03 3.90
      1 2014.25 64.25    0.00       A       A  TRUE 0.29  0.29   4.00 FALSE 4.62 2.03 3.90
      1 2014.25 64.25    0.26       A       A  TRUE 0.29  0.29   4.00 FALSE 4.62 2.03 3.90
      1 2014.51 64.51    0.00       A       A  TRUE 0.54  0.54   8.00 FALSE 4.88 2.03 3.90
      1 2014.51 64.51    0.09       A       A  TRUE 0.54  0.54   8.00 FALSE 4.88 2.03 3.90
      1 2014.60 64.60    0.39       A       A  TRUE 0.64  0.64   8.57 FALSE 4.97 2.03 3.90
      1 2014.99 64.99    0.00       A       A  TRUE 1.03  1.03  11.00 FALSE 5.36 2.03 3.90
      1 2014.99 64.99    0.01       A       A  TRUE 1.03  1.03  11.00 FALSE 5.36 2.03 3.90
      2 2008.00 57.00    0.60       A       A  TRUE 0.00  0.40   1.21 FALSE 0.00 0.00 0.00
      2 2008.60 57.60    0.00       A       A FALSE 0.60  1.00   3.00 FALSE 0.00 0.00 0.00
      2 2008.60 57.60    0.00       A       A FALSE 0.60  1.00   3.00 FALSE 0.00 0.00 0.00
      2 2008.60 57.60    0.49       A       A FALSE 0.60  1.00   3.00 FALSE 0.00 0.00 0.00
      2 2009.09 58.09    0.11       A       A FALSE 1.09  1.00   3.00  TRUE 0.00 0.00 0.00
      2 2009.20 58.20    0.60       A       A FALSE 1.20  1.00   3.00  TRUE 0.11 0.11 0.14
      2 2009.80 58.80    0.29       A       A FALSE 1.80  1.00   3.00  TRUE 0.71 0.71 0.92
      2 2010.09 59.09    0.31       A       A FALSE 2.09  1.00   3.00 FALSE 1.00 1.00 1.30
      2 2010.40 59.40    0.60       A       A FALSE 2.40  1.00   3.00 FALSE 1.31 1.00 1.30
      2 2011.00 60.00    0.60       A       A FALSE 3.00  1.00   3.00 FALSE 1.91 1.00 1.30
      2 2011.60 60.60    0.00       A       A FALSE 3.60  1.00   3.00  TRUE 2.51 1.00 1.30
      2 2011.60 60.60    0.11       A       A FALSE 3.60  1.00   3.00  TRUE 2.51 1.00 1.30
      2 2011.71 60.71    0.10       A       A  TRUE 3.71  1.00   3.00  TRUE 2.62 1.11 1.38
      2 2011.81 60.81    0.39       A       A  TRUE 3.81  1.10   7.00  TRUE 2.72 1.21 1.45
      2 2012.20 61.20    0.40       A       A  TRUE 4.20  1.49   8.16  TRUE 3.11 1.60 1.72
      2 2012.60 61.60    0.20       A       A  TRUE 4.60  1.89   9.36 FALSE 3.51 2.00 2.00
      2 2012.80 61.80    0.01       A       A  TRUE 4.80  2.09   9.96 FALSE 3.71 2.00 2.00
      2 2012.81 61.81    0.05       A       A FALSE 4.81  2.10  10.00 FALSE 3.72 2.00 2.00
      2 2012.87 61.87    0.47       A       A  TRUE 4.87  2.10  10.00 FALSE 3.78 2.00 2.00
      2 2013.33 62.33    0.07       A       A  TRUE 5.33  2.57  12.00 FALSE 4.24 2.00 2.00
      2 2013.40 62.40    0.02       A       A  TRUE 5.40  2.64  13.61 FALSE 4.31 2.00 2.00
      2 2013.42 62.42    0.51       A       A  TRUE 5.42  2.65  14.00 FALSE 4.33 2.00 2.00
```

```
2 2013.93 62.93    0.07        A       A   TRUE 5.93 3.17 16.00 FALSE 4.84 2.00 2.00
2 2014.00 63.00    0.57        A       A   TRUE 6.00 3.24 16.14 FALSE 4.91 2.00 2.00
2 2014.57 63.57    0.03        A       A   TRUE 6.57 3.80 17.27  TRUE 5.48 2.00 2.00
2 2014.60 63.60    0.33        A       A   TRUE 6.60 3.84 17.34  TRUE 5.51 2.03 2.03
2 2014.93 63.93    0.27        A       A  FALSE 6.93 4.17 18.00  TRUE 5.84 2.37 2.37
2 2015.20 64.20    0.37        A       A  FALSE 7.20 4.17 18.00  TRUE 6.11 2.63 2.63
2 2015.57 64.57    0.23        A       A  FALSE 7.57 4.17 18.00 FALSE 6.48 3.00 3.00
2 2015.80 64.80    0.60        A       A  FALSE 7.80 4.17 18.00 FALSE 6.71 3.00 3.00
2 2016.40 65.40    0.51        A       A  FALSE 8.40 4.17 18.00 FALSE 7.31 3.00 3.00
2 2016.91 65.91    0.09        A       A  FALSE 8.91 4.17 18.00  TRUE 7.82 3.00 3.00
2 2017.00 66.00    0.00        A       A  FALSE 9.00 4.17 18.00  TRUE 7.91 3.09 3.67
2 2017.00 66.00    0.60        A       A  FALSE 9.00 4.17 18.00  TRUE 7.91 3.09 3.70
2 2017.60 66.60    0.40        A       D  FALSE 9.60 4.17 18.00  TRUE 8.51 3.69 4.30
```

3.2 A more realistic example with run times

3.2.1 Follow-up data: `DMlate`

As example data we use rows from the `DMlate` example data from the `Epi` package:

```
> data(DMlate) ; str(DMlate)
'data.frame':        10000 obs. of  7 variables:
 $ sex  : Factor w/ 2 levels "M","F": 2 1 2 2 1 2 1 1 2 1 ...
 $ dobth: num  1940 1939 1918 1965 1933 ...
 $ dodm : num  1999 2003 2005 2009 2009 ...
 $ dodth: num  NA NA NA NA NA ...
 $ dooad: num  NA 2007 NA NA NA ...
 $ doins: num  NA NA NA NA NA NA NA NA NA NA ...
 $ dox  : num  2010 2010 2010 2010 2010 ...
> Lx <- Lexis(entry = list(per = dodm,
+                          age = dodm - dobth,
+                          tfd = 0),
+              exit = list(per = dox),
+       exit.status = factor(!is.na(dodth),
+                            labels = c("DM", "Dead")),
+              data = DMlate[sample(1:nrow(DMlate), 1000),])
NOTE: entry.status has been set to "DM" for all.

> summary(Lx)

Transitions:
     To
From  DM Dead  Records:  Events: Risk time:  Persons:
  DM 758  242      1000      242    5303.88       1000
```

We split the data along the age-scale (omitting the variables we shall not need):

```
> Sx <- splitLexis(Lx[,1:7], time.scale="age", breaks = 0:120)
> summary(Sx)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 6044  242      6286      242    5303.88       1000

> str(Sx)
```

```
Classes 'Lexis' and 'data.frame':       6286 obs. of  7 variables:
 $ lex.id : int  1 1 1 1 2 2 2 3 3 3 ...
 $ per    : num  1996 1996 1997 1998 2008 ...
 $ age    : num  75.51 76 77 78 7.51 ...
 $ tfd    : num  0 0.49 1.49 2.49 0 ...
 $ lex.dur: num  0.49 1 1 0.59 0.493 ...
 $ lex.Cst: Factor w/ 2 levels "DM","Dead": 1 1 1 1 1 1 1 1 1 1 ...
 $ lex.Xst: Factor w/ 2 levels "DM","Dead": 1 1 1 2 1 1 1 1 1 1 ...
 - attr(*, "breaks")=List of 3
  ..$ per: NULL
  ..$ age: int [1:121] 0 1 2 3 4 5 6 7 8 9 ...
  ..$ tfd: NULL
 - attr(*, "time.scales")= chr [1:3] "per" "age" "tfd"
 - attr(*, "time.since")= chr [1:3] "" "" ""
```

3.2.2   Artificial prescription data

To explore how `addDrug.Lexis` works, we need drug exposure data, but these are unfortunately not available, so we simulate three datasets representing `pur`chases of three types of drugs:

```
> set.seed(1952)
> purA <-
+   ( data.frame(lex.id = rep(Lx$lex.id,
+                             round(runif(nrow(Lx), 0, 20)))))
+ %>% left_join(Lx[,c("lex.id", "dodm", "dox")])
+ %>% mutate(per = dodm + runif(length(dodm), -0.1, 0.99) * (dox - dodm),
+            amt = sample(4:20*10, length(dodm), replace = TRUE),
+            dpt = amt * round(runif(length(dodm), 3, 7)))
+ %>% select(-dodm, -dox)
+ %>% arrange(lex.id, per)
+   )
> addmargins(table(table(purA$lex.id)))
  1   2   3   4   5   6   7   8   9  10  11  12  13  14  15  16  17  18  19  20 Sum
 51  46  47  45  49  58  51  44  53  48  50  48  54  64  52  47  37  50  46  28 968
> str(purA)
'data.frame':        9942 obs. of  4 variables:
 $ lex.id: int  1 1 1 1 1 1 1 1 1 1 ...
 $ per   : num  1995 1996 1996 1996 1996 ...
 $ amt   : num  80 120 170 100 180 60 190 90 80 180 ...
 $ dpt   : num  400 720 1020 300 1080 360 950 360 560 1080 ...
> purB <-
+   ( data.frame(lex.id = rep(Lx$lex.id,
+                             round(pmax(runif(nrow(Lx), -10, 15), 0))))
+ %>% left_join(Lx[,c("lex.id", "dodm", "dox")])
+ %>% mutate(per = dodm + runif(length(dodm), -0.1, 0.99) * (dox - dodm),
+            amt = sample(4:20*10, length(dodm), replace = TRUE),
+            dpt = amt * round(runif(length(dodm), 5, 9)))
+ %>% select(-dodm, -dox)
+ %>% arrange(lex.id, per)
+   ) -> purB
> addmargins(table(table(purB$lex.id)))
  1   2   3   4   5   6   7   8   9  10  11  12  13  14  15 Sum
 54  37  31  36  45  30  44  31  32  37  45  48  31  48  17 566
```

```
> str(purB)

'data.frame':         4385 obs. of  4 variables:
 $ lex.id: int  1 4 4 4 4 4 4 4 4 4 ...
 $ per   : num  1997 2001 2001 2001 2002 ...
 $ amt   : num  150 80 190 90 100 40 100 190 80 150 ...
 $ dpt   : num  1050 480 950 720 600 320 500 1520 480 1050 ...
> purC <-
+   ( data.frame(lex.id = rep(Lx$lex.id,
+                             round(pmax(runif(nrow(Lx), -5, 12), 0))))
+ %>% left_join(Lx[,c("lex.id", "dodm", "dox")])
+ %>% mutate(per = dodm + runif(length(dodm), -0.1, 0.99) * (dox - dodm),
+            amt = sample(4:20*10, length(dodm), replace = TRUE),
+            dpt = amt * round(runif(length(dodm), 5, 7)))
+ %>% select(-dodm, -dox)
+ %>% arrange(lex.id, per)
+   )
> addmargins(table(table(purC$lex.id)))

  1   2   3   4   5   6   7   8   9  10  11  12 Sum
 63  68  52  55  48  59  48  47  56  46  72  27 641

> str(purC)

'data.frame':         3961 obs. of  4 variables:
 $ lex.id: int  1 1 1 1 1 1 4 4 4 4 ...
 $ per   : num  1996 1996 1998 1998 1998 ...
 $ amt   : num  60 50 60 90 130 40 140 150 180 140 ...
 $ dpt   : num  360 300 300 540 780 240 840 900 1080 980 ...
> head(purC)

  lex.id      per amt dpt
1      1 1995.663  60 360
2      1 1996.442  50 300
3      1 1997.673  60 300
4      1 1997.855  90 540
5      1 1998.321 130 780
6      1 1998.431  40 240
```

Note that the time scale is in years, so the `dpt` must be in amount per year, so that `dpt/amt` is the approximate number of annual drug purchases.

We now have three artificial drug purchase datasets so we can see how `addDrug.Lexis` performs on larger datasets:

3.2.3   Using `addDrug`

100 and 500 persons

We start out with a small sample and a three month grace period to limit the number of gaps:

```
> Sx1 <- subset(Sx, lex.id < 100)
> pur <- list(A = subset(purA, lex.id < 1000),
+             B = subset(purB, lex.id < 1000),
+             C = subset(purC, lex.id < 1000))
> system.time(ad1 <- addDrug.Lexis(Sx1, pur, tnam = "per", grace = 1/4))
```

```
Values of grace has been recycled across 3 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).
  bruger    system forløbet
    4.28      0.13      4.41
> summary(Sx1)
Transitions:
     To
From  DM Dead  Records:  Events: Risk time:  Persons:
   DM 644   23       667       23     572.58        99
> summary(ad1)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
   DM 3051   23      3074       23     572.58        99
```

We then cut the number of persons in half to assess how run time depends on no. of persons in the data:

```
> Sx2 <- subset(Sx, lex.id < 500)
> pur <- list(A = subset(purA, lex.id < 500),
+             B = subset(purB, lex.id < 500),
+             C = subset(purC, lex.id < 500))
> system.time(ad2 <- addDrug.Lexis(Sx2, pur, tnam = "per", grace = 1/6))
Values of grace has been recycled across 3 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).
  bruger    system forløbet
   13.87      0.53     14.38
> summary(Sx2)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
   DM 3026  119      3145      119    2657.01       499
> summary(ad2)
Transitions:
     To
From    DM Dead  Records:  Events: Risk time:  Persons:
   DM 14734  119     14853      119    2657.01       499
```

...timing is broadly proportional to the number of persons.

Fewer prescription records

We can try to cut the number of purchases in half:

```
> pur <- list(A = subset(purA, lex.id < 100 & runif(nrow(purA)) < 0.5),
+             B = subset(purB, lex.id < 100 & runif(nrow(purB)) < 0.5),
+             C = subset(purC, lex.id < 100 & runif(nrow(purC)) < 0.5))
> sapply(pur, nrow)
  A   B   C
543 301 155

> system.time(ad3 <- addDrug.Lexis(Sx1, pur, tnam = "per", grace = 1/6))
```

```
Values of grace has been recycled across 3 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).
  bruger    system forløbet
    1.53      0.05      1.56
> summary(Sx1)

Transitions:
     To
From  DM Dead  Records:  Events: Risk time:  Persons:
  DM 644   23       667       23    572.58        99

> summary(ad3)

Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 2027   23      2050       23    572.58        99
```

It also appears that the number of purchases per person is also a determinant of the run time too; the timing is largely proportional to the number of drug records.

In any concrete application it is recommended to run the function on a fairly small sample of persons, say 1000 to get a feel for the run time. It may also be a good idea to run the function on chunks of the persons, to make sure that you do not lose all the processed data in a crash.

Fewer prescription types

Finally we try to cut the number of drugs, to assess how this influences the run time:

```
> pur <- list(B = subset(purB, lex.id < 100),
+             C = subset(purC, lex.id < 100))
> sapply(pur, nrow)
  B   C
558 307

> system.time(ad4 <- addDrug.Lexis(Sx1, pur, tnam = "per", grace = 1/6))

Values of grace has been recycled across 2 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).
  bruger    system forløbet
    1.33      0.06      1.39
> summary(Sx1)

Transitions:
     To
From  DM Dead  Records:  Events: Risk time:  Persons:
  DM 644   23       667       23    572.58        99

> summary(ad4)

Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 1855   23      1878       23    572.58        99
```

We see that the number of drugs also influence the run time proportionally.

3.2.4   Too many records —`coarse.Lexis`

If we look at the length of the intervals as given in `lex.dur` we see that some are are quite small:

```
> summary(ad1$lex.dur)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.00000 0.03178 0.10877 0.18626 0.26397 1.00000
```

Half are smaller then 0.11 years, 40 days. We could without much loss of precision in the analysis based on the `Lexis` object merge adjacent records that have total risk time less than 3 months.

The function `coarse.Lexis` will collapse records with short `lex.dur` with the subsequent record. The collapsing will use the covariates from the first record, and so the entire follow-up from the two records will have the characteristics of the first. Therefore it is wise to choose first records with reasonably short `lex.dur`—the approximation will be better than if the first record was with a larger `lex.dur`. Therefore there are two values supplied to `coarse.Lexis`; the maximal length of the first record's `lex.dur` and the maximal length of the `lex.dur` in the resulting combined record. The larger these parameters are, the more the `Lexis` object is coarsened.

```
> summary(ad1)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 3051   23      3074       23    572.58        99

> summary(adc <- coarse.Lexis(ad1, lim = c(1/6,1/2)))
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 1593   23      1616       23    572.58        99

> summary(adc$lex.dur)
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
 0.0000  0.2060  0.3072  0.3543  0.4420  1.0000
```

This could cut the number of units for analysis substantially, in this case from about 27,000 to some 13,000.

Records to be kept

When we are dealing with drug exposure data we will be interested keeping the record that holds the start of a drug exposure. Some may argue that it does not matter much, though.

The records (*i.e.* beginnings of FU intervals) that should be kept must be given in logical vector in the argument `keep`:

```
> summary(Sx2)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 3026  119      3145      119   2657.01       499
```

```
> system.time(ad4 <- addDrug.Lexis(Sx2,
+                                    pur,
+                                    tnam = "per",
+                                    grace = 1/6))
Values of grace has been recycled across 2 drugs
NOTE: end of exposure based on differences in purchase times (per)
 and amount purchased (amt).
  bruger    system forløbet
    2.86      0.18      3.05
> summary(ad4)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 4237  119      4356      119    2657.01       499
> #
> ad5 <- coarse.Lexis(ad4,
+                     lim = c(1/4, 1/2))
> summary(ad5)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 3497  119      3616      119    2657.01       499
```

We can identify the first date of exposure to drug B, say, by the exposure (B.ex) being true and the cumulative time on the drug (B.ct) being 0:

```
> ad4$keep <- with(ad4, (B.ex & B.ct == 0) |
+                       (C.ex & C.ct == 0))
> ad6 <- coarse.Lexis(ad4,
+                     lim = c(1/4, 1/2),
+                     keep = ad4$keep)
> summary(ad6)
Transitions:
     To
From   DM Dead  Records:  Events: Risk time:  Persons:
  DM 3522  119      3641      119    2657.01       499
```

We see the expected behaviour when we use coarse.Lexis: we get fewer records, but identical follow-up. And the keep argument gives the possibility to keep selected records, or more precisely beginnings. keep prevents a record to be collapsed with a previous one, but not with a subsequent one.

```
  Start time: 2024-07-18, 15:26:06
    End time: 2024-07-18, 15:26:35
Elapsed time: 0.48 minutes
```

Bibliography

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

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