

CIMT study

Ultrasound and metabolic data

SDC / LLCh

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Chapter 1

Construction of data

In this chapter we construct the analysis dataset that we shall be using for analysis of the primary outcome and the the two secondary ones.

```
> library( Epi )
> library( foreign )
```

1.1 Baseline dataset

We first construct a baseline-dataset, `base`, with one record per person.

1.1.1 Randomization data

We first read the randomization codes for those actually randomized, and also devise a list with the names for the groups to be used for annotation:

```
> rnd <- read.csv2("./data/PTNR_MetforminCode_InsulinTypeCode.csv" )
> rnd <- transform( rnd, subjid = PTNR,
+                 grp = factor(MetforminCode,
+                             labels=c("Plc","Met")),
+                 igr = factor(InsulinTypeCode,
+                             levels=c(3,1,2),
+                             labels=c("Biph","AspD","Detm"))) )
> rnd <- rnd[,c("subjid","grp","igr")]
> str( rnd )
'data.frame':      412 obs. of  3 variables:
 $ subjid: int   70002 70001 70004 70005 70006 70007 70010 70008 70009 70011 ...
 $ grp   : Factor w/ 2 levels "Plc","Met": 2 2 1 1 1 1 1 2 1 1 ...
 $ igr   : Factor w/ 3 levels "Biph","AspD",...: 1 1 1 3 3 1 3 3 3 2 ...
> addmargins( with( rnd, table( Ins=igr, Met=grp ) ) )
      Met
Ins   Plc Met Sum
Biph  67  70 137
AspD  73  65 138
Detm  66  71 137
Sum   206 206 412
```

For graphing and annotation purposes we define long sensible names for the groups and color schemes for groups:

```
> gN <- c("Placebo+Insulin","Metformin+Insulin")
> iN <- c("Biphasic","Aspart+Detemir","Detemir")
> clr <- c("red","blue","orange","black")
> iclr <- c("limegreen","red","blue","black")
```



```

+                               "Abnormal lab.",
+                               "Non-compl",
+                               "Admin pr.",
+                               "Other") ) )[,c("subjid","xdate","xtype")]
> str( ud )
'data.frame':      105 obs. of  3 variables:
 $ subjid: int  70003 70005 70011 70021 70030 70036 70013 70038 70041 40001 ...
 $ xdate : Date, format: "2009-01-22" "2009-03-19" ...
 $ xtype : Factor w/ 7 levels "Adverse","Other dis.",...: 1 1 7 1 7 7 7 7 3 ...
> cbind( table( ud$xtype ) )
      [,1]
Adverse      19
Other dis.     6
Excl. crit.   7
Abnormal lab. 10
Non-compl     11
Admin pr.     1
Other         51

```

This information will be merged into the base dataset shortly.

1.1.4 Baseline variables

We now retrieve the baseline measurements from a SAS-file:

```

> base <- read.ssd("./data","baseline")
> names( base ) <- gsub( "_", ".", tolower( names(base) ) )

```

Then we recode and groom the dataset, specifically we create categorical variable for GAD, one for any value over 0, and one for the usual definition of GAD-positivity, as well as properly coded date variables:

```

> base <- transform( base, dob = cal.yr( as.Date( birthdat, origin="1960-01-01" ) ),
+                               dov = cal.yr( as.Date( visitdat, origin="1960-01-01" ) ),
+                               dodm = cal.yr( as.Date( diabetes, origin="1960-01-01" ) ),
+                               dor = cal.yr( as.Date( substr(as.character(randdate),1,10 ),
+                                                       format="%d-%m-%Y" ) ),
+                               caucas = 1-ethnicity,
+                               gad.0 = gad65.b1==0,
+                               gad.pos = gad65.b1 > 24,
+                               retin = factor( retinopa, levels=0:2,
+                                               labels=c("None","Simplex","Prolif") ),
+                               cvd = pmax( ami, heartsur, ihd, heartins, vascsurg, apopl, tci, amp,
+                                             0, na.rm=TRUE ) == 1,
+                               ras = pmax( acei, acei.thi, arb, arcomb, arb.ccb,
+                                             0, na.rm=TRUE ) == 1,
+                               oah = pmax( loop, ccb, bblock, thiazid, spiron, aht,
+                                             0, na.rm=TRUE ) == 1,
+                               oad = pmax( rosiglit, glp1, dpp4, repaglin, glucagon,
+                                             0, na.rm=TRUE ) == 1 )

```

Note that in this recoding, missing values (NA) for any of the components of cvd, ras, oah or oad are taken as negative, that is as *not* being present in the person.

Then we throw out variables not needed:

```

> base <- transform( base, aav = dov-dob,
+                               dmdurav = dov-dodm )
> ( skip <- match( c("metform2","insulint","above.si","prior.in","sdc","insulin",
+                  "ethnicity","retinopa","randdate",
+                  "ami","heartsur","ihd","heartins","vascsurg","apopl","tci","amp",
+                  "acei","acei.thi","arb","arcomb","arb.ccb",
+                  "loop","ccb","bblock","thiazid","spiron","aht",
+                  "rosiglit","glp1","dpp4","repaglin","glucagon"),
+                  names( base ) ) )

```

```

      [1] 106 107 109 110 111 60 5 8 108 11 12 13 14 17 15 16 18 67 101 69 70
     [22] 105 68 71 72 73 74 75 62 63 64 65 66
> base <- base[,-skip]

```

1.1.4.1 Merging with randomization and drop-out data

We merge in the randomization and stratification variables, using the `all.x=TRUE` to make sure that we only include patients actually randomized:

```

> intersect( names(base), names(rnd) )
      [1] "subjid"
> dim( base )
      [1] 464 92
> base <- merge( rnd, base, all.x=TRUE )
> base <- merge( base, ud, all.x=TRUE )
> dim( base )
      [1] 412 99

```

1.1.5 Hypoglycaemia and serious adverse event data

We read the data from the SAS-file:

```

> hypo <- read.ssd("./data","hypo")[,-c(2:3,11:13)]
> names( hypo ) <- gsub( "_", ".", tolower( names(hypo) ) )
> str( hypo )
'data.frame':      415 obs. of  12 variables:
 $ subjid  : num  91200 91204 91218 10003 10007 ...
 $ total.sa: num  NA 2 NA 0 0 0 0 0 0 0 ...
 $ any.sae.: num  NA 1 NA 0 0 0 0 0 0 0 ...
 $ allhypos: num  0 1 0 0 26 4 1 6 5 3 ...
 $ sum.klar: num  0 0 0 0 26 4 1 6 5 3 ...
 $ sevhypos: num  0 1 0 0 0 0 0 0 0 0 ...
 $ any.hypo: num  0 1 0 0 1 1 1 1 1 1 ...
 $ any.seve: num  0 1 0 0 0 0 0 0 0 0 ...
 $ nonsevhy: num  0 0 0 0 26 4 1 6 5 3 ...
 $ sae.sevh: num  0 3 0 0 0 0 0 0 0 0 ...
 $ any.sae2: num  0 1 0 0 0 0 0 0 0 0 ...
 $ any.nons: num  0 0 0 0 1 1 1 1 1 1 ...

```

Although there are not strictly baseline variables, these are variables with only one value per person, so we include them with the `base` data frame.

```

> intersect( names(base), names(hypo) )
      [1] "subjid"
> dim( base )
      [1] 412 99
> base <- merge( base, hypo, all.x=TRUE )
> dim( base )
      [1] 412 110

```

This concludes the construction of the `base` dataframe, however we also want to include an indicator of whether a person completed the study per protocol or not. This however depends on the follow-up data, so we wait with the saving of the base data set till the per protocol indicator has been derived.

1.2 Ultrasound data

Then we read the ultrasound data for *all* participants. Note that some of the numerical variables are with “.” as decimal separator, even if we have a file from a Danish locale. We also rescale `csc2` to readable units (`()`):

```
> imt <- read.csv2("./data/imt.csv")
> names( imt ) <- gsub( "cca_", "", names(imt) )
> names( imt ) <- gsub( "mean_", "", names(imt) )
> str( imt )

'data.frame':      1544 obs. of  20 variables:
 $ subjid      : int  10002 70032 10002 10002 91089 60001 60001 80010 91081 91118 ...
 $ visit       : Factor w/ 2 levels "1a","7a": 1 2 1 2 1 1 1 2 1 1 ...
 $ side        : Factor w/ 2 levels "L","R": 1 1 2 2 1 1 2 2 2 1 ...
 $ datescanned : Factor w/ 805 levels "2008/05/06 - 10:45:19",...: 24 726 24 320 177 8 8 569 ...
 $ fimtavg     : Factor w/ 85 levels "0.44","0.46",...: 56 38 39 31 43 40 31 14 64 61 ...
 $ fimtmin     : num  0.91 0.69 0.68 0.58 0.63 0.69 0.6 0.45 0.94 0.86 ...
 $ fimtmax     : num  1.14 0.94 1 0.93 1.08 0.99 0.97 0.71 1.28 1.23 ...
 $ minvesseldia : num  NA NA NA NA NA NA NA NA NA NA ...
 $ maxvesseldia : Factor w/ 368 levels "", "10", "10.03",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ vesselareal : num  NA NA NA NA NA NA NA NA NA NA ...
 $ lumenareal  : num  NA NA NA NA NA NA NA NA NA NA ...
 $ imtareal    : Factor w/ 1120 levels "", "10.27300798",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ systolicpressure : int  115 163 115 140 119 145 145 151 145 124 ...
 $ diastolicpressure : int  69 84 69 72 73 89 89 97 68 69 ...
 $ ddpct       : num  NA NA NA NA NA NA NA NA NA NA ...
 $ csdpct     : num  NA NA NA NA NA NA NA NA NA NA ...
 $ dc         : num  NA NA NA NA NA NA NA NA NA NA ...
 $ csc1       : num  NA NA NA NA NA NA NA NA NA NA ...
 $ csc2       : num  NA NA NA NA NA NA NA NA NA NA ...
 $ iem        : num  NA NA NA NA NA NA NA NA NA NA ...

> wdp <- c(5,9,12) # variables Where Decimal Point was used instead of comma
> names( imt )[wdp]

[1] "fimtavg"      "maxvesseldia" "imtareal"

> for( i in wdp ) imt[,i] <- as.numeric(as.character(imt[,i]))
> imt$dosc <- cal.yr( as.Date( substr(imt$datescanned,1,10) ) )
> imt$csc2 <- imt$csc2*1000
> levels( imt$visit ) <- c("v1","v7")
```

We now have records for all patients scanned, *including* some that were never randomized. The dataset has one observation for each laterality and per visit 1 and 7:

```
> subset( imt, subjid==10001 )

  subjid visit side      datescanned fimtavg fimtmin fimtmax minvesseldia
17  10001   v1   R 2008/09/22 - 11:42:06   0.80   0.54   1.00           NA
32  10001   v1   L 2008/09/22 - 11:42:06   0.85   0.65   0.96          10.86
33  10001   v7   L 2010/03/22 - 11:47:32   0.84   0.63   1.03          10.76
34  10001   v7   R 2010/03/22 - 11:47:32   0.88   0.71   1.03           NA
  maxvesseldia vesselareal lumenareal imtareal systolicpressure diastolicpressure ddpct
17           NA           NA           NA           NA           142                86           NA
32      11.46      103.1476    74.81514 28.33245           142                86      5.51
33      11.52      104.2305    76.04665 28.18386           124                73      7.05
34           NA           NA           NA           NA           124                73           NA
  csdpct      dc csc1 csc2      iem      dosc
17      NA      NA  NA  NA      NA 2008.724
32  11.33 0.0107 0.19 2.02 2680.31 2008.724
33  14.60 0.0149 0.26 2.86 1913.97 2010.219
34      NA      NA  NA  NA      NA 2010.219
```

1.2.1 Merging with randomization data

By merging with the randomization dataset using `all.x=TRUE`, we ensure that only those from the randomization set are included:

```
> dim( imt )
[1] 1544  21
> rimt <- merge( rnd, imt, all.x=TRUE )
> dim( rimt )
[1] 1498  26
> with( rimt, addmargins(table(table(subjid))) )
      1  2  3  4 Sum
5    60 15 332 412
```

Fishily enough there is one person with 4 observations in `imt` that is not randomized:

```
> tt <- with( imt, table( subjid ) )
> has4i <- names( tt[tt==4] )
> isrnd <- rnd$subjid
> setdiff( has4i, isrnd )
[1] "91218"
```

This person is not included in the dataset `rimt`, excluded by the `all.x=TRUE` clause.

1.2.2 Data check and reshape for ultrasound measurements

We can now check how the three different measurements of the IMT relate across persons — as seen from figure 1.1, they do not differ much:

```
> with( rimt, pairs( cbind( avg = fimtavg,
+                          min = fimtmin,
+                          max = fimtmax,
+                          mn = (fimtmin+fimtmax)/2 ),
+               gap=0, pch=16, cex=0.5, col=c("red","limegreen")[side],
+               xlim=c(0.3,1.5), ylim=c(0.3,1.5), las=1,
+               panel = function(x,y,...){points(x,y,...);abline(0,1)} ) )
```

Figure 1.1: *Pairwise comparison of far wall intima media thickness (`fimt`) as the average, min, max and the mean of min and max measurements. There are two points for each participant, one from left (red) and one from right side (green).*

We now take the average for left and right-sided measurements, but also merge in the left and right side measurements as separate variables:

```
> qvar <- 10:25 # Quantitative variables
> cvar <- c(1:7,9) # Classification variables
> names( rimt )[qvar]
      [1] "fimtavg"          "fimtmin"          "fimtmax"          "minvesseldia"
      [5] "maxvesseldia"        "vesselareal"      "lumenareal"       "imtareal"
      [9] "systolicpressure"    "diastolicpressure" "ddpct"            "csdpct"
     [13] "dc"                  "csc1"             "csc2"             "iem"
> names( rimt )[cvar]
      [1] "subjid"      "grp"            "igr"            "over.65"        "pre.ins"        "sdc"
      [7] "visit"       "datescanned"
```

```

> mimt <- aggregate( rimt[,qvar],
+                   rimt[,cvar],
+                   FUN=mean,
+                   na.rm=TRUE )
> lvar <- c(10:17,23:25) # Laterality variables
> ( lvar <- names( rimt )[lvar] )

      [1] "fimtavg"      "fimtmin"      "fimtmax"      "minvesseldia" "maxvesseldia"
      [6] "vesselareal"    "lumenareal"   "imtareal"     "csc1"          "csc2"
      [11] "iem"

> wimt <- reshape( rimt[,c("subjid","visit","side",lvar)],
+                 direction = "wide",
+                 v.names = lvar,
+                 timevar = "side",
+                 idvar = c("subjid","visit") )
> cbind( sort( names( wimt ) ) )

      [,1]
      [1,] "csc1.L"
      [2,] "csc1.R"
      [3,] "csc2.L"
      [4,] "csc2.R"
      [5,] "fimtavg.L"
      [6,] "fimtavg.R"
      [7,] "fimtmax.L"
      [8,] "fimtmax.R"
      [9,] "fimtmin.L"
     [10,] "fimtmin.R"
     [11,] "iem.L"
     [12,] "iem.R"
     [13,] "imtareal.L"
     [14,] "imtareal.R"
     [15,] "lumenareal.L"
     [16,] "lumenareal.R"
     [17,] "maxvesseldia.L"
     [18,] "maxvesseldia.R"
     [19,] "minvesseldia.L"
     [20,] "minvesseldia.R"
     [21,] "subjid"
     [22,] "vesselareal.L"
     [23,] "vesselareal.R"
     [24,] "visit"

> mimt <- merge( mimt, wimt, all.x=TRUE )
> subset( rimt, subjid==10001 )

      subjid grp igr over.65 pre.ins sdc visit side      datescanned fimtavg fimtmin
1  10001 Met Biph >65 noIns notSDC v1 R 2008/09/22 - 11:42:06 0.80 0.54
2  10001 Met Biph >65 noIns notSDC v7 L 2010/03/22 - 11:47:32 0.84 0.63
3  10001 Met Biph >65 noIns notSDC v1 L 2008/09/22 - 11:42:06 0.85 0.65
4  10001 Met Biph >65 noIns notSDC v7 R 2010/03/22 - 11:47:32 0.88 0.71
      fimtmax minvesseldia maxvesseldia vesselareal lumenareal imtareal systolicpressure
1  1.00 NA NA NA NA NA NA 142
2  1.03 10.76 11.52 104.2305 76.04665 28.18386 124
3  0.96 10.86 11.46 103.1476 74.81514 28.33245 142
4  1.03 NA NA NA NA NA NA 124
      diastolicpressure ddpct csdpct dc csc1 csc2 iem dosc
1 86 NA NA NA NA NA NA NA 2008.724
2 73 7.05 14.60 0.0149 0.26 2.86 1913.97 2010.219
3 86 5.51 11.33 0.0107 0.19 2.02 2680.31 2008.724
4 73 NA NA NA NA NA NA NA 2010.219

> subset( mimt, subjid==10001 )

      subjid visit grp igr over.65 pre.ins sdc      datescanned fimtavg fimtmin
1  10001 v1 Met Biph >65 noIns notSDC 2008/09/22 - 11:42:06 0.825 0.595
2  10001 v7 Met Biph >65 noIns notSDC 2010/03/22 - 11:47:32 0.860 0.670
      fimtmax minvesseldia maxvesseldia vesselareal lumenareal imtareal systolicpressure
1  0.98 10.86 11.46 103.1476 74.81514 28.33245 142

```

```

2    1.03      10.76      11.52    104.2305    76.04665 28.18386                124
  diastolicpressure ddpct csdpct      dc csc1 csc2      iem fimtavg.R fimtmin.R fimtmax.R
1          86 5.51 11.33 0.0107 0.19 2.02 2680.31      0.80      0.54      1.00
2          73 7.05 14.60 0.0149 0.26 2.86 1913.97      0.88      0.71      1.03
  minvesseldia.R maxvesseldia.R vesselareal.R lumenareal.R imtareal.R csc1.R csc2.R iem.R
1          NA          NA          NA          NA          NA          NA          NA          NA
2          NA          NA          NA          NA          NA          NA          NA          NA
  fimtavg.L fimtmin.L fimtmax.L minvesseldia.L maxvesseldia.L vesselareal.L lumenareal.L
1      0.85      0.65      0.96          10.86          11.46      103.1476      74.81514
2      0.84      0.63      1.03          10.76          11.52      104.2305      76.04665
  imtareal.L csc1.L csc2.L iem.L
1 28.33245 0.19 2.02 2680.31
2 28.18386 0.26 2.86 1913.97

```

The resulting data set has one observation per visit (v1 and v7) among the randomized patients:

```

> with( mimt, ftable(addmargins(table(Met=grp, Ins=igr, visit ))) )
      visit  v1  v7 Sum
Met Ins
Plc Biph      67  61 128
    AspD      73  66 139
    Detm      66  55 121
    Sum      206 182 388
Met Biph      70  65 135
    AspD      65  59 124
    Detm      71  65 136
    Sum      206 189 395
Sum Biph      137 126 263
    AspD      138 125 263
    Detm      137 120 257
    Sum      412 371 783

```

1.2.3 Plaques data

We now read the plaques data:

```

> pl <- read.csv2( "./data/plaquesprgebet.csv" )[, -5]
> names( pl ) [5] <- "n"
> levels( pl$visit ) <- c("v1", "v7")
> levels( pl$side ) <- c("L", "R")
> pl$tp <- interaction( pl$gebet, pl$side )
> str( pl )
'data.frame':
 1255 obs. of 6 variables:
 $ subjid: int 10001 10001 10001 10001 10001 10002 10002 10002 10002 10002 10004 ...
 $ visit : Factor w/ 2 levels "v1","v7": 1 1 1 1 1 1 1 1 1 1 ...
 $ gebet : Factor w/ 3 levels "BIF","CCA","ICA": 1 1 2 2 1 1 2 2 3 1 ...
 $ side : Factor w/ 2 levels "L","R": 1 2 1 2 1 2 1 2 1 1 ...
 $ n : int 1 1 1 1 5 5 1 1 5 2 ...
 $ tp : Factor w/ 6 levels "BIF.L","CCA.L",...: 1 4 2 5 1 4 2 5 3 1 ...

```

We then reshape the data to have only one observation per subject and visit:

```

> wpl <- reshape( pl[, -(3:4)],
+               direction = "wide",
+               v.names = "n",
+               timevar = "tp",
+               idvar = c("subjid", "visit") )
> names( wpl ) <- gsub( "n.", "", names( wpl ) )
> wpl$n.pl <- apply( wpl[, 3:8], 1, sum, na.rm=TRUE )
> str( wpl )

```

```
'data.frame':      587 obs. of  9 variables:
 $ subjid: int  10001 10002 10004 10006 10007 10009 10010 10012 10016 10017 ...
 $ visit : Factor w/ 2 levels "v1","v7": 1 1 1 1 1 1 1 1 1 1 ...
 $ BIF.L : int  1 5 2 1 2 1 1 1 1 1 ...
 $ BIF.R : int  1 5 1 2 2 1 1 NA 1 1 ...
 $ CCA.L : int  1 1 NA NA NA NA NA NA NA NA ...
 $ CCA.R : int  1 1 2 NA 1 NA NA NA NA NA ...
 $ ICA.L : int  NA 5 NA NA NA NA NA NA NA NA ...
 $ ICA.R : int  NA NA NA NA NA NA NA NA NA NA ...
 $ n.pl  : int  4 17 5 3 5 2 2 1 2 2 ...
 - attr(*, "reshapeWide")=List of 5
 ..$ v.names: chr "n"
 ..$ timevar: chr "tp"
 ..$ idvar  : chr "subjid" "visit"
 ..$ times  : Factor w/ 6 levels "BIF.L","CCA.L",...: 1 4 2 5 3 6
 ..$ varying: chr [1, 1:6] "n.BIF.L" "n.BIF.R" "n.CCA.L" "n.CCA.R" ...
```

The plaques data are now merged into the `mimt` dataset:

```
> intersect( names(wpl), names(mimt) )
 [1] "subjid" "visit"
> dim( mimt )
 [1] 783 46
> mimt <- merge( mimt, wpl, all.x=TRUE )
> dim( mimt )
 [1] 783 53
```

1.2.4 Saving ultrasound data

Finally, we write the data frame both in Rda format and as a SAS data-file with corresponding script:

```
> save( mimt, file="./data/mimt.Rda" )
> write.foreign( mimt,
+               datafile = "./sas/mimt.dat",
+               codefile = "./sas/mimt.sas",
+               package = "SAS" )
```

1.3 Follow-up variables

We then retrieve the glucose-related measurements in an expanded data frame which will contain data for each of 7 visits, and not only the first (`v1`) and the last (`v7`) as `mimt`.

We start by reading the SAS-file:

```
> outc <- read.ssd("./data","outcome")
> names( outc ) <- gsub( "_", ".", tolower( names(outc) ) )
> str( outc )
'data.frame':      2639 obs. of  26 variables:
 $ subjid : num  10001 10001 10001 10001 10001 ...
 $ visit  : num  1 2 3 4 5 6 7 1 2 3 ...
 $ weight : num  122 122 121 124 125 ...
 $ bmi    : num  33 33.1 32.8 33.7 34 ...
 $ whr    : num  1.1 1.04 1.08 1.07 1.07 ...
 $ hba1c  : num  7.9 7.1 6.3 5.9 6.1 6.8 6.3 7.6 7.5 6.9 ...
 $ gluc   : num  12.6 6.7 4.8 3.4 8.8 9.3 8.9 10.4 NA 9.9 ...
 $ ins    : num  60 NA NA NA NA NA 132 56 NA NA ...
```

```

$ insdose.: num 14 54 64 64 64 70 NA 14 38 40 ...
$ insdose2: num 0.115 0.442 0.53 0.515 0.51 ...
$ cpep      : num 1192 NA NA NA NA ...
$ chol      : num 4.4 NA 4 NA 5.1 NA 4 3.8 NA 4 ...
$ ldl       : num 2.3 NA 2.2 NA 3 NA 2.3 1.7 NA 2 ...
$ hdl       : num 1.3 NA 1.3 NA 1.4 NA 1.22 1.66 NA 1.6 ...
$ vldl      : num 0.8 NA 0.5 NA 0.7 NA 0.5 0.5 NA 0.4 ...
$ trig      : num 1.82 NA 1.1 NA 1.6 NA 1.03 1.03 NA 0.9 ...
$ sys       : num 149 136 136 132 137 ...
$ dia       : num 86 65.5 69.5 69 78.5 76 77.5 75.5 72.5 65 ...
$ pulse     : num 89 98 85 87 82 95 87 77 68 77 ...
$ b2dato    : num 17902 17902 17902 17902 17902 ...
$ b3dato    : num 17990 17990 17990 17990 17990 ...
$ b4dato    : num 18067 18067 18067 18067 18067 ...
$ b5dato    : num 18169 18169 18169 18169 18169 ...
$ b6dato    : num 18267 18267 18267 18267 18267 ...
$ visitdat  : num 17797 17797 17797 17797 17797 ...
$ visitda2  : num 18343 18343 18343 18343 18343 ...

```

First we get the visit-dates from the dataset:

```

> names( outc )
 [1] "subjid"  "visit"    "weight"   "bmi"      "whr"      "hba1c"    "gluc"
 [8] "ins"     "insdose." "insdose2" "cpep"     "chol"     "ldl"      "hdl"
[15] "vldl"    "trig"     "sys"      "dia"      "pulse"    "b2dato"   "b3dato"
[22] "b4dato"  "b5dato"   "b6dato"   "visitdat" "visitda2"

> vdates <- aggregate( outc[,c(25,20:24,26)], outc["subjid",drop=F], mean )
> names( vdates ) [2:8] <- paste("v",1:7,sep="")
> head( vdates )
  subjid  v1    v2    v3    v4    v5    v6    v7
1 10001 17797 17902 17990 18067 18169 18267 18343
2 10002 17798 17885 17982 18136 18164 18253 18347
3 10003 17806 17903    NA    NA    NA    NA 18051
4 10004 17820 17932 18009 18107 18191 18282 18366
5 10005 17848 17946 18037 18128 18219 18318 18394
6 10006 17874 17967 18059 18150 18241 18338 18422

> vdat <- reshape( vdates,
+                 direction = "long",
+                 varying = 2:8,
+                 v.names = "vdate",
+                 times = 1:7,
+                 timevar = "visit",
+                 idvar = "subjid" )
> vdat <- vdat[order(vdat$subjid,vdat$visit),]
> head( vdat )
      subjid visit vdate
10001.1 10001    1 17797
10001.2 10001    2 17902
10001.3 10001    3 17990
10001.4 10001    4 18067
10001.5 10001    5 18169
10001.6 10001    6 18267

> vdat <- transform( vdat, visit = factor(visit,labels=paste("v",1:7,sep="")),
+                  vdate = as.Date(vdate,origin="1960-01-01") )
> vdat$dov <- cal.yr( vdat$vdate )
> head( vdat, 8 )
      subjid visit    vdate    dov
10001.1 10001    v1 2008-09-22 2008.724
10001.2 10001    v2 2009-01-05 2009.012
10001.3 10001    v3 2009-04-03 2009.253
10001.4 10001    v4 2009-06-19 2009.463
10001.5 10001    v5 2009-09-29 2009.743
10001.6 10001    v6 2010-01-05 2010.011
10001.7 10001    v7 2010-03-22 2010.219
10002.1 10002    v1 2008-09-23 2008.727

```

We then remove the date variables from `outc` too, notably the stratification variables, that we will get from the `rnd` dataset, in order to make sure that the coding of these is consistent throughout; and we rename the insulin variables to something sensible, `idos` for (total) insulin dose and `ipkg` for insulin per kg:

```
> outc <- outc[,1:19]
> outc$visit <- factor( outc$visit, levels=1:7, labels=paste("v",1:7,sep="") )
> outc <- merge( outc, vdat )
> names( outc )[grep("insdose2",names(outc))] <- "ipkg"
> names( outc )[grep("insdose.",names(outc))] <- "idos"
> head( outc, 7 )
```

	subjid	visit	weight	bmi	whr	hba1c	gluc	ins	idos	ipkg	cpep	chol	ldl	hdl
1	10001	v1	121.7	33.01324	1.103448	7.9	12.6	60	14	0.1150370	1192	4.4	2.3	1.30
2	10001	v2	122.1	33.12174	1.042017	7.1	6.7	NA	54	0.4422604	NA	NA	NA	NA
3	10001	v3	120.8	32.76910	1.081545	6.3	4.8	NA	64	0.5298013	NA	4.0	2.2	1.30
4	10001	v4	124.2	33.69141	1.067797	5.9	3.4	NA	64	0.5152979	NA	NA	NA	NA
5	10001	v5	125.4	34.01693	1.075000	6.1	8.8	NA	64	0.5103668	NA	5.1	3.0	1.40
6	10001	v6	121.9	33.06749	1.081545	6.8	9.3	NA	70	0.5742412	NA	NA	NA	NA
7	10001	v7	124.2	33.69141	1.057851	6.3	8.9	132	NA	NA	1017	4.0	2.3	1.22

```

vldl trig sys dia pulse vdate dov
1 0.8 1.82 149.0 86.0 89 2008-09-22 2008.724
2 NA NA 135.5 65.5 98 2009-01-05 2009.012
3 0.5 1.10 135.5 69.5 85 2009-04-03 2009.253
4 NA NA 132.0 69.0 87 2009-06-19 2009.463
5 0.7 1.60 137.0 78.5 82 2009-09-29 2009.743
6 NA NA 125.0 76.0 95 2010-01-05 2010.011
7 0.5 1.03 148.0 77.5 87 2010-03-22 2010.219
```

1.3.1 Merging with randomization data

Then we merge with the randomization data set, so that we have the correct grouping of the patients:

```
> intersect( names(outc), names(rnd) )
[1] "subjid"
> dim( outc )
[1] 2587 21
> outc <- merge( rnd, outc, all.x=TRUE )
> dim( outc )
[1] 2587 26
```

1.3.2 Adding actual insulin doses during study

We read the dataset with the actually prescribed insulin doses

```
> ins <- read.ssd( "./data", "ins" )
> names( ins ) <- tolower( names(ins) )
> ins <- ins[,c(1,3,2,4:12)]
> ins$visit <- factor( ins$visit, levels=1:7, labels=paste("v",1:7,sep="") )
> names( ins ) <- gsub( "instype", "typ", names(ins) )
> names( ins ) <- gsub( "insdose", "dos", names(ins) )
> names( ins )[3:12] <- paste( substr( names(ins)[3:12], 1, 3 ),
+                             rep(c("mor","lch","din","bed","ext"),each=2),
+                             sep="." )
> for( i in grep("typ",names(ins)) )
+ {
+   ins[is.na(ins[,i]),i] <- 0
```

```

+   ins[,i] <- factor( ins[,i],
+                     levels = 0:3,
+                     labels = c("non","Bip","Asp","Det") )
+ }
> str( ins )
'data.frame':      2478 obs. of  12 variables:
 $ subjid : num  10001 10001 10001 10001 10001 10001 ...
 $ visit  : Factor w/ 7 levels "v1","v2","v3",...: 1 2 3 4 5 6 1 2 3 4 ...
 $ typ.mor: Factor w/ 4 levels "non","Bip","Asp",...: 1 2 2 2 2 2 1 2 2 2 ...
 $ dos.mor: num   NA 30 38 38 38 44 NA 18 20 20 ...
 $ typ.lch: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ dos.lch: num   NA NA NA NA NA NA NA NA NA NA ...
 $ typ.din: Factor w/ 4 levels "non","Bip","Asp",...: 2 2 2 2 2 2 2 2 2 2 ...
 $ dos.din: num  14 24 26 26 26 26 14 20 20 20 ...
 $ typ.bed: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ dos.bed: num   NA NA NA NA NA NA NA NA NA NA ...
 $ typ.ext: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ dos.ext: num   NA NA NA NA NA NA NA NA NA NA ...

```

Having read these data we merge them into the outcomes dataset:

```

> outc <- merge( outc, ins, all.x=TRUE )
> save( outc, file="./data/outc.Rda" )

```

1.4 Construction of total analysis data set

We will construct a dataset with all secondary outcomes, of which most are measured at all visits, but a few only at visits 1, 3, 5, and 7. The structure of the datasets will be with `subjid` and `visit` as key variables, that is with one record for each combination of these. There will be no records for visits where a person did not attend, and only persons randomized are included.

1.4.1 The intention to treat data

The intention to treat data is basically just the entire dataset with the relevant randomization as the primary explanatory variable.

How many persons with how many measurements, and what visits they attended:

```

> addmargins( with( outc, table( grp, visit ) ), 1 )
      visit
grp   v1 v2 v3 v4 v5 v6 v7
Plc 206 189 180 175 167 158 184
Met 206 194 191 187 183 177 190
Sum 412 383 371 362 350 335 374

> pattn <- data.frame( as.table( apply( with( outc, table( grp, subjid, visit ) ),
+                                     1:2, paste, collapse="-" ) ) )
> tpt <- addmargins( with( subset( pattn, Freq!="0-0-0-0-0-0-0" ),
+                         table( Visit.pattern=Freq, grp )[-1,] ) )
> cbind( tpt, round( 100*sweep(tpt,2,tpt["Sum",],"/"), 1 ) )
      Plc Met Sum   Plc   Met   Sum
1-0-0-0-0-0-0 13   8  21   6.3   3.9   5.1
1-0-0-0-0-0-1  4   4   8   1.9   1.9   1.9
1-1-0-0-0-0-0  5   3   8   2.4   1.5   1.9
1-1-0-0-0-0-1  4   0   4   1.9   0.0   1.0
1-1-1-0-0-0-0  1   1   2   0.5   0.5   0.5
1-1-1-0-0-0-1  4   3   7   1.9   1.5   1.7
1-1-1-1-0-0-1  8   4  12   3.9   1.9   2.9

```



```

1-1-1-1-1-0-0  2  2  4  1.0  1.0  1.0
1-1-1-1-1-0-1  7  4 11  3.4  1.9  2.7
1-1-1-1-1-1-0  1  2  3  0.5  1.0  0.7
1-1-1-1-1-1-1 157 175 332 76.2 85.0 80.6
Sum            206 206 412 100.0 100.0 100.0

```

1.4.2 The per protocol data

We also point out the patients with follow-up at least 3 visits (the per protocol analysis), that is the patients *not* in the 3 first lines of the above table, thus excluding 22 patients from the placebo group and 15 from the metformin group:

```

> vv <- with( outc, table(subjid) )
> base$pp <- base$subjid %in% names( vv[vv>2] )
> with( base, ftable( grp, igr, pp, col.vars=3 ) )
      pp FALSE TRUE
grp igr
Plc Biph      5  62
    AspD      5  68
    Detm     12  54
Met Biph      3  67
    AspD      5  60
    Detm      7  64

```

1.4.3 Saving the base data set

We save the long versions of the group names and the color scemes along the base data:

```

> save( base, gN, iN, clr, iclr, file="./data/base.Rda" )

```

1.4.4 Merging it all together

Finally we construct the total analysis data set, AD, to be used in all subsequent analyses.

```

> names(base)[85] <- "doV"
> intersect( names(outc), names(base) )
 [1] "subjid" "grp" "igr" "over.65" "pre.ins" "sdc"
> rbind( base=dim(base), outc=dim(outc) )
      [,1] [,2]
base  412  111
outc 2587   36
> AD <- merge( outc, base, all.x = TRUE )
> dim( AD )
 [1] 2587  141
> intersect( names(AD), names(mimt) )
 [1] "subjid" "grp" "igr" "over.65" "pre.ins" "sdc" "visit"
> AD <- merge( AD, mimt, all.x=TRUE )
> dim( AD )
 [1] 2587  187
> c( names( AD )[ 1:6 ],
+ sort( names( AD )[-(1:6)] ) )

```

[1]	"subjid"	"grp"	"igr"	"over.65"
[5]	"pre.ins"	"sdc"	"alcohol."	"alendr"
[9]	"allhypos"	"antibiot"	"antidep"	"any.hypo"
[13]	"any.nons"	"any.sae."	"any.sae2"	"any.seve"
[17]	"apurin"	"asa"	"auto.neu"	"avgnatu2"
[21]	"avgnatua"	"b1bdato"	"BIF.L"	"BIF.R"
[25]	"birthdat"	"bmi"	"bvit"	"bvit.iro"
[29]	"calc"	"caucas"	"CCA.L"	"CCA.R"
[33]	"chol"	"chol.b1a"	"chol.b7a"	"contrace"
[37]	"cpep"	"cpep.b1a"	"cpep.b7a"	"csc1"
[41]	"csc1.L"	"csc1.R"	"csc2"	"csc2.L"
[45]	"csc2.R"	"csdpct"	"cvd"	"datescanned"
[49]	"dc"	"ddpct"	"dia"	"dia1.b0"
[53]	"dia2.b0"	"diabetes"	"diastolicpressure"	"dmdurav"
[57]	"dob"	"dodm"	"dor"	"dos.bed"
[61]	"dos.din"	"dos.ext"	"dos.lch"	"dos.mor"
[65]	"dov"	"doV"	"dvit"	"dvit.cal"
[69]	"e.gfr"	"fibrat"	"fimtavg"	"fimtavg.L"
[73]	"fimtavg.R"	"fimtmax"	"fimtmax.L"	"fimtmax.R"
[77]	"fimtmin"	"fimtmin.L"	"fimtmin.R"	"fishoil"
[81]	"gaba"	"gad.0"	"gad.pos"	"gad65.b1"
[85]	"gastro"	"gluc"	"gluc.b1a"	"gluc.b7a"
[89]	"hba1c"	"hba1c.b1"	"hba1c.b7"	"hdl"
[93]	"hdlc.b1a"	"hdlc.b7a"	"height.2"	"height.b"
[97]	"hofte.b1"	"hofte.b7"	"ICA.L"	"ICA.R"
[101]	"idos"	"iem"	"iem.L"	"iem.R"
[105]	"impo"	"imtareal"	"imtareal.L"	"imtareal.R"
[109]	"ins"	"ins.b1a"	"ins.b7a"	"ipkg"
[113]	"iron"	"laserbeh"	"ldl"	"ldl.b1a"
[117]	"ldl.b7a"	"lipids"	"loop.ccb"	"lumenareal"
[121]	"lumenareal.L"	"lumenareal.R"	"lung"	"macroalb"
[125]	"maxvesseldia"	"maxvesseldia.L"	"maxvesseldia.R"	"metformi"
[129]	"microalb"	"minvesseldia"	"minvesseldia.L"	"minvesseldia.R"
[133]	"n.pl"	"nonsevhy"	"nsaid"	"ntg"
[137]	"oad"	"oah"	"other"	"othernat"
[141]	"painkill"	"peri.neu"	"plataggr"	"pp"
[145]	"pulse"	"pulse.b0"	"ras"	"retin"
[149]	"sae.sevh"	"sevhypos"	"sex"	"smoking."
[153]	"statin"	"su"	"sum.klar"	"sys"
[157]	"sys1.b0"	"sys2.b0"	"systolicpressure"	"talje.b1"
[161]	"talje.b7"	"thyre"	"total.sa"	"trig"
[165]	"trig.b1a"	"trig.b7a"	"typ.bed"	"typ.din"
[169]	"typ.ext"	"typ.lch"	"typ.mor"	"vdate"
[173]	"vesselareal"	"vesselareal.L"	"vesselareal.R"	"visit"
[177]	"visitdat"	"vldl"	"vldl.b1a"	"vldl.b7a"
[181]	"weight"	"weight.2"	"weight.b"	"whr"
[185]	"xdate"	"xtype"	"aav"	

```
> save( AD, gN, iN, clr, iclr, file="./data/AD.Rda" )
```

Chapter 2

Base tables for the study

2.1 Descriptive tables by Met / Plc

These descriptive tables are based on two datasets, `base` and `AD`.

```
> load( file="./data/AD.Rda" )
> load( file="./data/base.Rda" )
> addmargins( with( base, table(table(subjid)) ) )
  1 Sum
 412 412

> names( base )

 [1] "subjid"    "grp"      "igr"      "over.65"  "pre.ins"  "sdc"      "birthdat"
 [8] "visitdat" "sex"      "diabetes" "peri.neu" "auto.neu" "laserbeh" "sys1.b0"
[15] "dia1.b0"   "sys2.b0"  "dia2.b0"  "pulse.b0" "microalb" "macroalb" "e.gfr"
[22] "b1bdat0"  "smoking." "alcohol." "hba1c.b1" "hba1c.b7" "gluc.b1a" "gluc.b7a"
[29] "cpep.b1a" "cpep.b7a" "ins.b1a"  "ins.b7a"  "chol.b1a" "chol.b7a" "trig.b1a"
[36] "trig.b7a" "ldl.b1a"  "ldl.b7a"  "vldl.b1a" "vldl.b7a" "hdlc.b1a" "hdlc.b7a"
[43] "gad65.b1" "weight.b" "weight.2" "height.b" "height.2" "talje.b1" "talje.b7"
[50] "hofte.b1" "hofte.b7" "avgnatua" "avgnatu2" "metformi" "su"        "statin"
[57] "fibrat"   "lipids"   "asa"      "thyre"    "apurin"   "nsaid"    "painkill"
[64] "antidep"  "gaba"     "impo"     "ntg"      "gastro"   "contrace" "antibiot"
[71] "dvit"     "calc"     "alendr"   "bvit"     "lung"     "other"    "plataggr"
[78] "iron"     "fishoil"  "othernat" "loop.ccb" "dvit.cal" "bvit.iro" "dob"
[85] "dov"     "dodm"     "dor"      "caucas"   "gad.0"    "gad.pos"  "retin"
[92] "cvd"     "ras"      "oah"      "oad"      "aav"      "dmdurav"  "xdate"
[99] "xtype"   "total.sa" "any.sae." "allhypos" "sum.klar" "sevhypos" "any.hypo"
[106] "any.seve" "nonsevhy" "sae.sevh" "any.sae2" "any.nons" "pp"
```

2.1.1 Table 1

This is a table of patient characteristics at entry into the study on variables that are not measured (or of any particular interest) at follow-up. We now set up a table to hold the values in the baseline table, first defining what variables to use:

```
> base <- transform( base, s.ret = (retin=="Simplex"),
+                   p.ret = (retin=="Prolif"),
+                   ini.ins = pre.ins=="preIns" )
> bvars <- c( "aav",
+            "sex",
+            "smoking.",
+            "alcohol.",
+            "caucas",
+            "dmdurav",
```

```

+      "gad65.b1", "gad.0", "gad.pos",
+      "cvd",
+      "microalb", "macroalb", "avgnatua", "e.gfr",
+      "s.ret", "p.ret", "laserbeh", "auto.neu", "peri.neu",
+      "metformi", "ini.ins", "su", "oad", "ras", "oah", "statin", "asa" )
> bin <- rep( 1, length(bvars) )
> wh.cont <- c(1,4,6,7,13,14)
> bin[wh.cont] <- 0
> dec <- c(1,0,1,1,1,0)
> dig <- bin*0
> dig[bin==0] <- dec
> data.frame( bin, dig, bvars )
  bin dig  bvars
1   0  1   aav
2   1  0   sex
3   1  0 smoking.
4   0  0 alcohol.
5   1  0 caucas
6   0  1 dmdurav
7   0  1 gad65.b1
8   1  0   gad.0
9   1  0   gad.pos
10  1  0   cvd
11  1  0 microalb
12  1  0 macroalb
13  0  1 avgnatua
14  0  0   e.gfr
15  1  0   s.ret
16  1  0   p.ret
17  1  0 laserbeh
18  1  0 auto.neu
19  1  0 peri.neu
20  1  0 metformi
21  1  0 ini.ins
22  1  0    su
23  1  0   oad
24  1  0   ras
25  1  0   oah
26  1  0   statin
27  1  0    asa

```

Once we have defined the variables, which of them that are categorical and the number of digits after the decimal point to use for printing we can set up the array to hold the relevant numbers:

```

> QQ <- NArray( list( bvars,
+                    levels(base$grp),
+                    c( paste( c(2,1,3)/4), "mean", "sd" ) ) )
> str( QQ )
logi [1:27, 1:2, 1:5] NA NA NA NA NA NA ...
- attr(*, "dimnames")=List of 3
..$ : chr [1:27] "aav" "sex" "smoking." "alcohol." ...
..$ : chr [1:2] "Plc" "Met"
..$ : chr [1:5] "0.5" "0.25" "0.75" "mean" ...

> for( vv in 1:dim(QQ)[1] )
+ for( gg in dimnames(QQ)[[2]] )
+ {
+ if( bin[vv] == 0 )
+ QQ[vv,gg,] <- c( quantile( base[base$grp==gg,bvars[vv]],
+                          probs=c(2,1,3)/4, na.rm=TRUE ),
+                mean( base[base$grp==gg,bvars[vv]], na.rm=TRUE ),
+                sd( base[base$grp==gg,bvars[vv]], na.rm=TRUE ) )
+ else
+ QQ[vv,gg,1:2] <-

```

```
+ QQ[vv,gg,4:5] <- c( sum( base[base$grp==gg,bvars[vv]], na.rm=TRUE ),
+                   mean( base[base$grp==gg,bvars[vv]], na.rm=TRUE )*100 )
+ }
```

Then we print out the median and IQR from this array for the continuous variables and the number and percentage of the categorical ones:

```
> round( tt <- ftable( QQ[,1:3], col.vars=2:3), 3 )
      Plc      Met
      0.5    0.25  0.75  0.5    0.25  0.75
aav      62.479 54.119 66.287 62.449 55.699 66.632
sex     141.000 68.447   NA 140.000 67.961   NA
smoking. 27.000 13.171   NA 36.000 17.561   NA
alcohol.  1.000  0.000  5.250  2.000  0.000  6.000
caucas  201.000 97.573   NA 201.000 97.573   NA
dmdurav 11.209  7.366 15.341 12.537  8.747 17.985
gad65.b1 0.000  0.000  0.000  0.000  0.000  0.000
gad.0   174.000 84.466   NA 173.000 83.981   NA
gad.pos  11.000  5.340   NA 19.000  9.223   NA
cvd     55.000 26.699   NA 45.000 21.845   NA
microalb 40.000 19.802   NA 48.000 24.000   NA
macroalb  8.000  3.941   NA 12.000  6.000   NA
avgnatua 10.783  6.044 19.834 11.871  6.475 32.863
e.gfr   117.500 93.000 156.750 121.000 101.000 145.750
s.ret   63.000 31.188   NA 59.000 29.500   NA
p.ret   10.000  4.950   NA 15.000  7.500   NA
laserbeh 16.000  7.882   NA 21.000 10.345   NA
auto.neu 36.000 17.647   NA 33.000 16.098   NA
peri.neu 78.000 38.049   NA 76.000 37.073   NA
metformi 176.000 85.854   NA 167.000 81.068   NA
ini.ins 142.000 68.932   NA 143.000 69.417   NA
su      55.000 26.829   NA 61.000 29.612   NA
oad     27.000 13.107   NA 32.000 15.534   NA
ras    149.000 72.330   NA 159.000 77.184   NA
oah    111.000 53.883   NA 122.000 59.223   NA
statin  181.000 87.864   NA 170.000 82.524   NA
asa    119.000 57.767   NA 112.000 54.369   NA

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Plc ;      ; Met ;      \n",
+      "; Med ; IQR ; Med ; IQR \n",
+      "; N ;   % ; N ;   % \n",
+      file="./results/LLCh-Tab1.csv" )
> for( i in 1:nrow(tt) )
+ write.table( if( bin[i]==1 ) cbind( tt[i,1],
+                                   formatC( tt[i,2], format="f", dig=1 ),
+                                   tt[i,4],
+                                   formatC( tt[i,5], format="f", dig=1 ) )
+           else cbind( formatC( tt[i,1,drop=F], format="f", digits=dig[i] ),
+           paste( "(", formatC( tt[i,2,drop=F], format="f", digits=dig[i] ), " ",
+           formatC( tt[i,3,drop=F], format="f", digits=dig[i] ), " )" ),
+           formatC( tt[i,4,drop=F], format="f", digits=dig[i] ),
+           paste( "(", formatC( tt[i,5,drop=F], format="f", digits=dig[i] ), " ",
+           formatC( tt[i,6,drop=F], format="f", digits=dig[i] ), " )" ) ),
+           file="./results/LLCh-Tab1.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+           quote=F, sep=";", dec="," )
```

Then we print the table with mean and sd of the continuous baseline-variables:

```
> round( tt <- ftable( QQ[,4:5], col.vars=2:3), 2 )
      Plc      Met
      mean    sd  mean    sd
aav      60.31  9.13 60.95  8.67
```

```

sex      141.00  68.45 140.00  67.96
smoking. 27.00  13.17  36.00  17.56
alcohol.  4.20  12.46   4.76   7.35
caucas   201.00  97.57 201.00  97.57
dmdurav  12.23   6.52  13.53   6.22
gad65.b1 10.21  44.59   9.64  38.36
gad.0    174.00  84.47 173.00  83.98
gad.pos   11.00   5.34  19.00   9.22
cvd      55.00  26.70  45.00  21.84
microalb 40.00  19.80  48.00  24.00
macroalb  8.00   3.94  12.00   6.00
avgnatua 50.29 184.57  84.73 364.96
e.gfr    125.71  44.73 130.02  43.94
s.ret    63.00  31.19  59.00  29.50
p.ret    10.00   4.95  15.00   7.50
laserbeh 16.00   7.88  21.00  10.34
auto.neu 36.00  17.65  33.00  16.10
peri.neu 78.00  38.05  76.00  37.07
metformi 176.00  85.85 167.00  81.07
ini.ins  142.00  68.93 143.00  69.42
su       55.00  26.83  61.00  29.61
oad      27.00  13.11  32.00  15.53
ras     149.00  72.33 159.00  77.18
oah     111.00  53.88 122.00  59.22
statin  181.00  87.86 170.00  82.52
asa     119.00  57.77 112.00  54.37

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Plc ;      ; Met ;      \n",
+      "; Mean ; SD ; Mean ; SD \n",
+      "; N ; % ; N ; % \n",
+      file="./results/LLCh-Tab1m.csv" )
> for( i in 1:nrow(tt) )
+ write.table( if( bin[i]==1 ) cbind( tt[i,1],
+                                     formatC( tt[i,2], format="f", dig=1 ),
+                                     tt[i,3],
+                                     formatC( tt[i,4], format="f", dig=1 ) )
+           else formatC( tt[i,,drop=F], format="f", digits=dig[i] ),
+           file="./results/LLCh-Tab1m.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+           quote=F, sep=";", dec="," )
+

```

2.1.2 Table 2

We first retrieve the outcome data, and produce an overview of the number of records per visit and randomization group:

```

> load( file="./data/AD.Rda" )
> with( AD, addmargins( table( grp, visit ) ) )
      visit
grp   v1  v2  v3  v4  v5  v6  v7  Sum
Plc  206 189 180 175 167 158 184 1259
Met  206 194 191 187 183 177 190 1328
Sum  412 383 371 362 350 335 374 2587

> ftable( with( AD,
+             addmargins( table( grp, visit, hb7=hba1c<=7, useNA="ifany" ),
+                               3 ) ), col.vars=2 )
      visit v1 v2 v3 v4 v5 v6 v7
grp hb7
Plc FALSE 201 174 144 142 134 123 155
      TRUE   5 13 33 31 32 31 28
      NA    0  2  3  2  1  4  1

```

```

      Sum      206 189 180 175 167 158 184
Met FALSE      202 160 139 135 131 121 137
  TRUE         4  33  51  51  51  54  53
  NA           0   1   1   1   1   2   0
  Sum         206 194 191 187 183 177 190

> ftable( with( AD,
+           addmargins( table( pp, grp, visit, hb7=hba1c<=7, useNA="ifany" ),
+                             4 ) ), col.vars=3 )

```

	visit	v1	v2	v3	v4	v5	v6	v7
pp	grp	hb7						
FALSE	Plc	FALSE	20	4	0	0	0	3
		TRUE	2	0	0	0	0	1
		NA	0	1	0	0	0	0
		Sum	22	5	0	0	0	4
	Met	FALSE	14	2	0	0	0	4
		TRUE	1	0	0	0	0	0
		NA	0	1	0	0	0	0
		Sum	15	3	0	0	0	4
TRUE	Plc	FALSE	181	170	144	142	134	123
		TRUE	3	13	33	31	32	31
		NA	0	1	3	2	1	4
		Sum	184	184	180	175	167	158
	Met	FALSE	188	158	139	135	131	121
		TRUE	3	33	51	51	51	54
		NA	0	0	1	1	1	2
		Sum	191	191	191	187	183	177

```

>

```

Since we want to use the insulin dose at visit 6 to be used as the final insulin dose, and since insulin dose at visit 7 is always NA, we substitute insulin values from time 6 to time 7:

```

> wh <- match( c("idos","ipkg"), names(AD) )
> for( ii in unique(AD$subjid) )
+ if( all( dim(AD[AD$subjid==ii & AD$visit %in% c("v6","v7"),wh] )==c(2,2) ) )
+   AD[AD$subjid==ii & AD$visit == "v7",wh] <-
+   AD[AD$subjid==ii & AD$visit == "v6",wh]

```

The we define the variables we want to show at visit 1 and visit 7:

```

> vars <- c( "fimtavg",
+           "fimtmax",
+           "csc2",
+           "iem",
+           "imtareal",
+           "n.pl",
+           "weight",
+           "bmi",
+           "whr",
+           "hba1c",
+           "gluc",
+           "ins",
+           "cpep",
+           "idos",
+           "ipkg",
+           "sys",
+           "dia",
+           "pulse",
+           "chol",
+           "ldl",
+           "hdl",
+           "vldl",
+           "trig" )
> dig <- c(3,3,4,0,1,0,1,1,2,1,1,0,0,0,2,0,0,0,1,1,1,2,1)
> data.frame( vars, dig )

```

```

      vars dig
1  fimtavg  3
2  fimtmax  3
3   csc2   4
4   iem    0
5  imtareal 1
6   n.pl   0
7  weight  1
8   bmi    1
9   whr    2
10  hba1c  1
11  gluc   1
12  ins    0
13  cpep   0
14  idos   0
15  ipkg   2
16  sys    0
17  dia    0
18  pulse  0
19  chol   1
20  ldl    1
21  hdl    1
22  vldl   2
23  trig   1

> QQ <- NArray( list( vars,
+                   levels(AD$grp),
+                   levels(AD$visit),
+                   c( paste( c(2,1,3)/4), "mean", "sd" ) ) )
> str( QQ )

logi [1:23, 1:2, 1:7, 1:5] NA NA NA NA NA NA ...
- attr(*, "dimnames")=List of 4
..$ : chr [1:23] "fimtavg" "fimtmax" "csc2" "iem" ...
..$ : chr [1:2] "Plc" "Met"
..$ : chr [1:7] "v1" "v2" "v3" "v4" ...
..$ : chr [1:5] "0.5" "0.25" "0.75" "mean" ...

> for( vv in dimnames(QQ)[[1]] )
+ for( gg in dimnames(QQ)[[2]] )
+ for( tt in dimnames(QQ)[[3]] )
+ QQ[vv,gg,tt,] <- c( quantile( AD[AD$grp==gg & AD$visit==tt,vv],
+                             probs=c(2,1,3)/4, na.rm=TRUE ),
+                   mean( AD[AD$grp==gg & AD$visit==tt,vv], na.rm=TRUE ),
+                   sd( AD[AD$grp==gg & AD$visit==tt,vv], na.rm=TRUE ) )

```

Then we can print the median and IQR for these variables to a .csv-file:

```

> round( ftable( QQ[,,,1:3], col.vars=3 ), 3 )

```

			v1	v2	v3	v4	v5	v6	v7	
fimtavg	Plc	0.5	0.785	NA	NA	NA	NA	NA	0.758	
		0.25	0.700	NA	NA	NA	NA	NA	0.675	
		0.75	0.884	NA	NA	NA	NA	NA	0.865	
	Met	0.5	0.778	NA	NA	NA	NA	NA	0.780	
		0.25	0.691	NA	NA	NA	NA	NA	0.685	
		0.75	0.870	NA	NA	NA	NA	NA	0.875	
	fimtmax	Plc	0.5	0.950	NA	NA	NA	NA	NA	0.928
			0.25	0.855	NA	NA	NA	NA	NA	0.836
			0.75	1.045	NA	NA	NA	NA	NA	1.044
Met		0.5	0.942	NA	NA	NA	NA	NA	0.940	
		0.25	0.851	NA	NA	NA	NA	NA	0.835	
		0.75	1.035	NA	NA	NA	NA	NA	1.040	
csc2		Plc	0.5	2.473	NA	NA	NA	NA	NA	2.540
			0.25	1.865	NA	NA	NA	NA	NA	1.990
			0.75	3.196	NA	NA	NA	NA	NA	3.310
	Met	0.5	2.348	NA	NA	NA	NA	NA	2.393	

		0.25	1.771	NA	NA	NA	NA	NA	1.789
		0.75	3.015	NA	NA	NA	NA	NA	3.115
iem	Plc	0.5	2086.383	NA	NA	NA	NA	NA	2005.258
		0.25	1629.700	NA	NA	NA	NA	NA	1512.266
		0.75	2798.068	NA	NA	NA	NA	NA	2482.720
	Met	0.5	2190.363	NA	NA	NA	NA	NA	2131.930
		0.25	1722.326	NA	NA	NA	NA	NA	1575.994
		0.75	2871.215	NA	NA	NA	NA	NA	2847.847
imtareal	Plc	0.5	18.737	NA	NA	NA	NA	NA	18.227
		0.25	15.928	NA	NA	NA	NA	NA	15.646
		0.75	21.702	NA	NA	NA	NA	NA	21.169
	Met	0.5	18.409	NA	NA	NA	NA	NA	18.180
		0.25	15.403	NA	NA	NA	NA	NA	15.351
		0.75	21.797	NA	NA	NA	NA	NA	22.071
n.pl	Plc	0.5	3.000	NA	NA	NA	NA	NA	3.000
		0.25	2.000	NA	NA	NA	NA	NA	2.000
		0.75	5.000	NA	NA	NA	NA	NA	5.000
	Met	0.5	3.000	NA	NA	NA	NA	NA	3.000
		0.25	1.000	NA	NA	NA	NA	NA	2.000
		0.75	4.000	NA	NA	NA	NA	NA	5.000
weight	Plc	0.5	95.700	97.100	98.100	99.650	98.800	100.300	99.500
		0.25	86.525	87.800	88.600	89.450	89.700	89.800	90.050
		0.75	106.225	107.350	107.900	109.925	109.500	108.900	110.000
	Met	0.5	96.550	96.200	97.100	97.600	96.550	97.250	97.100
		0.25	86.100	86.600	86.600	86.425	87.000	87.325	86.925
		0.75	105.800	106.800	107.250	108.525	107.950	109.125	108.600
bmi	Plc	0.5	31.771	32.010	32.187	32.499	32.583	32.783	32.824
		0.25	29.129	29.383	29.712	30.058	29.971	29.931	30.188
		0.75	34.705	34.973	35.963	36.255	36.502	36.499	36.475
	Met	0.5	31.964	32.454	32.039	32.297	32.077	32.519	32.408
		0.25	29.389	29.152	29.298	29.295	29.005	29.100	29.024
		0.75	35.062	35.361	35.605	35.188	35.276	35.921	35.803
whr	Plc	0.5	1.009	1.000	1.009	1.009	1.009	1.009	1.018
		0.25	0.962	0.962	0.958	0.958	0.951	0.949	0.962
		0.75	1.057	1.047	1.059	1.057	1.049	1.059	1.062
	Met	0.5	1.000	1.000	1.000	0.998	1.000	1.000	1.000
		0.25	0.949	0.942	0.941	0.949	0.957	0.951	0.959
		0.75	1.051	1.054	1.051	1.055	1.059	1.056	1.059
hba1c	Plc	0.5	8.300	8.500	8.200	8.100	8.000	7.800	7.900
		0.25	7.725	7.800	7.200	7.300	7.200	7.300	7.250
		0.75	9.100	9.500	9.000	8.900	8.900	8.775	8.700
	Met	0.5	8.300	7.900	7.600	7.600	7.500	7.600	7.500
		0.25	7.800	7.300	7.000	7.000	7.000	6.900	7.000
		0.75	9.400	8.600	8.200	8.300	8.275	8.200	8.400
gluc	Plc	0.5	9.400	8.350	8.400	8.100	8.100	7.700	8.100
		0.25	7.900	6.625	6.800	6.300	6.500	6.400	6.400
		0.75	11.600	11.175	10.500	10.000	10.150	9.825	9.800
	Met	0.5	9.800	8.300	7.700	7.500	7.600	7.500	7.650
		0.25	7.900	6.700	6.500	5.775	6.400	6.200	6.500
		0.75	12.600	10.000	9.275	9.400	9.300	9.300	10.125
ins	Plc	0.5	72.500	NA	NA	NA	NA	NA	47.000
		0.25	44.000	NA	NA	NA	NA	NA	23.000
		0.75	127.500	NA	NA	NA	NA	NA	91.250
	Met	0.5	65.000	NA	NA	NA	NA	NA	45.000
		0.25	37.250	NA	NA	NA	NA	NA	19.500
		0.75	107.000	NA	NA	NA	NA	NA	81.500
cpep	Plc	0.5	861.000	NA	NA	NA	NA	NA	522.000
		0.25	484.500	NA	NA	NA	NA	NA	317.250
		0.75	1257.500	NA	NA	NA	NA	NA	858.500
	Met	0.5	746.000	NA	NA	NA	NA	NA	564.000
		0.25	451.250	NA	NA	NA	NA	NA	339.500
		0.75	1186.500	NA	NA	NA	NA	NA	869.500
idos	Plc	0.5	40.000	90.000	100.000	110.000	113.000	112.000	112.000
		0.25	20.000	60.000	68.000	70.000	68.000	64.000	64.000
		0.75	66.000	125.000	152.000	167.250	174.500	165.750	166.000
	Met	0.5	40.000	70.000	80.000	80.000	82.000	82.000	82.000

		0.25	22.000	44.000	50.000	48.000	50.000	51.000	51.000
		0.75	66.000	100.000	110.000	118.000	120.000	130.000	128.500
ipkg	Plc	0.5	0.415	0.915	1.001	1.087	1.114	1.097	1.098
		0.25	0.214	0.641	0.752	0.726	0.697	0.688	0.700
		0.75	0.662	1.234	1.493	1.627	1.585	1.596	1.606
	Met	0.5	0.427	0.708	0.798	0.807	0.824	0.832	0.831
		0.25	0.227	0.486	0.525	0.545	0.551	0.562	0.559
		0.75	0.656	1.027	1.124	1.146	1.174	1.261	1.251
sys	Plc	0.5	137.000	135.750	132.500	132.500	132.500	133.000	131.250
		0.25	128.000	125.625	123.250	122.875	125.000	123.000	122.375
		0.75	147.875	148.375	143.750	143.625	142.500	140.500	142.000
	Met	0.5	138.500	134.000	135.000	133.500	132.500	131.500	134.000
		0.25	129.500	122.500	125.250	124.000	124.000	124.375	124.250
		0.75	151.000	144.500	145.750	142.750	143.500	142.000	144.000
dia	Plc	0.5	82.000	82.000	80.000	80.500	81.000	80.000	78.500
		0.25	75.625	75.625	74.000	75.000	74.000	75.000	73.875
		0.75	86.875	87.500	86.250	86.625	85.375	85.750	85.625
	Met	0.5	82.500	79.500	80.500	81.000	79.000	79.000	78.500
		0.25	76.000	74.000	74.000	74.000	73.500	72.875	72.500
		0.75	88.500	85.000	86.000	86.500	85.000	86.000	85.000
pulse	Plc	0.5	77.000	75.000	73.000	74.000	72.000	72.000	73.000
		0.25	69.000	67.000	67.000	66.000	65.000	65.250	67.000
		0.75	83.000	82.000	81.000	81.000	80.000	79.000	80.000
	Met	0.5	75.000	75.000	75.000	75.000	75.000	73.000	74.000
		0.25	68.000	68.000	67.000	67.000	67.000	67.000	67.000
		0.75	83.000	83.000	82.000	81.000	82.000	81.000	84.000
chol	Plc	0.5	4.000	NA	4.200	NA	4.200	NA	4.100
		0.25	3.500	NA	3.700	NA	3.700	NA	3.650
		0.75	4.675	NA	4.700	NA	4.800	NA	4.800
	Met	0.5	4.100	NA	4.200	NA	4.100	NA	4.100
		0.25	3.500	NA	3.600	NA	3.600	NA	3.600
		0.75	4.700	NA	4.800	NA	4.800	NA	4.700
ldl	Plc	0.5	2.100	NA	2.200	NA	2.300	NA	2.300
		0.25	1.700	NA	1.800	NA	1.800	NA	1.800
		0.75	2.600	NA	2.700	NA	2.800	NA	2.750
	Met	0.5	2.050	NA	2.200	NA	2.100	NA	2.100
		0.25	1.500	NA	1.800	NA	1.600	NA	1.700
		0.75	2.600	NA	2.700	NA	2.575	NA	2.600
hdl	Plc	0.5	1.080	NA	1.100	NA	1.100	NA	1.100
		0.25	0.912	NA	0.950	NA	0.900	NA	0.915
		0.75	1.397	NA	1.433	NA	1.400	NA	1.385
	Met	0.5	1.085	NA	1.110	NA	1.115	NA	1.100
		0.25	0.930	NA	0.947	NA	0.942	NA	0.920
		0.75	1.350	NA	1.400	NA	1.400	NA	1.340
vldl	Plc	0.5	0.700	NA	0.600	NA	0.700	NA	0.600
		0.25	0.500	NA	0.500	NA	0.500	NA	0.500
		0.75	0.900	NA	0.900	NA	0.900	NA	0.900
	Met	0.5	0.800	NA	0.700	NA	0.800	NA	0.700
		0.25	0.500	NA	0.500	NA	0.500	NA	0.500
		0.75	1.000	NA	1.000	NA	1.000	NA	1.000
trig	Plc	0.5	1.485	NA	1.400	NA	1.480	NA	1.430
		0.25	1.100	NA	1.030	NA	1.042	NA	1.035
		0.75	2.072	NA	2.150	NA	2.002	NA	2.080
	Met	0.5	1.710	NA	1.550	NA	1.640	NA	1.630
		0.25	1.162	NA	1.200	NA	1.170	NA	1.190
		0.75	2.300	NA	2.198	NA	2.170	NA	2.345

> round(tt <- ftable(QQ[, ,c(1,7),1:3], col.vars=2:4), 3)

	Plc						Met			
	v1		v7				v1			v
	0.5	0.25	0.75	0.5	0.25	0.75	0.5	0.25	0.75	0
fimtavg	0.785	0.700	0.884	0.758	0.675	0.865	0.778	0.691	0.870	0.78
fimtmax	0.950	0.855	1.045	0.928	0.836	1.044	0.942	0.851	1.035	0.94
csc2	2.473	1.865	3.196	2.540	1.990	3.310	2.348	1.771	3.015	2.39
iem	2086.383	1629.700	2798.068	2005.258	1512.266	2482.720	2190.363	1722.326	2871.215	2131.93
imtareal	18.737	15.928	21.702	18.227	15.646	21.169	18.409	15.403	21.797	18.18

n.pl	3.000	2.000	5.000	3.000	2.000	5.000	3.000	1.000	4.000	3.000
weight	95.700	86.525	106.225	99.500	90.050	110.000	96.550	86.100	105.800	97.100
bmi	31.771	29.129	34.705	32.824	30.188	36.475	31.964	29.389	35.062	32.400
whr	1.009	0.962	1.057	1.018	0.962	1.062	1.000	0.949	1.051	1.000
hba1c	8.300	7.725	9.100	7.900	7.250	8.700	8.300	7.800	9.400	7.500
gluc	9.400	7.900	11.600	8.100	6.400	9.800	9.800	7.900	12.600	7.600
ins	72.500	44.000	127.500	47.000	23.000	91.250	65.000	37.250	107.000	45.000
cpep	861.000	484.500	1257.500	522.000	317.250	858.500	746.000	451.250	1186.500	564.000
idos	40.000	20.000	66.000	112.000	64.000	166.000	40.000	22.000	66.000	82.000
ipkg	0.415	0.214	0.662	1.098	0.700	1.606	0.427	0.227	0.656	0.830
sys	137.000	128.000	147.875	131.250	122.375	142.000	138.500	129.500	151.000	134.000
dia	82.000	75.625	86.875	78.500	73.875	85.625	82.500	76.000	88.500	78.500
pulse	77.000	69.000	83.000	73.000	67.000	80.000	75.000	68.000	83.000	74.000
chol	4.000	3.500	4.675	4.100	3.650	4.800	4.100	3.500	4.700	4.100
ldl	2.100	1.700	2.600	2.300	1.800	2.750	2.050	1.500	2.600	2.100
hdl	1.080	0.912	1.397	1.100	0.915	1.385	1.085	0.930	1.350	1.100
vldl	0.700	0.500	0.900	0.600	0.500	0.900	0.800	0.500	1.000	0.700
trig	1.485	1.100	2.072	1.430	1.035	2.080	1.710	1.162	2.300	1.630

```

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Plc ; ; ; Met ; ; ; \n",
+      "; V1 ; ; V7 ; ; V1 ; ; V7 ; \n",
+      "; Med ; IQR ; Med ; IQR ; Med ; IQR ; Med ; IQR \n",
+      file="./results/LLCh-Tab2.csv" )
> for( i in 1:nrow(tt) )
+ write.table(      cbind( formatC( tt[i,1,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,2,drop=F], format="f", digits=dig[i] ), ", ",
+       formatC( tt[i,3,drop=F], format="f", digits=dig[i] ), ")" ),
+       formatC( tt[i,4,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,5,drop=F], format="f", digits=dig[i] ), ", ",
+       formatC( tt[i,6,drop=F], format="f", digits=dig[i] ), ")" ),
+       formatC( tt[i,7,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,8,drop=F], format="f", digits=dig[i] ), ", ",
+       formatC( tt[i,9,drop=F], format="f", digits=dig[i] ), ")" ),
+       formatC( tt[i,10,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,11,drop=F], format="f", digits=dig[i] ), ", ",
+       formatC( tt[i,12,drop=F], format="f", digits=dig[i] ), ")" ),
+       file="./results/LLCh-Tab2.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+       quote=F, sep=";", dec="," )

```

Print the mean and the sd instead

```

> round( ftable( QQ[,,,4:5], col.vars=3 ), 3 )

```

		v1	v2	v3	v4	v5	v6	v7
fimtavg	Plc mean	0.799	NaN	NaN	NaN	NaN	NaN	0.785
	sd	0.139	NA	NA	NA	NA	NA	0.138
	Met mean	0.788	NaN	NaN	NaN	NaN	NaN	0.785
	sd	0.135	NA	NA	NA	NA	NA	0.136
fimtmax	Plc mean	0.959	NaN	NaN	NaN	NaN	NaN	0.944
	sd	0.156	NA	NA	NA	NA	NA	0.155
	Met mean	0.953	NaN	NaN	NaN	NaN	NaN	0.948
	sd	0.151	NA	NA	NA	NA	NA	0.159
csc2	Plc mean	2.606	NaN	NaN	NaN	NaN	NaN	2.698
	sd	1.000	NA	NA	NA	NA	NA	0.907
	Met mean	2.539	NaN	NaN	NaN	NaN	NaN	2.545
	sd	1.075	NA	NA	NA	NA	NA	1.031
iem	Plc mean	2307.172	NaN	NaN	NaN	NaN	NaN	2120.009
	sd	1079.673	NA	NA	NA	NA	NA	796.594
	Met mean	2386.637	NaN	NaN	NaN	NaN	NaN	2345.254
	sd	978.223	NA	NA	NA	NA	NA	1055.920
imtareal	Plc mean	19.377	NaN	NaN	NaN	NaN	NaN	18.939
	sd	4.794	NA	NA	NA	NA	NA	4.310
	Met mean	18.875	NaN	NaN	NaN	NaN	NaN	18.898
	sd	4.660	NA	NA	NA	NA	NA	4.609
n.pl	Plc mean	3.935	NaN	NaN	NaN	NaN	NaN	4.289

	sd	3.403	NA	NA	NA	NA	NA	3.838
	Met mean	3.353	NaN	NaN	NaN	NaN	NaN	3.987
	sd	2.981	NA	NA	NA	NA	NA	3.772
weight	Plc mean	97.149	98.460	99.821	100.798	100.688	100.755	101.405
	sd	14.749	15.140	15.888	16.187	15.987	15.920	16.315
	Met mean	97.183	97.262	97.868	98.017	98.007	98.070	98.387
	sd	15.242	15.352	15.992	16.271	16.525	16.644	16.865
bmi	Plc mean	32.061	32.389	32.762	33.069	33.092	33.108	33.341
	sd	4.189	4.264	4.462	4.610	4.630	4.755	4.743
	Met mean	32.258	32.437	32.596	32.568	32.573	32.651	32.679
	sd	4.230	4.340	4.547	4.457	4.576	4.553	4.649
whr	Plc mean	1.011	1.001	1.007	1.004	1.000	1.003	1.013
	sd	0.082	0.074	0.079	0.077	0.079	0.081	0.078
	Met mean	0.996	0.998	0.998	0.997	1.004	1.001	1.007
	sd	0.080	0.083	0.082	0.079	0.079	0.078	0.081
hba1c	Plc mean	8.492	8.719	8.214	8.168	8.138	7.999	8.086
	sd	0.999	1.293	1.160	1.172	1.177	1.075	1.180
	Met mean	8.608	8.031	7.728	7.717	7.727	7.671	7.829
	sd	1.101	1.069	1.080	0.994	1.035	0.974	1.185
gluc	Plc mean	10.081	8.918	8.858	8.490	8.683	8.246	8.368
	sd	3.249	3.228	2.864	3.065	3.425	3.042	2.936
	Met mean	10.513	8.524	8.033	7.922	7.978	8.077	8.369
	sd	3.254	2.669	2.613	3.013	2.591	3.105	2.964
ins	Plc mean	103.225	NaN	NaN	NaN	NaN	NaN	69.086
	sd	103.211	NA	NA	NA	NA	NA	73.710
	Met mean	83.466	NaN	NaN	NaN	NaN	NaN	80.799
	sd	70.282	NA	NA	NA	NA	NA	284.162
cpep	Plc mean	916.718	NaN	NaN	NaN	NaN	NaN	642.846
	sd	565.616	NA	NA	NA	NA	NA	436.037
	Met mean	849.806	NaN	NaN	NaN	NaN	NaN	639.620
	sd	555.119	NA	NA	NA	NA	NA	450.410
idos	Plc mean	47.356	103.674	120.576	128.080	128.976	129.228	129.936
	sd	30.321	62.456	77.196	80.758	81.053	86.252	86.066
	Met mean	48.712	81.503	91.453	95.011	96.071	98.989	98.552
	sd	36.452	51.627	59.507	63.031	63.205	68.190	68.273
ipkg	Plc mean	0.481	1.035	1.190	1.251	1.249	1.247	1.254
	sd	0.291	0.589	0.702	0.726	0.742	0.775	0.774
	Met mean	0.497	0.827	0.918	0.948	0.963	0.990	0.987
	sd	0.346	0.482	0.541	0.578	0.581	0.612	0.613
sys	Plc mean	138.173	136.901	133.913	134.073	133.590	132.706	132.348
	sd	15.465	15.773	15.142	16.131	13.883	13.385	14.922
	Met mean	140.517	134.824	136.537	135.091	134.099	134.142	134.851
	sd	15.138	16.147	15.637	15.430	15.146	14.882	16.385
dia	Plc mean	81.953	81.790	80.313	80.532	80.012	80.090	79.327
	sd	9.192	9.070	8.759	8.258	8.659	8.684	8.929
	Met mean	82.234	79.756	80.490	80.199	78.995	79.179	78.517
	sd	9.386	9.312	9.914	9.848	9.212	10.155	9.270
pulse	Plc mean	76.734	74.692	73.942	74.300	72.594	72.591	73.554
	sd	11.760	12.250	11.578	12.307	10.979	10.938	12.384
	Met mean	75.927	75.437	74.805	75.263	74.811	74.377	75.485
	sd	11.996	11.809	11.457	12.974	11.950	12.374	12.817
chol	Plc mean	4.121	NaN	4.264	NaN	4.275	NaN	4.279
	sd	0.905	NA	0.950	NA	0.886	NA	0.941
	Met mean	4.208	NaN	4.291	NaN	4.202	NaN	4.271
	sd	0.979	NA	0.943	NA	0.875	NA	0.928
ldl	Plc mean	2.167	NaN	2.328	NaN	2.333	NaN	2.358
	sd	0.799	NA	0.855	NA	0.800	NA	0.840
	Met mean	2.168	NaN	2.276	NaN	2.137	NaN	2.207
	sd	0.824	NA	0.825	NA	0.707	NA	0.728
hdl	Plc mean	1.166	NaN	1.212	NaN	1.190	NaN	1.162
	sd	0.350	NA	0.361	NA	0.379	NA	0.326
	Met mean	1.164	NaN	1.200	NaN	1.220	NaN	1.166
	sd	0.334	NA	0.346	NA	0.400	NA	0.330
vldl	Plc mean	0.762	NaN	0.735	NaN	0.718	NaN	0.738
	sd	0.373	NA	0.343	NA	0.350	NA	0.366
	Met mean	0.821	NaN	0.776	NaN	0.858	NaN	0.817

```

      sd      0.404      NA      0.343      NA      0.637      NA      0.399
trig  Plc mean  1.771      NaN      1.639      NaN      1.736      NaN      1.677
      sd      1.112      NA      0.769      NA      1.169      NA      0.973
      Met mean  1.991      NaN      1.864      NaN      1.956      NaN      1.989
      sd      1.266      NA      1.274      NA      1.558      NA      1.312

> round( ( tt <- ftable( QQ[,c(1,7),4:5], col.vars=2:4) ), 3 )

      Plc          Met
      v1          v1
      mean      sd  mean      sd  mean      sd  mean      sd

fimtavg  0.799  0.139  0.785  0.138  0.788  0.135  0.785  0.136
fimtmax  0.959  0.156  0.944  0.155  0.953  0.151  0.948  0.159
csc2     2.606  1.000  2.698  0.907  2.539  1.075  2.545  1.031
iem      2307.172 1079.673 2120.009 796.594 2386.637 978.223 2345.254 1055.920
imtareal 19.377  4.794  18.939  4.310  18.875  4.660  18.898  4.609
n.pl     3.935  3.403  4.289  3.838  3.353  2.981  3.987  3.772
weight   97.149 14.749 101.405 16.315  97.183 15.242  98.387 16.865
bmi      32.061 4.189  33.341  4.743  32.258  4.230  32.679  4.649
whr      1.011 0.082  1.013  0.078  0.996  0.080  1.007  0.081
hba1c    8.492 0.999  8.086  1.180  8.608  1.101  7.829  1.185
gluc     10.081 3.249  8.368  2.936  10.513  3.254  8.369  2.964
ins      103.225 103.211 69.086  73.710  83.466  70.282  80.799 284.162
cpep     916.718 565.616 642.846 436.037 849.806 555.119 639.620 450.410
idos     47.356 30.321 129.936 86.066  48.712 36.452  98.552 68.273
ipkg     0.481 0.291  1.254  0.774  0.497  0.346  0.987  0.613
sys      138.173 15.465 132.348 14.922 140.517 15.138 134.851 16.385
dia      81.953  9.192  79.327  8.929  82.234  9.386  78.517  9.270
pulse    76.734 11.760  73.554 12.384  75.927 11.996  75.485 12.817
chol     4.121 0.905  4.279  0.941  4.208  0.979  4.271  0.928
ldl      2.167 0.799  2.358  0.840  2.168  0.824  2.207  0.728
hdl      1.166 0.350  1.162  0.326  1.164  0.334  1.166  0.330
vldl     0.762 0.373  0.738  0.366  0.821  0.404  0.817  0.399
trig     1.771 1.112  1.677  0.973  1.991  1.266  1.989  1.312

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Plc ; ; ; Met ; ; ; \n",
+      "; V1 ; ; V7 ; ; V1 ; ; V7 ; \n",
+      "; Mean ; SD ; Mean ; SD ; Mean ; SD ; Mean ; SD \n",
+      file="./results/LLCh-Tab2m.csv" )
> for( i in 1:nrow(tt) )
+ write.table( formatC( tt[i,,drop=F], format="f", digits=dig[i] ),
+             file="./results/LLCh-Tab2m.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+             quote=F, sep=";", dec="," )

```

2.2 Descriptive tables by insulin regimen

2.2.1 Table 1

This is a table of patient characteristics at entry into the study on variables that are not measured (or of any particular interest) at follow-up. We now set up a table to hold the values in the baseline table, first defining what variables to use:

```

> base <- transform( base, s.ret = (retin=="Simplex"),
+                   p.ret = (retin=="Prolif"),
+                   ini.ins = pre.ins=="preIns" )
> bvars <- c( "aav",
+            "sex",
+            "smoking.",
+            "alcohol.",
+            "caucas",
+            "dmdurav",

```

```

+      "gad65.b1", "gad.0", "gad.pos",
+      "cvd",
+      "microalb", "macroalb", "avgnatua", "e.gfr",
+      "s.ret", "p.ret", "laserbeh", "auto.neu", "peri.neu",
+      "metformi", "ini.ins", "su", "oad", "ras", "oah", "statin", "asa" )
> bin <- rep( 1, length(bvars) )
> wh.cont <- c(1,4,6,7,13,14)
> bin[wh.cont] <- 0
> dec <- c(1,0,1,1,1,0)
> dig <- bin*0
> dig[bin==0] <- dec
> data.frame( bin, dig, bvars )
  bin dig  bvars
1   0  1   aav
2   1  0   sex
3   1  0 smoking.
4   0  0 alcohol.
5   1  0  caucas
6   0  1 dmdurav
7   0  1 gad65.b1
8   1  0   gad.0
9   1  0  gad.pos
10  1  0   cvd
11  1  0 microalb
12  1  0 macroalb
13  0  1 avgnatua
14  0  0   e.gfr
15  1  0   s.ret
16  1  0   p.ret
17  1  0 laserbeh
18  1  0 auto.neu
19  1  0 peri.neu
20  1  0 metformi
21  1  0 ini.ins
22  1  0    su
23  1  0   oad
24  1  0   ras
25  1  0   oah
26  1  0  statin
27  1  0   asa

```

Once we have defined the variables, which of them that are categorical and the number of digits after the decimal point to use for printing we can set up the array to hold the relevant numbers:

```

> QQ <- NArray( list( bvars,
+                    levels(base$igr),
+                    c( paste( c(2,1,3)/4), "mean", "sd" ) ) )
> str( QQ )
logi [1:27, 1:3, 1:5] NA NA NA NA NA NA ...
- attr(*, "dimnames")=List of 3
..$ : chr [1:27] "aav" "sex" "smoking." "alcohol." ...
..$ : chr [1:3] "AspD" "Detm" "Biph"
..$ : chr [1:5] "0.5" "0.25" "0.75" "mean" ...

> for( vv in 1:dim(QQ)[1] )
+ for( gg in dimnames(QQ)[[2]] )
+ {
+ if( bin[vv] == 0 )
+ QQ[vv,gg,] <- c( quantile( base[base$igr==gg,bvars[vv]],
+                          probs=c(2,1,3)/4, na.rm=TRUE ),
+                mean( base[base$igr==gg,bvars[vv]], na.rm=TRUE ),
+                sd( base[base$igr==gg,bvars[vv]], na.rm=TRUE ) )
+ else
+ QQ[vv,gg,1:2] <-

```

```
+ QQ[vv,gg,4:5] <- c( sum( base[base$igr==gg,bvars[vv]], na.rm=TRUE ),
+                   mean( base[base$igr==gg,bvars[vv]], na.rm=TRUE )*100 )
+ }
```

Then we print out the median and IQR from this array for the continuous variables and the number and percentage of the categorical ones:

```
> round( tt <- ftable( QQ[, ,1:3], col.vars=2:3), 3 )
      AspD      Detm      Biph
      0.5    0.25    0.75    0.5    0.25    0.75    0.5    0.25    0.75
aav      62.263  54.294  66.446  62.650  56.413  66.081  62.779  55.195  66.856
sex      96.000  69.565      NA  95.000  69.343      NA  90.000  65.693      NA
smoking. 19.000  13.768      NA  17.000  12.593      NA  27.000  19.708      NA
alcohol.  2.000   0.000   5.000   2.000   0.000   6.000   2.000   0.000   5.000
caucas  133.000  96.377      NA 136.000  99.270      NA 133.000  97.080      NA
dmdurav 12.056   8.038  16.958  11.933   8.197  17.220  11.335   8.238  16.780
gad65.b1 0.000   0.000   0.000   0.000   0.000   0.000   0.000   0.000   0.000
gad.0   116.000  84.058      NA 116.000  84.672      NA 115.000  83.942      NA
gad.pos  9.000   6.522      NA  11.000   8.029      NA  10.000   7.299      NA
cvd     29.000  21.014      NA  36.000  26.277      NA  35.000  25.547      NA
microalb 23.000  17.037      NA  30.000  22.222      NA  35.000  26.515      NA
macroalb 8.000   5.926      NA   7.000   5.185      NA   5.000   3.759      NA
avgnatua 9.911   5.433  17.815  13.052   7.018  31.440  12.017   5.880  25.270
e.gfr   121.500  98.250 156.250 117.000  91.000 144.000 119.000  99.000 151.000
s.ret   42.000  31.343      NA  42.000  31.343      NA  38.000  28.358      NA
p.ret    6.000   4.478      NA   9.000   6.716      NA  10.000   7.463      NA
laserbeh 7.000   5.072      NA  14.000  10.526      NA  16.000  11.852      NA
auto.neu 22.000  16.058      NA  24.000  17.647      NA  23.000  16.912      NA
peri.neu 46.000  33.577      NA  60.000  44.118      NA  48.000  35.036      NA
metformi 114.000  82.609      NA 118.000  86.765      NA 111.000  81.022      NA
ini.ins  96.000  69.565      NA  95.000  69.343      NA  94.000  68.613      NA
su      40.000  28.986      NA  37.000  27.206      NA  39.000  28.467      NA
oad     17.000  12.319      NA  25.000  18.248      NA  17.000  12.409      NA
ras     102.000  73.913      NA 100.000  72.993      NA 106.000  77.372      NA
oah     73.000  52.899      NA  81.000  59.124      NA  79.000  57.664      NA
statin  116.000  84.058      NA 119.000  86.861      NA 116.000  84.672      NA
asa     79.000  57.246      NA  72.000  52.555      NA  80.000  58.394      NA

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Asp+Det ;      ; Detemir ;      ; Biphasic ;      \n",
+      "; Med ; IQR ; Med ; IQR ; Med ; IQR \n",
+      "; N ; % ; N ; % ; N ; % \n",
+      file="./results/LLCh-Tabli.csv" )
> for( i in 1:nrow(tt) )
+ write.table( if( bin[i]==1 ) cbind( tt[i,1],
+                                   formatC( tt[i,2], format="f", dig=1 ),
+                                   tt[i,4],
+                                   formatC( tt[i,5], format="f", dig=1 ) )
+ else cbind( formatC( tt[i,1,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,2,drop=F], format="f", digits=dig[i] ), " ",
+         formatC( tt[i,3,drop=F], format="f", digits=dig[i] ), " )" ),
+         formatC( tt[i,4,drop=F], format="f", digits=dig[i] ),
+ paste( "(", formatC( tt[i,5,drop=F], format="f", digits=dig[i] ), " ",
+         formatC( tt[i,6,drop=F], format="f", digits=dig[i] ), " )" ) ),
+ file="./results/LLCh-Tabli.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+ quote=F, sep=";", dec="," )
```

Then we print the table with mean and sd of the continuous baseline-variables:

```
> round( tt <- ftable( QQ[, ,4:5], col.vars=2:3), 2 )
      AspD      Detm      Biph
      mean    sd  mean    sd  mean    sd
aav      60.23  9.32  60.52  8.85  61.14  8.55
```



```

sex          96.00 69.57 95.00 69.34 90.00 65.69
smoking.    19.00 13.77 17.00 12.59 27.00 19.71
alcohol.    3.74 14.11 4.98 8.04 4.75 6.99
caucas      133.00 96.38 136.00 99.27 133.00 97.08
dmdurav     12.90 6.51 12.85 6.23 12.90 6.49
gad65.b1    9.00 40.01 9.89 39.50 10.89 45.17
gad.0       116.00 84.06 116.00 84.67 115.00 83.94
gad.pos     9.00 6.52 11.00 8.03 10.00 7.30
cvd         29.00 21.01 36.00 26.28 35.00 25.55
microalb    23.00 17.04 30.00 22.22 35.00 26.52
macroalb    8.00 5.93 7.00 5.19 5.00 3.76
avgnatua    47.65 188.45 85.08 426.94 69.02 176.85
e.gfr       130.76 45.02 123.86 43.07 128.94 44.93
s.ret       42.00 31.34 42.00 31.34 38.00 28.36
p.ret       6.00 4.48 9.00 6.72 10.00 7.46
laserbeh    7.00 5.07 14.00 10.53 16.00 11.85
auto.neu    22.00 16.06 24.00 17.65 23.00 16.91
peri.neu    46.00 33.58 60.00 44.12 48.00 35.04
metformi    114.00 82.61 118.00 86.76 111.00 81.02
ini.ins     96.00 69.57 95.00 69.34 94.00 68.61
su          40.00 28.99 37.00 27.21 39.00 28.47
oad         17.00 12.32 25.00 18.25 17.00 12.41
ras         102.00 73.91 100.00 72.99 106.00 77.37
oah         73.00 52.90 81.00 59.12 79.00 57.66
statin      116.00 84.06 119.00 86.86 116.00 84.67
asa         79.00 57.25 72.00 52.55 80.00 58.39

```

```

> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Asp+Det ;      ; Detemir ;      ; Biphasic ;      \n",
+      "; Mean ; SD ; Mean ; SD \n",
+      "; N ; % ; N ; % ; N ; % \n",
+      file="./results/LLCh-Tab1mi.csv" )
> for( i in 1:nrow(tt) )
+ write.table( if( bin[i]==1 ) cbind( tt[i,1],
+                                     formatC( tt[i,2], format="f", dig=1 ),
+                                     tt[i,3],
+                                     formatC( tt[i,4], format="f", dig=1 ) )
+           else formatC( tt[i,,drop=F], format="f", digits=dig[i] ),
+           file="./results/LLCh-Tab1mi.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+           quote=F, sep=";", dec="," )
+

```

2.2.2 Table 2

We first retrieve the outcome data, and produce an overview of the number of records per visit and randomization group:

```

> load( file="./data/AD.Rda" )
> with( AD, addmargins( table( igr, visit ) ) )
      visit
igr   v1  v2  v3  v4  v5  v6  v7 Sum
AspD 138 130 126 120 116 109 127 866
Detm 137 122 117 114 107 103 120 820
Biph 137 131 128 128 127 123 127 901
Sum  412 383 371 362 350 335 374 2587

> ftable( with( AD,
+             addmargins( table( igr, visit, hb7=hba1c<=7, useNA="ifany" ),
+                               3 ) ), col.vars=2 )
      visit v1 v2 v3 v4 v5 v6 v7
igr hb7
AspD FALSE 136 104 93 85 77 74 96
      TRUE 2 24 32 34 38 33 31

```


	NA	0	2	1	1	1	2	0
Sum	138	130	126	120	116	109	127	
Detm	FALSE	134	115	102	100	93	83	108
	TRUE	3	6	15	14	13	16	12
	NA	0	1	0	0	1	4	0
Sum		137	122	117	114	107	103	120
Biph	FALSE	133	115	88	92	95	87	88
	TRUE	4	16	37	34	32	36	38
	NA	0	0	3	2	0	0	1
Sum		137	131	128	128	127	123	127

```

> ftable( with( AD,
+           addmargins( table( pp, igr, visit, hb7=hba1c<=7, useNA="ifany" ),
+                           4 ) ), col.vars=3 )

```

pp	igr	hb7	visit	v1	v2	v3	v4	v5	v6	v7	
FALSE	AspD	FALSE		10	1	0	0	0	0	3	
		TRUE		0	0	0	0	0	0	0	
		NA		0	1	0	0	0	0	0	
		Sum		10	2	0	0	0	0	0	3
	Detm	FALSE		17	3	0	0	0	0	0	4
		TRUE		2	0	0	0	0	0	0	0
		NA		0	1	0	0	0	0	0	0
		Sum		19	4	0	0	0	0	0	4
	Biph	FALSE		7	2	0	0	0	0	0	0
		TRUE		1	0	0	0	0	0	0	1
		NA		0	0	0	0	0	0	0	0
		Sum		8	2	0	0	0	0	0	1
TRUE	AspD	FALSE		126	103	93	85	77	74	93	
		TRUE		2	24	32	34	38	33	31	
		NA		0	1	1	1	1	2	0	
		Sum		128	128	126	120	116	109	124	
	Detm	FALSE		117	112	102	100	93	83	104	
		TRUE		1	6	15	14	13	16	12	
		NA		0	0	0	0	1	4	0	
		Sum		118	118	117	114	107	103	116	
	Biph	FALSE		126	113	88	92	95	87	88	
		TRUE		3	16	37	34	32	36	37	
		NA		0	0	3	2	0	0	1	
		Sum		129	129	128	128	127	123	126	

Since we want to use the insulin dose at visit 6 to be used as the final insulin dose, and since insulin dose at visit 7 is always NA, we substitute insulin values from time 6 to time 7:

```

> wh <- match( c("idos","ipkg"), names(AD) )
> for( ii in unique(AD$subjid) )
+ if( all( dim(AD[AD$subjid==ii & AD$visit %in% c("v6","v7"),wh] )==c(2,2) ) )
+   AD[AD$subjid==ii & AD$visit == "v7",wh] <-
+   AD[AD$subjid==ii & AD$visit == "v6",wh]

```

The we define the variables we want to show at visit 1 and visit 7:

```

> vars <- c( "fimtavg",
+           "fimtmax",
+           "csc2",
+           "iem",
+           "imtareal",
+           "n.pl",
+           "weight",
+           "bmi",
+           "whr",
+           "hba1c",
+           "gluc",
+           "ins",
+           "cpep",

```

```

+         "idos",
+         "ipkg",
+         "sys",
+         "dia",
+         "pulse",
+         "chol",
+         "ldl",
+         "hdl",
+         "vldl",
+         "trig" )
> dig <- c(3,3,4,0,1,0,1,1,2,1,1,0,0,0,2,0,0,0,1,1,1,2,1)
> data.frame( vars, dig )
      vars dig
1  fimtavg   3
2  fimtmax   3
3    csc2    4
4     iem    0
5 imtareal   1
6     n.pl   0
7   weight   1
8     bmi    1
9     whr    2
10  hba1c    1
11    gluc    1
12     ins    0
13    cpep    0
14    idos    0
15    ipkg    2
16     sys    0
17     dia    0
18  pulse    0
19    chol    1
20     ldl    1
21     hdl    1
22    vldl    2
23    trig    1
> QQ <- NArray( list( vars,
+                     levels(AD$igr),
+                     levels(AD$visit),
+                     c( paste( c(2,1,3)/4), "mean", "sd" ) ) )
> str( QQ )

logi [1:23, 1:3, 1:7, 1:5] NA NA NA NA NA NA ...
- attr(*, "dimnames")=List of 4
..$ : chr [1:23] "fimtavg" "fimtmax" "csc2" "iem" ...
..$ : chr [1:3] "AspD" "Detm" "Biph"
..$ : chr [1:7] "v1" "v2" "v3" "v4" ...
..$ : chr [1:5] "0.5" "0.25" "0.75" "mean" ...

> for( vv in dimnames(QQ)[[1]] )
+ for( gg in dimnames(QQ)[[2]] )
+ for( tt in dimnames(QQ)[[3]] )
+ QQ[vv,gg,tt,] <- c( quantile( AD[AD$igr==gg & AD$visit==tt,vv],
+                             probs=c(2,1,3)/4, na.rm=TRUE ),
+                     mean( AD[AD$igr==gg & AD$visit==tt,vv], na.rm=TRUE ),
+                     sd( AD[AD$igr==gg & AD$visit==tt,vv], na.rm=TRUE ) )

```

Then we can print the median and IQR for these variables to a .csv-file:

```

> round( ftable( QQ[,,,1:3], col.vars=3 ), 3 )
      v1      v2      v3      v4      v5      v6      v7
fimtavg AspD 0.5      0.778      NA      NA      NA      NA      0.780
          0.25      0.690      NA      NA      NA      NA      0.685
          0.75      0.874      NA      NA      NA      NA      0.880
          Detm 0.5      0.790      NA      NA      NA      NA      0.768

```

		0.25	0.700	NA	NA	NA	NA	NA	0.684
		0.75	0.870	NA	NA	NA	NA	NA	0.866
	Biph	0.5	0.780	NA	NA	NA	NA	NA	0.765
		0.25	0.700	NA	NA	NA	NA	NA	0.691
		0.75	0.870	NA	NA	NA	NA	NA	0.874
fimtmax	AspD	0.5	0.940	NA	NA	NA	NA	NA	0.925
		0.25	0.836	NA	NA	NA	NA	NA	0.835
		0.75	1.034	NA	NA	NA	NA	NA	1.055
	Detm	0.5	0.970	NA	NA	NA	NA	NA	0.938
		0.25	0.865	NA	NA	NA	NA	NA	0.834
		0.75	1.045	NA	NA	NA	NA	NA	1.041
	Biph	0.5	0.935	NA	NA	NA	NA	NA	0.933
		0.25	0.855	NA	NA	NA	NA	NA	0.836
		0.75	1.045	NA	NA	NA	NA	NA	1.035
csc2	AspD	0.5	2.400	NA	NA	NA	NA	NA	2.420
		0.25	1.838	NA	NA	NA	NA	NA	1.990
		0.75	3.270	NA	NA	NA	NA	NA	3.175
	Detm	0.5	2.425	NA	NA	NA	NA	NA	2.350
		0.25	1.780	NA	NA	NA	NA	NA	1.900
		0.75	3.075	NA	NA	NA	NA	NA	3.255
	Biph	0.5	2.390	NA	NA	NA	NA	NA	2.610
		0.25	1.806	NA	NA	NA	NA	NA	1.890
		0.75	3.010	NA	NA	NA	NA	NA	3.174
iem	AspD	0.5	2125.370	NA	NA	NA	NA	NA	2061.485
		0.25	1587.483	NA	NA	NA	NA	NA	1519.065
		0.75	2822.757	NA	NA	NA	NA	NA	2572.135
	Detm	0.5	2122.635	NA	NA	NA	NA	NA	2144.210
		0.25	1687.640	NA	NA	NA	NA	NA	1551.470
		0.75	2849.805	NA	NA	NA	NA	NA	2634.580
	Biph	0.5	2161.050	NA	NA	NA	NA	NA	1935.722
		0.25	1712.285	NA	NA	NA	NA	NA	1515.717
		0.75	2839.812	NA	NA	NA	NA	NA	2848.595
imtareal	AspD	0.5	18.564	NA	NA	NA	NA	NA	17.774
		0.25	15.444	NA	NA	NA	NA	NA	15.057
		0.75	22.346	NA	NA	NA	NA	NA	22.778
	Detm	0.5	18.872	NA	NA	NA	NA	NA	18.226
		0.25	15.840	NA	NA	NA	NA	NA	15.750
		0.75	21.771	NA	NA	NA	NA	NA	21.114
	Biph	0.5	18.354	NA	NA	NA	NA	NA	18.738
		0.25	15.897	NA	NA	NA	NA	NA	15.882
		0.75	21.009	NA	NA	NA	NA	NA	21.295
n.pl	AspD	0.5	2.000	NA	NA	NA	NA	NA	3.000
		0.25	1.000	NA	NA	NA	NA	NA	2.000
		0.75	4.000	NA	NA	NA	NA	NA	5.000
	Detm	0.5	3.000	NA	NA	NA	NA	NA	3.000
		0.25	2.000	NA	NA	NA	NA	NA	2.000
		0.75	5.000	NA	NA	NA	NA	NA	6.000
	Biph	0.5	3.000	NA	NA	NA	NA	NA	3.000
		0.25	2.000	NA	NA	NA	NA	NA	2.000
		0.75	4.000	NA	NA	NA	NA	NA	5.000
weight	AspD	0.5	96.150	98.000	99.550	100.700	99.600	99.700	99.600
		0.25	86.125	88.100	88.275	89.500	89.700	88.300	86.900
		0.75	104.575	107.200	107.175	109.000	108.500	107.100	108.200
	Detm	0.5	97.700	96.600	97.400	97.000	97.800	98.100	98.500
		0.25	87.700	86.000	86.400	87.600	87.300	88.100	89.350
		0.75	107.700	106.800	107.475	108.300	108.200	108.700	110.200
	Biph	0.5	93.500	94.900	95.350	96.550	96.900	97.800	97.000
		0.25	85.200	87.425	87.800	87.775	89.300	89.300	88.100
		0.75	104.300	106.625	107.425	109.425	110.950	111.650	109.100
bmi	AspD	0.5	32.014	32.606	32.537	33.143	32.625	32.606	32.824
		0.25	29.523	30.046	30.253	30.266	30.248	30.097	30.009
		0.75	34.691	35.382	35.893	35.923	35.480	35.932	35.917
	Detm	0.5	31.965	31.686	31.889	31.774	32.250	32.402	32.429
		0.25	29.436	28.886	28.901	28.780	28.756	28.784	29.140
		0.75	35.511	35.156	35.600	36.179	36.131	36.157	36.229
	Biph	0.5	31.508	32.070	32.004	32.312	32.237	32.809	32.948

		0.25	28.597	29.091	29.233	29.303	29.091	29.425	29.608
		0.75	34.412	34.846	35.896	36.002	36.211	36.697	36.763
whr	AspD	0.5	1.009	1.009	1.009	1.009	1.014	1.009	1.009
		0.25	0.955	0.953	0.958	0.956	0.965	0.960	0.958
		0.75	1.059	1.055	1.052	1.064	1.059	1.059	1.064
	Detm	0.5	1.009	1.007	1.010	1.000	1.000	1.000	1.022
		0.25	0.951	0.950	0.951	0.958	0.951	0.951	0.965
		0.75	1.054	1.052	1.062	1.059	1.055	1.064	1.066
	Biph	0.5	0.993	0.991	0.992	1.000	1.008	1.000	1.000
		0.25	0.954	0.944	0.935	0.951	0.945	0.947	0.952
		0.75	1.051	1.034	1.043	1.048	1.049	1.050	1.053
hba1c	AspD	0.5	8.200	7.900	7.700	7.600	7.500	7.500	7.700
		0.25	7.800	7.200	7.000	6.950	6.950	6.900	7.100
		0.75	9.300	8.700	8.300	8.400	8.500	8.200	8.700
	Detm	0.5	8.300	8.700	8.200	8.300	8.100	8.000	8.100
		0.25	7.700	8.000	7.500	7.700	7.500	7.400	7.400
		0.75	9.200	9.500	9.200	8.975	8.975	8.700	8.900
	Biph	0.5	8.500	8.000	7.600	7.500	7.500	7.500	7.400
		0.25	7.900	7.450	6.900	7.000	7.050	7.000	6.900
		0.75	9.300	8.800	8.300	8.300	8.300	8.400	8.200
gluc	AspD	0.5	9.400	8.150	8.000	8.000	7.900	7.650	7.900
		0.25	7.700	6.600	6.700	6.325	6.700	6.325	6.600
		0.75	11.600	10.325	9.900	10.400	9.800	9.750	9.900
	Detm	0.5	10.000	8.000	7.700	7.400	7.100	6.900	7.200
		0.25	8.300	6.300	6.300	5.400	5.575	6.150	6.100
		0.75	12.000	10.100	9.500	9.125	8.700	9.050	9.475
	Biph	0.5	9.700	8.500	8.300	7.850	8.400	8.050	8.300
		0.25	7.900	7.200	6.900	6.300	6.850	6.400	6.725
		0.75	12.400	10.700	10.000	9.725	10.250	10.325	9.975
ins	AspD	0.5	75.500	NA	NA	NA	NA	NA	43.000
		0.25	45.250	NA	NA	NA	NA	NA	19.000
		0.75	132.000	NA	NA	NA	NA	NA	101.000
	Detm	0.5	65.000	NA	NA	NA	NA	NA	36.500
		0.25	37.000	NA	NA	NA	NA	NA	15.750
		0.75	114.000	NA	NA	NA	NA	NA	65.500
	Biph	0.5	68.000	NA	NA	NA	NA	NA	56.500
		0.25	38.000	NA	NA	NA	NA	NA	35.500
		0.75	103.000	NA	NA	NA	NA	NA	92.250
cpep	AspD	0.5	828.000	NA	NA	NA	NA	NA	499.000
		0.25	507.000	NA	NA	NA	NA	NA	297.000
		0.75	1217.250	NA	NA	NA	NA	NA	961.000
	Detm	0.5	877.000	NA	NA	NA	NA	NA	467.000
		0.25	466.000	NA	NA	NA	NA	NA	270.000
		0.75	1280.000	NA	NA	NA	NA	NA	751.250
	Biph	0.5	782.000	NA	NA	NA	NA	NA	638.500
		0.25	418.000	NA	NA	NA	NA	NA	436.750
		0.75	1150.000	NA	NA	NA	NA	NA	851.750
idos	AspD	0.5	42.500	88.000	94.000	98.000	98.000	96.000	96.000
		0.25	22.000	60.000	64.000	67.750	64.000	64.000	64.000
		0.75	64.000	120.000	130.000	142.000	150.500	148.000	145.000
	Detm	0.5	38.000	90.000	107.000	114.000	116.000	114.000	118.000
		0.25	20.000	60.000	65.750	70.000	67.500	73.000	74.000
		0.75	61.500	128.000	160.000	180.000	182.000	195.000	196.000
	Biph	0.5	40.000	63.000	72.000	72.000	72.000	70.000	70.000
		0.25	20.000	43.250	47.250	46.000	47.000	46.500	46.500
		0.75	70.000	99.250	105.000	108.500	117.500	127.250	127.250
ipkg	AspD	0.5	0.448	0.879	0.923	0.984	0.978	0.951	0.944
		0.25	0.261	0.635	0.693	0.715	0.657	0.653	0.653
		0.75	0.621	1.138	1.239	1.269	1.398	1.364	1.354
	Detm	0.5	0.392	0.945	1.110	1.139	1.181	1.168	1.185
		0.25	0.229	0.616	0.728	0.758	0.772	0.797	0.801
		0.75	0.626	1.311	1.654	1.696	1.768	1.852	1.857
	Biph	0.5	0.466	0.661	0.742	0.729	0.726	0.754	0.754
		0.25	0.209	0.457	0.528	0.529	0.534	0.543	0.543
		0.75	0.720	0.945	0.990	1.013	1.090	1.157	1.157
sys	AspD	0.5	138.000	135.000	133.000	132.000	132.000	131.500	133.750

		0.25	128.375	123.500	124.500	124.625	125.000	124.000	122.625
		0.75	151.000	146.000	142.750	141.875	143.250	140.125	143.000
	Detm	0.5	139.000	135.000	135.000	133.750	132.250	132.000	133.500
		0.25	130.000	124.000	124.500	122.625	124.000	121.750	126.000
		0.75	149.000	146.000	144.500	143.375	143.000	139.625	142.500
	Biph	0.5	136.500	135.250	134.500	132.750	133.000	133.500	131.000
		0.25	127.750	123.750	125.500	124.125	123.500	124.500	121.375
		0.75	149.500	145.500	146.250	140.875	143.750	142.250	140.000
dia	AspD	0.5	82.250	81.000	81.000	80.500	79.500	79.000	78.500
		0.25	75.500	75.000	74.125	75.250	73.500	73.375	74.500
		0.75	88.125	86.625	85.500	85.500	85.000	87.000	86.000
	Detm	0.5	82.000	80.000	80.500	81.500	80.000	77.500	77.000
		0.25	75.500	74.500	74.500	73.250	73.000	72.500	72.500
		0.75	88.000	86.000	87.000	87.500	85.500	84.625	84.500
	Biph	0.5	82.500	82.000	80.000	80.250	80.500	81.000	78.500
		0.25	76.500	75.000	74.000	74.625	73.750	75.500	72.500
		0.75	87.500	87.375	86.000	86.375	84.500	86.000	84.625
pulse	AspD	0.5	75.500	74.000	75.000	74.000	72.000	72.000	73.000
		0.25	68.000	67.000	67.000	65.250	65.500	65.250	67.000
		0.75	84.000	83.500	81.000	82.000	81.000	79.000	82.500
	Detm	0.5	77.000	74.500	74.000	73.500	74.000	73.000	74.000
		0.25	70.000	65.000	64.750	65.000	66.750	64.000	64.000
		0.75	82.500	81.000	82.000	80.000	81.250	81.000	80.000
	Biph	0.5	76.000	76.500	74.000	75.000	74.000	73.000	74.000
		0.25	69.000	71.000	67.000	69.000	68.000	68.000	69.000
		0.75	83.000	83.000	81.000	80.750	80.750	80.000	82.000
chol	AspD	0.5	4.100	NA	4.200	NA	4.100	NA	4.100
		0.25	3.500	NA	3.700	NA	3.600	NA	3.650
		0.75	4.800	NA	4.900	NA	4.700	NA	4.700
	Detm	0.5	4.000	NA	4.100	NA	4.100	NA	4.100
		0.25	3.400	NA	3.500	NA	3.400	NA	3.600
		0.75	4.700	NA	4.700	NA	4.800	NA	4.800
	Biph	0.5	4.000	NA	4.200	NA	4.200	NA	4.200
		0.25	3.600	NA	3.700	NA	3.700	NA	3.700
		0.75	4.500	NA	4.700	NA	4.800	NA	4.800
ldl	AspD	0.5	2.100	NA	2.200	NA	2.200	NA	2.100
		0.25	1.600	NA	1.800	NA	1.700	NA	1.800
		0.75	2.700	NA	2.800	NA	2.700	NA	2.650
	Detm	0.5	2.000	NA	2.200	NA	2.100	NA	2.200
		0.25	1.500	NA	1.800	NA	1.700	NA	1.700
		0.75	2.600	NA	2.700	NA	2.775	NA	2.600
	Biph	0.5	2.100	NA	2.200	NA	2.100	NA	2.200
		0.25	1.600	NA	1.700	NA	1.600	NA	1.700
		0.75	2.500	NA	2.600	NA	2.600	NA	2.700
hdl	AspD	0.5	1.045	NA	1.105	NA	1.100	NA	1.070
		0.25	0.920	NA	0.947	NA	0.900	NA	0.920
		0.75	1.350	NA	1.400	NA	1.400	NA	1.330
	Detm	0.5	1.080	NA	1.100	NA	1.100	NA	1.080
		0.25	0.910	NA	0.900	NA	0.900	NA	0.885
		0.75	1.290	NA	1.400	NA	1.300	NA	1.325
	Biph	0.5	1.150	NA	1.210	NA	1.190	NA	1.160
		0.25	0.930	NA	1.000	NA	1.000	NA	0.960
		0.75	1.480	NA	1.470	NA	1.510	NA	1.482
vldl	AspD	0.5	0.700	NA	0.700	NA	0.700	NA	0.700
		0.25	0.500	NA	0.500	NA	0.600	NA	0.500
		0.75	0.925	NA	1.000	NA	0.900	NA	0.950
	Detm	0.5	0.700	NA	0.700	NA	0.700	NA	0.700
		0.25	0.500	NA	0.500	NA	0.500	NA	0.500
		0.75	1.000	NA	1.000	NA	1.000	NA	1.000
	Biph	0.5	0.700	NA	0.600	NA	0.600	NA	0.600
		0.25	0.500	NA	0.500	NA	0.500	NA	0.500
		0.75	1.000	NA	0.800	NA	0.900	NA	0.900
trig	AspD	0.5	1.630	NA	1.605	NA	1.580	NA	1.610
		0.25	1.175	NA	1.170	NA	1.263	NA	1.155
		0.75	2.143	NA	2.200	NA	2.088	NA	2.275
	Detm	0.5	1.630	NA	1.530	NA	1.600	NA	1.630

	0.25	1.150	NA	1.200	NA	1.100	NA	1.185
	0.75	2.400	NA	2.225	NA	2.100	NA	2.190
Biph	0.5	1.480	NA	1.365	NA	1.445	NA	1.420
	0.25	1.030	NA	1.000	NA	1.053	NA	1.030
	0.75	2.280	NA	1.900	NA	2.067	NA	2.130

```
> round( ftable( QQ[,c(1,7),1:3], col.vars=3:4), 3 )
```

		v1			v7		
		0.5	0.25	0.75	0.5	0.25	0.75
fimtavg	AspD	0.778	0.690	0.874	0.780	0.685	0.880
	Detm	0.790	0.700	0.870	0.768	0.684	0.866
	Biph	0.780	0.700	0.870	0.765	0.691	0.874
fimtmax	AspD	0.940	0.836	1.034	0.925	0.835	1.055
	Detm	0.970	0.865	1.045	0.938	0.834	1.041
	Biph	0.935	0.855	1.045	0.933	0.836	1.035
csc2	AspD	2.400	1.838	3.270	2.420	1.990	3.175
	Detm	2.425	1.780	3.075	2.350	1.900	3.255
	Biph	2.390	1.806	3.010	2.610	1.890	3.174
iem	AspD	2125.370	1587.483	2822.757	2061.485	1519.065	2572.135
	Detm	2122.635	1687.640	2849.805	2144.210	1551.470	2634.580
	Biph	2161.050	1712.285	2839.812	1935.722	1515.717	2848.595
imtareal	AspD	18.564	15.444	22.346	17.774	15.057	22.778
	Detm	18.872	15.840	21.771	18.226	15.750	21.114
	Biph	18.354	15.897	21.009	18.738	15.882	21.295
n.pl	AspD	2.000	1.000	4.000	3.000	2.000	5.000
	Detm	3.000	2.000	5.000	3.000	2.000	6.000
	Biph	3.000	2.000	4.000	3.000	2.000	5.000
weight	AspD	96.150	86.125	104.575	99.600	86.900	108.200
	Detm	97.700	87.700	107.700	98.500	89.350	110.200
	Biph	93.500	85.200	104.300	97.000	88.100	109.100
bmi	AspD	32.014	29.523	34.691	32.824	30.009	35.917
	Detm	31.965	29.436	35.511	32.429	29.140	36.229
	Biph	31.508	28.597	34.412	32.948	29.608	36.763
whr	AspD	1.009	0.955	1.059	1.009	0.958	1.064
	Detm	1.009	0.951	1.054	1.022	0.965	1.066
	Biph	0.993	0.954	1.051	1.000	0.952	1.053
hba1c	AspD	8.200	7.800	9.300	7.700	7.100	8.700
	Detm	8.300	7.700	9.200	8.100	7.400	8.900
	Biph	8.500	7.900	9.300	7.400	6.900	8.200
gluc	AspD	9.400	7.700	11.600	7.900	6.600	9.900
	Detm	10.000	8.300	12.000	7.200	6.100	9.475
	Biph	9.700	7.900	12.400	8.300	6.725	9.975
ins	AspD	75.500	45.250	132.000	43.000	19.000	101.000
	Detm	65.000	37.000	114.000	36.500	15.750	65.500
	Biph	68.000	38.000	103.000	56.500	35.500	92.250
cpep	AspD	828.000	507.000	1217.250	499.000	297.000	961.000
	Detm	877.000	466.000	1280.000	467.000	270.000	751.250
	Biph	782.000	418.000	1150.000	638.500	436.750	851.750
idos	AspD	42.500	22.000	64.000	96.000	64.000	145.000
	Detm	38.000	20.000	61.500	118.000	74.000	196.000
	Biph	40.000	20.000	70.000	70.000	46.500	127.250
ipkg	AspD	0.448	0.261	0.621	0.944	0.653	1.354
	Detm	0.392	0.229	0.626	1.185	0.801	1.857
	Biph	0.466	0.209	0.720	0.754	0.543	1.157
sys	AspD	138.000	128.375	151.000	133.750	122.625	143.000
	Detm	139.000	130.000	149.000	133.500	126.000	142.500
	Biph	136.500	127.750	149.500	131.000	121.375	140.000
dia	AspD	82.250	75.500	88.125	78.500	74.500	86.000
	Detm	82.000	75.500	88.000	77.000	72.500	84.500
	Biph	82.500	76.500	87.500	78.500	72.500	84.625
pulse	AspD	75.500	68.000	84.000	73.000	67.000	82.500
	Detm	77.000	70.000	82.500	74.000	64.000	80.000
	Biph	76.000	69.000	83.000	74.000	69.000	82.000
chol	AspD	4.100	3.500	4.800	4.100	3.650	4.700
	Detm	4.000	3.400	4.700	4.100	3.600	4.800
	Biph	4.000	3.600	4.500	4.200	3.700	4.800

ldl	AspD	2.100	1.600	2.700	2.100	1.800	2.650
	Detm	2.000	1.500	2.600	2.200	1.700	2.600
	Biph	2.100	1.600	2.500	2.200	1.700	2.700
hdl	AspD	1.045	0.920	1.350	1.070	0.920	1.330
	Detm	1.080	0.910	1.290	1.080	0.885	1.325
	Biph	1.150	0.930	1.480	1.160	0.960	1.482
vldl	AspD	0.700	0.500	0.925	0.700	0.500	0.950
	Detm	0.700	0.500	1.000	0.700	0.500	1.000
	Biph	0.700	0.500	1.000	0.600	0.500	0.900
trig	AspD	1.630	1.175	2.143	1.610	1.155	2.275
	Detm	1.630	1.150	2.400	1.630	1.185	2.190
	Biph	1.480	1.030	2.280	1.420	1.030	2.130

```
> round( tt <- ftable( QQ[,c(1,7),1:3], col.vars=2:4), 3 )
```

	AspD			v7			Detm			v
	v1			v1			v1			
	0.5	0.25	0.75	0.5	0.25	0.75	0.5	0.25	0.75	
fimtavg	0.778	0.690	0.874	0.780	0.685	0.880	0.790	0.700	0.870	0.76
fimtmax	0.940	0.836	1.034	0.925	0.835	1.055	0.970	0.865	1.045	0.93
csc2	2.400	1.838	3.270	2.420	1.990	3.175	2.425	1.780	3.075	2.35
iem	2125.370	1587.483	2822.757	2061.485	1519.065	2572.135	2122.635	1687.640	2849.805	2144.2
imtareal	18.564	15.444	22.346	17.774	15.057	22.778	18.872	15.840	21.771	18.22
n.pl	2.000	1.000	4.000	3.000	2.000	5.000	3.000	2.000	5.000	3.00
weight	96.150	86.125	104.575	99.600	86.900	108.200	97.700	87.700	107.700	98.50
bmi	32.014	29.523	34.691	32.824	30.009	35.917	31.965	29.436	35.511	32.42
whr	1.009	0.955	1.059	1.009	0.958	1.064	1.009	0.951	1.054	1.02
hba1c	8.200	7.800	9.300	7.700	7.100	8.700	8.300	7.700	9.200	8.10
gluc	9.400	7.700	11.600	7.900	6.600	9.900	10.000	8.300	12.000	7.20
ins	75.500	45.250	132.000	43.000	19.000	101.000	65.000	37.000	114.000	36.50
cpep	828.000	507.000	1217.250	499.000	297.000	961.000	877.000	466.000	1280.000	467.00
idos	42.500	22.000	64.000	96.000	64.000	145.000	38.000	20.000	61.500	118.00
ipkg	0.448	0.261	0.621	0.944	0.653	1.354	0.392	0.229	0.626	1.18
sys	138.000	128.375	151.000	133.750	122.625	143.000	139.000	130.000	149.000	133.50
dia	82.250	75.500	88.125	78.500	74.500	86.000	82.000	75.500	88.000	77.00
pulse	75.500	68.000	84.000	73.000	67.000	82.500	77.000	70.000	82.500	74.00
chol	4.100	3.500	4.800	4.100	3.650	4.700	4.000	3.400	4.700	4.10
ldl	2.100	1.600	2.700	2.100	1.800	2.650	2.000	1.500	2.600	2.20
hdl	1.045	0.920	1.350	1.070	0.920	1.330	1.080	0.910	1.290	1.08
vldl	0.700	0.500	0.925	0.700	0.500	0.950	0.700	0.500	1.000	0.70
trig	1.630	1.175	2.143	1.610	1.155	2.275	1.630	1.150	2.400	1.63

```
> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Asp+Det ; ; ; Detemir ; ; ; Biphasic ; ; ; \n",
+      "; V1 ; ; V7 ; ; V1 ; ; V7 ; \n",
+      "; Med ; IQR ; Med ; IQR ; Med ; IQR ; Med ; IQR \n",
+      file="./results/LLCh-Tab2i.csv" )
> for( i in 1:nrow(tt) )
+ write.table( cbind( formatC( tt[i,1,drop=F], format="f", digits=dig[i] ),
+                       paste( "(", formatC( tt[i,2,drop=F], format="f", digits=dig[i] ), " ",
+                                   formatC( tt[i,3,drop=F], format="f", digits=dig[i] ), " )" ),
+                       formatC( tt[i,4,drop=F], format="f", digits=dig[i] ),
+                       paste( "(", formatC( tt[i,5,drop=F], format="f", digits=dig[i] ), " ",
+                                   formatC( tt[i,6,drop=F], format="f", digits=dig[i] ), " )" ),
+                       formatC( tt[i,7,drop=F], format="f", digits=dig[i] ),
+                       paste( "(", formatC( tt[i,8,drop=F], format="f", digits=dig[i] ), " ",
+                                   formatC( tt[i,9,drop=F], format="f", digits=dig[i] ), " )" ),
+                       formatC( tt[i,10,drop=F], format="f", digits=dig[i] ),
+                       paste( "(", formatC( tt[i,11,drop=F], format="f", digits=dig[i] ), " ",
+                                   formatC( tt[i,12,drop=F], format="f", digits=dig[i] ), " )" ),
+                       file="./results/LLCh-Tab2i.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+                       quote=F, sep=";", dec="," )
```

Print the mean and the sd instead

```
> round( ftable( QQ[,c(4:5), col.vars=3 ], 3 )
```


			v1	v2	v3	v4	v5	v6	v7
fimtavg	AspD	mean	0.796	NaN	NaN	NaN	NaN	NaN	0.795
		sd	0.148	NA	NA	NA	NA	NA	0.150
	Detm	mean	0.798	NaN	NaN	NaN	NaN	NaN	0.778
		sd	0.139	NA	NA	NA	NA	NA	0.129
	Biph	mean	0.786	NaN	NaN	NaN	NaN	NaN	0.781
		sd	0.121	NA	NA	NA	NA	NA	0.130
fimtmax	AspD	mean	0.954	NaN	NaN	NaN	NaN	NaN	0.954
		sd	0.165	NA	NA	NA	NA	NA	0.170
	Detm	mean	0.965	NaN	NaN	NaN	NaN	NaN	0.940
		sd	0.155	NA	NA	NA	NA	NA	0.149
	Biph	mean	0.949	NaN	NaN	NaN	NaN	NaN	0.943
		sd	0.140	NA	NA	NA	NA	NA	0.151
csc2	AspD	mean	2.626	NaN	NaN	NaN	NaN	NaN	2.654
		sd	1.103	NA	NA	NA	NA	NA	0.992
	Detm	mean	2.575	NaN	NaN	NaN	NaN	NaN	2.649
		sd	1.053	NA	NA	NA	NA	NA	0.992
	Biph	mean	2.518	NaN	NaN	NaN	NaN	NaN	2.558
		sd	0.956	NA	NA	NA	NA	NA	0.939
iem	AspD	mean	2314.408	NaN	NaN	NaN	NaN	NaN	2188.873
		sd	1012.908	NA	NA	NA	NA	NA	858.809
	Detm	mean	2348.003	NaN	NaN	NaN	NaN	NaN	2192.966
		sd	1009.038	NA	NA	NA	NA	NA	867.971
	Biph	mean	2376.867	NaN	NaN	NaN	NaN	NaN	2321.016
		sd	1073.070	NA	NA	NA	NA	NA	1086.385
imtareal	AspD	mean	19.277	NaN	NaN	NaN	NaN	NaN	19.071
		sd	5.144	NA	NA	NA	NA	NA	5.151
	Detm	mean	19.493	NaN	NaN	NaN	NaN	NaN	18.752
		sd	4.885	NA	NA	NA	NA	NA	4.074
	Biph	mean	18.638	NaN	NaN	NaN	NaN	NaN	18.939
		sd	4.103	NA	NA	NA	NA	NA	4.117
n.pl	AspD	mean	3.511	NaN	NaN	NaN	NaN	NaN	4.056
		sd	3.573	NA	NA	NA	NA	NA	4.171
	Detm	mean	3.938	NaN	NaN	NaN	NaN	NaN	4.273
		sd	3.284	NA	NA	NA	NA	NA	3.691
	Biph	mean	3.437	NaN	NaN	NaN	NaN	NaN	4.059
		sd	2.714	NA	NA	NA	NA	NA	3.569
weight	AspD	mean	97.454	98.816	99.818	100.590	100.324	99.547	100.176
		sd	14.957	15.258	15.751	16.426	16.405	16.151	17.021
	Detm	mean	98.468	97.559	98.361	98.883	98.429	98.851	100.208
		sd	15.113	15.312	16.217	16.260	15.886	16.284	16.642
	Biph	mean	95.572	97.168	98.232	98.638	99.043	99.547	99.282
		sd	14.831	15.223	15.979	16.192	16.627	16.667	16.370
bmi	AspD	mean	32.234	32.754	33.025	33.202	33.112	32.925	33.101
		sd	3.929	4.077	4.283	4.335	4.414	4.370	4.546
	Detm	mean	32.399	32.148	32.389	32.487	32.490	32.649	32.868
		sd	4.291	4.372	4.625	4.551	4.526	4.656	4.685
	Biph	mean	31.845	32.322	32.592	32.732	32.828	32.994	33.046
		sd	4.396	4.448	4.607	4.696	4.845	4.904	4.899
whr	AspD	mean	1.003	1.004	1.006	1.006	1.008	1.007	1.010
		sd	0.078	0.074	0.079	0.077	0.075	0.078	0.075
	Detm	mean	1.008	1.002	1.008	1.002	1.001	1.006	1.022
		sd	0.090	0.084	0.085	0.084	0.087	0.081	0.087
	Biph	mean	0.999	0.993	0.993	0.994	0.997	0.995	0.998
		sd	0.075	0.077	0.077	0.075	0.076	0.080	0.076
hba1c	AspD	mean	8.497	8.041	7.790	7.796	7.810	7.750	8.024
		sd	1.023	1.085	1.134	1.141	1.177	1.095	1.321
	Detm	mean	8.531	8.918	8.444	8.325	8.239	8.084	8.266
		sd	1.119	1.342	1.168	1.112	1.080	1.031	1.190
	Biph	mean	8.622	8.185	7.683	7.711	7.761	7.680	7.590
		sd	1.012	1.092	0.986	0.971	1.060	0.948	0.928
gluc	AspD	mean	9.861	8.527	8.467	8.613	8.444	8.065	8.537
		sd	3.082	2.789	2.598	3.126	2.600	2.704	3.349
	Detm	mean	10.375	8.503	8.114	7.837	7.387	7.569	7.944
		sd	3.085	3.223	2.780	3.221	2.624	2.569	2.863

	Biph	mean	10.653	9.098	8.685	8.132	8.990	8.708	8.603
		sd	3.549	2.838	2.893	2.781	3.507	3.621	2.544
ins	AspD	mean	104.600	NaN	NaN	NaN	NaN	NaN	67.408
		sd	94.633	NA	NA	NA	NA	NA	66.371
	Detm	mean	94.956	NaN	NaN	NaN	NaN	NaN	80.588
		sd	101.143	NA	NA	NA	NA	NA	351.195
cpep	Biph	mean	80.399	NaN	NaN	NaN	NaN	NaN	77.311
		sd	65.171	NA	NA	NA	NA	NA	79.639
	AspD	mean	925.971	NaN	NaN	NaN	NaN	NaN	684.880
		sd	591.349	NA	NA	NA	NA	NA	508.924
idos	Detm	mean	903.146	NaN	NaN	NaN	NaN	NaN	561.075
		sd	544.527	NA	NA	NA	NA	NA	390.283
	Biph	mean	820.358	NaN	NaN	NaN	NaN	NaN	674.742
		sd	543.249	NA	NA	NA	NA	NA	410.797
ipkg	AspD	mean	48.486	94.884	102.683	108.575	110.603	106.651	105.935
		sd	30.975	48.661	53.889	59.334	62.898	59.653	59.459
	Detm	mean	47.110	108.661	131.810	139.062	137.425	143.272	145.040
		sd	36.025	75.788	93.147	94.326	91.422	101.039	101.117
sys	Biph	mean	48.500	74.838	84.359	88.359	91.291	93.918	93.918
		sd	33.552	41.178	49.026	55.772	59.732	63.574	63.574
	AspD	mean	0.494	0.957	1.019	1.068	1.076	1.054	1.048
		sd	0.304	0.480	0.510	0.549	0.580	0.558	0.557
dia	Detm	mean	0.470	1.086	1.307	1.364	1.361	1.406	1.423
		sd	0.325	0.693	0.819	0.824	0.812	0.877	0.877
	Biph	mean	0.504	0.755	0.845	0.879	0.903	0.920	0.920
		sd	0.330	0.383	0.461	0.525	0.560	0.576	0.576
pulse	AspD	mean	139.754	136.426	135.091	134.919	133.448	133.106	133.864
		sd	14.808	16.136	14.924	15.275	12.864	12.939	16.573
	Detm	mean	139.820	135.764	135.043	134.518	133.038	132.335	135.429
		sd	16.120	17.130	17.380	17.210	14.536	16.118	15.550
chol	Biph	mean	138.481	135.342	135.650	134.381	134.909	134.711	131.879
		sd	15.097	14.768	14.084	14.926	15.953	13.596	14.959
	AspD	mean	82.404	81.008	80.135	80.242	79.378	79.148	79.276
		sd	9.272	9.818	8.920	8.951	9.047	10.171	9.258
hdl	Detm	mean	81.801	80.074	80.808	80.355	79.222	78.630	78.529
		sd	9.443	9.169	9.883	9.570	8.932	9.593	8.960
	Biph	mean	82.078	81.138	80.299	80.472	79.787	80.801	78.907
		sd	9.181	8.736	9.356	8.894	8.950	8.710	9.132
vldl	AspD	mean	75.836	75.087	74.352	74.119	72.991	72.443	74.495
		sd	11.441	12.312	11.011	12.169	11.949	10.951	12.109
	Detm	mean	76.570	73.850	73.750	74.304	73.788	73.950	73.379
		sd	11.328	12.681	11.741	14.453	12.673	13.475	13.349
ldl	Biph	mean	76.563	76.195	75.032	75.889	74.413	74.154	75.537
		sd	12.857	11.028	11.815	11.341	10.123	10.883	12.467
	AspD	mean	4.246	NaN	4.374	NaN	4.207	NaN	4.256
		sd	0.958	NA	0.931	NA	0.766	NA	0.903
vldl	Detm	mean	4.121	NaN	4.267	NaN	4.239	NaN	4.297
		sd	0.997	NA	1.114	NA	1.057	NA	1.050
	Biph	mean	4.126	NaN	4.196	NaN	4.261	NaN	4.273
		sd	0.870	NA	0.770	NA	0.812	NA	0.847
hdl	AspD	mean	2.256	NaN	2.398	NaN	2.239	NaN	2.315
		sd	0.826	NA	0.890	NA	0.658	NA	0.803
	Detm	mean	2.155	NaN	2.324	NaN	2.287	NaN	2.287
		sd	0.847	NA	0.927	NA	0.904	NA	0.842
vldl	Biph	mean	2.093	NaN	2.185	NaN	2.173	NaN	2.246
		sd	0.753	NA	0.679	NA	0.705	NA	0.726
	AspD	mean	1.142	NaN	1.184	NaN	1.174	NaN	1.133
		sd	0.323	NA	0.301	NA	0.335	NA	0.291
vldl	Detm	mean	1.133	NaN	1.151	NaN	1.171	NaN	1.117
		sd	0.330	NA	0.356	NA	0.415	NA	0.307
	Biph	mean	1.221	NaN	1.278	NaN	1.265	NaN	1.241
		sd	0.367	NA	0.386	NA	0.410	NA	0.368
vldl	AspD	mean	0.776	NaN	0.772	NaN	0.839	NaN	0.778
		sd	0.351	NA	0.344	NA	0.733	NA	0.365
	Detm	mean	0.814	NaN	0.804	NaN	0.799	NaN	0.807
		sd	0.415	NA	0.360	NA	0.393	NA	0.411

```

      Biph mean      0.783      NaN      0.695      NaN      0.739      NaN      0.748
      sd          0.400      NA       0.319      NA       0.373      NA       0.377
  trig  AspD mean      1.924      NaN      1.820      NaN      1.785      NaN      1.851
      sd          1.325      NA       0.987      NA       0.921      NA       1.205
      Detm mean      1.898      NaN      1.766      NaN      1.838      NaN      1.906
      sd          1.158      NA       0.860      NA       1.146      NA       1.226
      Biph mean      1.821      NaN      1.685      NaN      1.923      NaN      1.749
      sd          1.096      NA       1.295      NA       1.860      NA       1.065
> round( ftable( QQ[, ,c(1,7),4:5], col.vars=3:4), 3 )
      v1          v7
      mean      sd      mean      sd
  fimtavg  AspD      0.796      0.148      0.795      0.150
      Detm      0.798      0.139      0.778      0.129
      Biph      0.786      0.121      0.781      0.130
  fimtmax  AspD      0.954      0.165      0.954      0.170
      Detm      0.965      0.155      0.940      0.149
      Biph      0.949      0.140      0.943      0.151
  csc2     AspD      2.626      1.103      2.654      0.992
      Detm      2.575      1.053      2.649      0.992
      Biph      2.518      0.956      2.558      0.939
  iem      AspD 2314.408 1012.908 2188.873 858.809
      Detm 2348.003 1009.038 2192.966 867.971
      Biph 2376.867 1073.070 2321.016 1086.385
  imtareal AspD      19.277      5.144      19.071      5.151
      Detm      19.493      4.885      18.752      4.074
      Biph      18.638      4.103      18.939      4.117
  n.pl     AspD      3.511      3.573      4.056      4.171
      Detm      3.938      3.284      4.273      3.691
      Biph      3.437      2.714      4.059      3.569
  weight   AspD      97.454      14.957     100.176     17.021
      Detm      98.468      15.113     100.208     16.642
      Biph      95.572      14.831      99.282     16.370
  bmi      AspD      32.234      3.929      33.101      4.546
      Detm      32.399      4.291      32.868      4.685
      Biph      31.845      4.396      33.046      4.899
  whr      AspD      1.003      0.078      1.010      0.075
      Detm      1.008      0.090      1.022      0.087
      Biph      0.999      0.075      0.998      0.076
  hba1c    AspD      8.497      1.023      8.024      1.321
      Detm      8.531      1.119      8.266      1.190
      Biph      8.622      1.012      7.590      0.928
  gluc     AspD      9.861      3.082      8.537      3.349
      Detm     10.375      3.085      7.944      2.863
      Biph     10.653      3.549      8.603      2.544
  ins      AspD     104.600     94.633      67.408      66.371
      Detm     94.956     101.143     80.588     351.195
      Biph      80.399      65.171      77.311      79.639
  cpep     AspD     925.971     591.349     684.880     508.924
      Detm     903.146     544.527     561.075     390.283
      Biph     820.358     543.249     674.742     410.797
  idos     AspD      48.486      30.975     105.935      59.459
      Detm      47.110      36.025     145.040     101.117
      Biph      48.500      33.552      93.918      63.574
  ipkg     AspD      0.494      0.304      1.048      0.557
      Detm      0.470      0.325      1.423      0.877
      Biph      0.504      0.330      0.920      0.576
  sys      AspD     139.754     14.808     133.864     16.573
      Detm     139.820     16.120     135.429     15.550
      Biph     138.481     15.097     131.879     14.959
  dia      AspD      82.404      9.272      79.276      9.258
      Detm      81.801      9.443      78.529      8.960
      Biph      82.078      9.181      78.907      9.132
  pulse   AspD      75.836     11.441      74.495     12.109
      Detm      76.570     11.328      73.379     13.349
      Biph      76.563     12.857      75.537     12.467

```

```

chol    AspD    4.246    0.958    4.256    0.903
        Detm    4.121    0.997    4.297    1.050
        Biph    4.126    0.870    4.273    0.847
ldl     AspD    2.256    0.826    2.315    0.803
        Detm    2.155    0.847    2.287    0.842
        Biph    2.093    0.753    2.246    0.726
hdl     AspD    1.142    0.323    1.133    0.291
        Detm    1.133    0.330    1.117    0.307
        Biph    1.221    0.367    1.241    0.368
vldl    AspD    0.776    0.351    0.778    0.365
        Detm    0.814    0.415    0.807    0.411
        Biph    0.783    0.400    0.748    0.377
trig    AspD    1.924    1.325    1.851    1.205
        Detm    1.898    1.158    1.906    1.226
        Biph    1.821    1.096    1.749    1.065

> tt <- ftable( QQ[,c(1,7),4:5], col.vars=2:4)
> row.names(tt) <- attr(tt,"row.vars")[[1]]
> cat( "; Asp+Det ; ; ; Detemir ; ; ; Biphasic ; ; ; \n",
+      "; V1 ; ; V7 ; ; V1 ; ; V7 ; \n",
+      "; Mean ; SD ; Mean ; SD ; Mean ; SD ; Mean ; SD \n",
+      file="./results/LLCh-Tab2mi.csv" )
> for( i in 1:nrow(tt) )
+ write.table( formatC( tt[i,,drop=F], format="f", digits=dig[i] ),
+             file="./results/LLCh-Tab2mi.csv", append=TRUE, row.names=TRUE, col.names=FALSE,
+             quote=F, sep=";", dec="," )

```

2.3 Dropouts during the study

In the baseline file we have the drop-out date for those that did not complete the study:

```

> with( base, ftable( addmargins( table( grp, igr, is.na(xdate) ) ) ) )

```

		FALSE	TRUE	Sum
grp	igr			
Plc	AspD	15	58	73
	Detm	25	41	66
	Biph	9	58	67
	Sum	49	157	206
Met	AspD	13	52	65
	Detm	13	58	71
	Biph	5	65	70
	Sum	31	175	206
Sum	AspD	28	110	138
	Detm	38	99	137
	Biph	14	123	137
	Sum	80	332	412

2.3.1 Drop-out by Metformin status

This is a simple binomial regression, using log-link, so that we both get the estimated probabilities of drop-out and the relevant tests. Since the Metformin/Placebo classification only has 2 levels we could also use a simple 2×2 -table approach:

```

> with( base, twoby2( table(grp,is.na(xdate))[2:1,] ) )
2 by 2 table analysis:
-----
Outcome      : FALSE
Comparing    : Met vs. Plc

```

```

      FALSE TRUE   P(FALSE) 95% conf. interval
Met    31  175    0.1505   0.1079  0.2061
Plc    49  157    0.2379   0.1847  0.3008

                                95% conf. interval
      Relative Risk: 0.6327   0.4214  0.9497
      Sample Odds Ratio: 0.5676   0.3447  0.9346
      Conditional MLE Odds Ratio: 0.5684   0.3324  0.9604
      Probability difference: -0.0874   -0.1630 -0.0109

      Exact P-value: 0.0338
      Asymptotic P-value: 0.026
-----
> mm <- glm( !is.na(xdate) ~ grp-1, family=binomial(link=log), data=base )
> CM <- rbind( diag(2), c(-1,1) )
> rownames( CM ) <- c(levels(base$grp),
+                     paste( levels(base$grp)[2], "vs.",
+                             levels(base$grp)[1] ) )
> CM

      [,1] [,2]
Plc      1   0
Met      0   1
Met vs. Plc -1  1

> cbind( round( ci.exp( mm, ctr.mat=CM ), 2 ),
+        P=round( ci.lin( mm, ctr.mat=CM )[, "P"], 3 ) )

      exp(Est.) 2.5% 97.5%   P
Plc      0.24 0.19  0.30 0.000
Met      0.15 0.11  0.21 0.000
Met vs. Plc 0.63 0.42  0.95 0.027

```

2.3.2 Drop-out by Insulin group

This is again a simple binomial regression, using log-link, so that we both get the estimated drop-out rates and the differences. But there is no simple table approach here:

```

> mi <- glm( !is.na(xdate) ~ igr-1, family=binomial(link=log), data=base )
> ci.exp( mi )

      exp(Est.)   2.5%   97.5%
igrAspD 0.2028986 0.14576745 0.2824212
igrDetm 0.2773723 0.21168106 0.3634495
igrBiph 0.1021898 0.06220883 0.1678661

> CM <- rbind( diag(3), c(0,1,-1), c(-1,1,0), c(1,0,-1) )
> colnames( CM ) <- levels(base$igr)
> rownames( CM ) <- c(levels(base$igr),
+                     paste( levels(base$igr)[2], "vs.",
+                             levels(base$igr)[3] ),
+                     paste( levels(base$igr)[2], "vs.",
+                             levels(base$igr)[1] ),
+                     paste( levels(base$igr)[1], "vs.",
+                             levels(base$igr)[3] ) )
> CM

      AspD Detm Biph
AspD      1   0   0
Detm      0   1   0
Biph      0   0   1
Detm vs. Biph 0   1  -1
Detm vs. AspD -1  1   0
AspD vs. Biph 1   0  -1

> cbind( round( ci.exp( mi, ctr.mat=CM ), 2 ),
+        P=round( ci.lin( mi, ctr.mat=CM )[, "P"], 3 ) )

```

	exp(Est.)	2.5%	97.5%	P
AspD	0.20	0.15	0.28	0.000
Detm	0.28	0.21	0.36	0.000
Biph	0.10	0.06	0.17	0.000
Detm vs. Biph	2.71	1.54	4.78	0.001
Detm vs. AspD	1.37	0.89	2.10	0.151
AspD vs. Biph	1.99	1.09	3.60	0.024

2.3.3 Drop-out by randomization group

It would be of interest to see how the drop-out rate depends on *both* randomizations simultaneously:

```
> m2 <- glm( !is.na(xdate) ~ grp + relevel(igr,2),
+           family=binomial(link=log), data=base )
> round( ci.exp( m2 ), 2 )

              exp(Est.) 2.5% 97.5%
(Intercept)          0.35 0.26  0.47
grpMet              0.62 0.42  0.93
relevel(igr, 2)AspD  0.70 0.46  1.07
relevel(igr, 2)Biph  0.36 0.21  0.64

> m2i <- glm( !is.na(xdate) ~ grp:igr-1,
+            family=binomial(link=log), data=base )
> round( 100*ci.exp( m2i ), 1 )

              exp(Est.) 2.5% 97.5%
grpPlc:igrAspD    20.5 13.1  32.3
grpMet:igrAspD    20.0 12.3  32.5
grpPlc:igrDetm    37.9 27.8  51.6
grpMet:igrDetm    18.3 11.2  29.9
grpPlc:igrBiph    13.4  7.3  24.7
grpMet:igrBiph     7.1  3.1  16.6

> anova( m2i, m2, test="Chisq" )

Analysis of Deviance Table

Model 1: !is.na(xdate) ~ grp:igr - 1
Model 2: !is.na(xdate) ~ grp + relevel(igr, 2)
  Resid. Df Resid. Dev Df Deviance Pr(>Chi)
1       406      383.28
2        408      385.82 -2  -2.5421  0.2805
```

Even if there is clearly no evidence for differential effect of Metformin in the different insulin groups, we could evaluate the Metformin vs. Placebo relative risk of dropout in the three insulin groups, using the interaction model:

```
> CI <- rbind( c(-1,1,0,0,0,0),
+             c(0,0,-1,1,0,0),
+             c(0,0,0,0,-1,1) )
> rownames( CI ) <- levels( base$igr )
> cbind( round( ci.exp( m2i, ctr.mat=CI ), 2 ),
+       P=round( ci.lin( m2i, ctr.mat=CI )["P"], 3 ) )

              exp(Est.) 2.5% 97.5%      P
AspD          0.97 0.50  1.89 0.936
Detm          0.48 0.27  0.86 0.014
Biph          0.53 0.19  1.51 0.234
```

2.4 Insulin doses during study

We load the outcones dataset which included the actually prescribed insulin doses

```
> load( file="./data/outc.Rda" )
> str( outc )
'data.frame':      2587 obs. of  36 variables:
 $ subjid : int  10001 10001 10001 10001 10001 10001 10001 10001 10002 10002 ...
 $ visit  : Factor w/ 7 levels "v1","v2","v3",...: 1 2 3 4 5 6 7 1 2 3 ...
 $ grp    : Factor w/ 2 levels "Plc","Met": 2 2 2 2 2 2 2 1 1 1 ...
 $ igr    : Factor w/ 3 levels "AspD","Detm",...: 3 3 3 3 3 3 3 3 3 3 ...
 $ over.65: Factor w/ 2 levels "<65",">65": 2 2 2 2 2 2 2 2 2 2 ...
 $ pre.ins: Factor w/ 2 levels "preIns","noIns": 2 2 2 2 2 2 2 2 2 2 ...
 $ sdc    : Factor w/ 2 levels "SDC","notSDC": 2 2 2 2 2 2 2 2 2 2 ...
 $ weight : num  122 122 121 124 125 ...
 $ bmi    : num  33 33.1 32.8 33.7 34 ...
 $ whr    : num  1.1 1.04 1.08 1.07 1.07 ...
 $ hba1c  : num  7.9 7.1 6.3 5.9 6.1 6.8 6.3 7.6 7.5 6.9 ...
 $ gluc   : num  12.6 6.7 4.8 3.4 8.8 9.3 8.9 10.4 NA 9.9 ...
 $ ins    : num  60 NA NA NA NA NA 132 56 NA NA ...
 $ idos   : num  14 54 64 64 64 70 NA 14 38 40 ...
 $ ipkg   : num  0.115 0.442 0.53 0.515 0.51 ...
 $ cpep   : num  1192 NA NA NA NA ...
 $ chol   : num  4.4 NA 4 NA 5.1 NA 4 3.8 NA 4 ...
 $ ldl    : num  2.3 NA 2.2 NA 3 NA 2.3 1.7 NA 2 ...
 $ hdl    : num  1.3 NA 1.3 NA 1.4 NA 1.22 1.66 NA 1.6 ...
 $ vldl   : num  0.8 NA 0.5 NA 0.7 NA 0.5 0.5 NA 0.4 ...
 $ trig   : num  1.82 NA 1.1 NA 1.6 NA 1.03 1.03 NA 0.9 ...
 $ sys    : num  149 136 136 132 137 ...
 $ dia    : num  86 65.5 69.5 69 78.5 76 77.5 75.5 72.5 65 ...
 $ pulse  : num  89 98 85 87 82 95 87 77 68 77 ...
 $ vdate  : Date, format: "2008-09-22" "2009-01-05" ...
 $ dov    : num  2009 2009 2009 2009 2010 ...
 $ typ.mor: Factor w/ 4 levels "non","Bip","Asp",...: 1 2 2 2 2 2 NA 1 2 2 ...
 $ dos.mor: num  NA 30 38 38 38 44 NA NA 18 20 ...
 $ typ.lch: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 NA 1 1 1 ...
 $ dos.lch: num  NA NA NA NA NA NA NA NA NA NA ...
 $ typ.din: Factor w/ 4 levels "non","Bip","Asp",...: 2 2 2 2 2 2 NA 2 2 2 ...
 $ dos.din: num  14 24 26 26 26 26 NA 14 20 20 ...
 $ typ.bed: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 NA 1 1 1 ...
 $ dos.bed: num  NA NA NA NA NA NA NA NA NA NA ...
 $ typ.ext: Factor w/ 4 levels "non","Bip","Asp",...: 1 1 1 1 1 1 NA 1 1 1 ...
 $ dos.ext: num  NA NA NA NA NA NA NA NA NA NA ...
```

We want to know how many persons are on each treatment at each point in time. Since the analyses here only relate to visits 1-6, we make a version of the data where visit 7 is not included:

```
> out6 <- transform( subset( outc, visit != "v7" ), visit=factor(visit) )
```

With this we can make a quick overview of how many patients that at a given time is on a given type of insulin in the morning, and at the other times too — this should give a sanity check on the derived dataset.

```
> with( out6, print( ftable( addmargins( table( grp, igr, visit, typ.mor ),
+                                     margin = 1:2 ),
+                       col.vars=c(1,3) ),
+                       zero.print="." ) )
```

		grp Plc					Met					Sum								
		visit	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6
igr	typ.mor																			
AspD	non		2	.	2	.	.	1	1	1	1	.	.	.	3	1	3	.	.	1
	Bip		.	1	2	1	3	3	.	.	.	2	.	1	.	1	2	3	3	4

	Asp	71	68	62	61	58	53	64	60	59	56	55	51	135	128	121	117	113	104
	Det
Detm	non	56	16	7	4	3	2	53	22	14	13	9	7	109	38	21	17	12	9
	Bip
	Asp	.	1	3	3	4	4	1	3	3	4	4
	Det	10	40	43	45	39	37	17	43	50	49	52	53	27	83	93	94	91	90
Biph	non	22	6	1	1	1	1	19	9	8	6	6	6	41	15	9	7	7	7
	Bip	44	56	60	60	59	57	50	59	59	61	61	59	94	115	119	121	120	116
	Asp	1	1
	Det
Sum	non	80	22	10	5	4	4	73	32	23	19	15	13	153	54	33	24	19	17
	Bip	44	57	62	61	62	60	50	59	59	63	61	60	94	116	121	124	123	120
	Asp	71	69	65	64	62	57	65	60	59	56	55	51	136	129	124	120	117	108
	Det	10	40	43	45	39	37	17	43	50	49	52	53	27	83	93	94	91	90

```
> with( out6, print( ftable( addmargins( table( grp, igr, visit, typ.lch ),
+                               margin = 1:2 ),
+                               col.vars=c(1,3) ),
+                               zero.print="." ) )
```

		grp	Plc							Met							Sum						
		visit	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6			
igr	typ.lch																						
AspD	non		1	.	2	.	.	.	1	1	1	.	.	.	2	1	3	.	.	.			
	Bip		.	2	1	1	3	3	.	1	.	2	.	3	.	3	1	3	3	6			
	Asp		72	67	63	61	58	54	64	59	59	56	55	49	136	126	122	117	113	103			
	Det				
Detm	non		66	55	50	46	39	34	69	64	63	60	60	58	135	119	113	106	99	92			
	Bip				
	Asp		.	2	3	6	7	9	1	1	1	2	1	2	1	3	4	8	8	11			
	Det				
Biph	non		60	42	33	30	28	25	66	50	46	44	43	39	126	92	79	74	71	64			
	Bip		6	20	28	31	32	33	4	18	21	23	24	26	10	38	49	54	56	59			
	Asp				
	Det				
Sum	non		127	97	85	76	67	59	136	115	110	104	103	97	263	212	195	180	170	156			
	Bip		6	22	29	32	35	36	4	19	21	25	24	29	10	41	50	57	59	65			
	Asp		72	69	66	67	65	63	65	60	60	58	56	51	137	129	126	125	121	114			
	Det				

```
> with( out6, print( ftable( addmargins( table( grp, igr, visit, typ.din ),
+                               margin = 1:2 ),
+                               col.vars=c(1,3) ),
+                               zero.print="." ) )
```

		grp	Plc							Met							Sum						
		visit	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6	v1	v2	v3	v4	v5	v6			
igr	typ.din																						
AspD	non		1	.	2	.	.	.	1	1	1	.	.	.	2	1	3	.	.	.			
	Bip		.	.	1	3	4	3	.	.	.	2	.	2	.	.	1	5	4	5			
	Asp		72	69	63	59	57	54	64	60	59	56	55	50	136	129	122	115	112	104			
	Det				
Detm	non		66	55	48	40	31	27	69	63	62	59	55	53	135	118	110	99	86	80			
	Bip		1	1			
	Asp		.	2	5	12	15	16	.	2	2	3	6	7	.	4	7	15	21	23			
	Det				
Biph	non		4	.	1	1	2	3	5	.	.	.	1	2	9	.	1	1	3	5			
	Bip		62	62	60	60	58	55	65	68	67	67	66	63	127	130	127	127	124	118			
	Asp				
	Det				
Sum	non		71	55	51	41	33	30	75	64	63	59	56	55	146	119	114	100	89	85			
	Bip		62	62	61	63	62	58	66	68	67	69	66	65	128	130	128	132	128	123			
	Asp		72	71	68	71	72	70	64	62	61	59	61	57	136	133	129	130	133	127			
	Det				

```
> with( out6, print( ftable( addmargins( table( grp, igr, visit, typ.bed ),
+                               margin = 1:2 ),
+                               col.vars=c(1,3) ),
+                               zero.print="." ) )
```

```

      grp Plc      Met      Sum
      visit v1 v2 v3 v4 v5 v6 v1 v2 v3 v4 v5 v6 v1 v2 v3 v4 v5 v6
igr typ.bed
AspD non      .      .      2      .      .      .      .      1      1      .      .      .      .      1      3      .      .      .
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Det      73     69     64     62     61     57     65     60     59     58     55     52    138    129    123    120    116    109
Detm non      .      1      3      4      4      2      4      1      2      1      2      2      4      2      5      5      6      4
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Det      66     56     50     48     42     41     66     64     62     61     59     58    132    120    112    109    101     99
Biph non      66     62     61     61     60     58     70     68     67     67     67     65    136    130    128    128    127    123
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Det      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
Sum non      66     63     66     65     64     60     74     70     70     68     69     67    140    133    136    133    133    127
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Det     139    125    114    110    103     98    131    124    121    119    114    110    270    249    235    229    217    208

```

```

> with( out6, print( ftable( addmargins( table( grp, igr, visit, typ.ext ),
+                               margin = 1:2 ),
+                               col.vars=c(1,3) ),
+                               zero.print="." ) )

```

```

      grp Plc      Met      Sum
      visit v1 v2 v3 v4 v5 v6 v1 v2 v3 v4 v5 v6 v1 v2 v3 v4 v5 v6
igr typ.ext
AspD non      73     69     66     61     61     56     65     60     59     57     54     50    138    129    125    118    115    106
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      1      .      1      .      1      1      1      1      2      .      1      1      2      1      3
      Det      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
Detm non      66     56     51     50     43     38     70     64     64     59     60     58    136    120    115    109    103     96
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      1      2      2      3      5      .      1      .      3      1      2      .      2      2      5      4      7
      Det      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
Biph non      66     62     61     61     60     58     70     68     67     67     67     65    136    130    128    128    127    123
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Det      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
Sum non      205    187    178    172    164    152    205    192    190    183    181    173    410    379    368    355    345    325
      Bip      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .
      Asp      .      1      2      3      3      6      .      2      1      4      2      4      .      3      3      7      5    10
      Det      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .      .

```

If we want to know how many persons have had more than once per day Detemir at a given visit, we derive this variable on the fly:

```

> with( out6, ftable( table( grp, igr, visit,
+                               nDet2 = ( (typ.mor=="Det") +
+                               (typ.lch=="Det") +
+                               (typ.din=="Det") +
+                               (typ.bed=="Det") +
+                               (typ.ext=="Det") ) > 1, useNA="ifany" ),
+                               col.vars=c(1,3) ) )

```

```

      grp Plc      Met
      visit v1 v2 v3 v4 v5 v6 v1 v2 v3 v4 v5 v6
igr nDet2
AspD FALSE      73     69     66     62     61     57     65     61     60     58     55     52
      TRUE       0      0      0      0      0      0      0      0      0      0      0      0
      NA         0      0      0      0      0      0      0      0      0      0      0      0
Detm FALSE      56     17     12     10     10      8      57     23     16     14     11      9
      TRUE      10     40     41     42     36     35     13     42     48     48     50     51
      NA         0      0      0      0      0      0      1      0      0      0      0      0
Biph FALSE      66     62     61     61     60     58     70     68     67     67     67     65
      TRUE       0      0      0      0      0      0      0      0      0      0      0      0
      NA         1      1      0      0      0      0      0      0      0      0      0      0

```


But we actually want to know how many persons that at *any* time during the follow-up has been on a given type of insulin. Thus for each type of insulin we want to classify persons by the maximal no of times a day of this type of insulin they get. To this end we first compute how many times each person at each visit gets a given type of insulin:

```
> out6 <- transform( out6,
+                   nBip = ( (typ.mor=="Bip") +
+                           (typ.lch=="Bip") +
+                           (typ.din=="Bip") +
+                           (typ.bed=="Bip") +
+                           (typ.ext=="Bip") ),
+                   nAsp = ( (typ.mor=="Asp") +
+                           (typ.lch=="Asp") +
+                           (typ.din=="Asp") +
+                           (typ.bed=="Asp") +
+                           (typ.ext=="Asp") ),
+                   nDet = ( (typ.mor=="Det") +
+                           (typ.lch=="Det") +
+                           (typ.din=="Det") +
+                           (typ.bed=="Det") +
+                           (typ.ext=="Det") ) )
> names( out6 )
 [1] "subjid" "visit" "grp" "igr" "over.65" "pre.ins" "sdc" "weight"
 [9] "bmi" "whr" "hba1c" "gluc" "ins" "idos" "ipkg" "cpep"
[17] "chol" "ldl" "hdl" "vldl" "trig" "sys" "dia" "pulse"
[25] "vdate" "dov" "typ.mor" "dos.mor" "typ.lch" "dos.lch" "typ.din" "dos.din"
[33] "typ.bed" "dos.bed" "typ.ext" "dos.ext" "nBip" "nAsp" "nDet"
```

Then we aggregate over visits, computing the maximum number of doses of a given type across visits within each person. We take the randomization groupings into the the classification in order to have these for tabulation of the resulting dataset

```
> wh <- c(1,3,4,37:39)
> names( out6 )[wh]
 [1] "subjid" "grp" "igr" "nBip" "nAsp" "nDet"
> Nmax <- aggregate( out6[,37:39],
+                   out6[,c(1,3,4)],
+                   FUN = max )
> str( Nmax )
'data.frame': 412 obs. of 6 variables:
 $ subjid: int 10003 10007 10022 10028 20012 20014 20029 20037 20041 40010 ...
 $ grp : Factor w/ 2 levels "Plc","Met": 1 1 1 1 1 1 1 1 1 1 ...
 $ igr : Factor w/ 3 levels "AspD","Detm",...: 1 1 1 1 1 1 1 1 1 1 ...
 $ nBip : int 0 3 0 0 0 0 0 0 0 0 ...
 $ nAsp : int 3 3 3 3 3 3 3 3 3 3 ...
 $ nDet : int 1 1 1 1 1 1 1 1 1 1 ...
> summary( Nmax )
      subjid      grp      igr      nBip      nAsp      nDet
Min.   :10001 Plc:206 AspD:138 Min.   :0.000 Min.   :0.000 Min.   :0.0000
1st Qu.:60015 Met:206 Detm:137 1st Qu.:0.000 1st Qu.:0.000 1st Qu.:0.0000
Median :90015          Biph:137 Median :0.000 Median :0.000 Median :1.0000
Mean   :70154          Mean   :0.878 Mean   :1.141 Mean   :0.9366
3rd Qu.:91107          3rd Qu.:2.000 3rd Qu.:3.000 3rd Qu.:2.0000
Max.   :91231          Max.   :3.000 Max.   :4.000 Max.   :2.0000
      NA's      :2      NA's      :2      NA's      :2
> with( Nmax, ftable( addmargins( table( grp, igr, maxBip=nBip ), margin=1:3 ) ) )
      maxBip  0  1  2  3 Sum
grp igr
Plc AspD      64  4  0  5  73
Detm      66  0  0  0  66
```

```

      Biph      0  3 30 33 66
      Sum     130  7 30 38 205
Met AspD     58  4  0  3 65
  Detm      69  1  0  0 70
  Biph      0  5 35 30 70
  Sum     127 10 35 33 205
Sum AspD    122  8  0  8 138
  Detm     135  1  0  0 136
  Biph      0  8 65 63 136
  Sum     257 17 65 71 410

```

```

> with( Nmax, ftable( addmargins( table( grp, igr, maxAsp=nAsp ), margin=1:3 ) ) )
      maxAsp  0  1  2  3  4 Sum
grp igr
Plc AspD      0  0  1 71  1 73
  Detm     45  9  6  6  0 66
  Biph     66  0  0  0  0 66
  Sum     111  9  7 77  1 205
Met AspD      1  0  0 62  2 65
  Detm     59  8  2  1  0 70
  Biph     69  1  0  0  0 70
  Sum     129  9  2 63  2 205
Sum AspD      1  0  1 133  3 138
  Detm     104 17  8  7  0 136
  Biph     135  1  0  0  0 136
  Sum     240 18  9 140  3 410

```

```

> with( Nmax, ftable( addmargins( table( grp, igr, maxDet=nDet ), margin=1:3 ) ) )
      maxDet  0  1  2 Sum
grp igr
Plc AspD      0 73  0 73
  Detm      0 13 53 66
  Biph     66  0  0 66
  Sum     66 86 53 205
Met AspD      0 65  0 65
  Detm      0 13 57 70
  Biph     70  0  0 70
  Sum     70 78 57 205
Sum AspD      0 138  0 138
  Detm      0 26 110 136
  Biph    136  0  0 136
  Sum    136 164 110 410

```

Chapter 3

Serious adverse events

The adverse events are part of the base dataset, so we retrieve this:

```
> library(Epi)
> load( file="./data/base.Rda" )
> wh <- c(102,105,98,106)
> names( base )[wh]
[1] "sevhypos" "nonsevhy" "total.sa" "sae.sevh"
```

These variables are all counts of number of episodes for each person. Analyses of adverse events between patient groups is done by using

1. a Poisson model for the rate of events for each person
2. a logistic regression for the odds-ratio of any event

Both models are controlled for the stratification variables.

3.1 Analysis by Metformin/Placebo group

```
> for( i in wh )
+ {
+   cat( "\n-----\n",
+       names(base)[i], "\n" )
+   tt <- table(base[,i], base[, "grp" ] )
+   tt <- rbind( tt, apply( tt[-1,], 2, sum ),
+               apply( tt*as.numeric(dimnames(tt)[[1]]), 2, sum ) )
+   rownames(tt)[nrow(tt)-1:0] <- c("n.Ptt", "n.Epi")
+   print( t(tt)[2:1,] )
+   cat( "\n" )
+   RR <- ci.lin( glm( base[,i] ~ grp + pre.ins + over.65 + sdc,
+                     family=poisson, data=base ), E=T ) [2,c(5:7,4),drop=FALSE]
+   OR <- ci.lin( glm( (base[,i]>0) ~ grp + pre.ins + over.65 + sdc,
+                     family=binomial, data=base ), E=T ) [2,c(5:7,4),drop=FALSE]
+   est <- rbind( RR, OR )
+   rownames( est ) <- c("RR (N events)", "OR (Any event)")
+   colnames( est )[1] <- "Met vs. Plc"
+   print( round( est, 4 ) )
+ }
```

```
sevhypos
  0 1 2 4 6 n.Ptt n.Epi
Met 199 3 2 2 0      7    15
```

```
Plc 199 6 0 0 1      7      12
```

```
Met vs. Plc  2.5% 97.5%      P
RR (N events)      1.2494 0.5848 2.6694 0.5654
OR (Any event)     0.9972 0.3432 2.8970 0.9958
```

```
-----
nonsevhy
```

```
  0  1  2  3  4  5  6  7  8  9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
Met 49 15 12 10 12 3 3 7 6 5  4  3  3  1  3  1  2  3  1  5  0  0  2  2  2  2  1  3  1  0
Plc 50 15 12 16  6  9  3  6  5  2  7  4  3  2  3  4  2  2  1  2  3  2  1  2  2  0  3  1  2  1
  30 31 32 33 34 35 36 37 38 40 42 43 44 48 51 52 53 54 56 57 59 64 66 68 70 71 72 74
Met  2  2  3  0  1  2  0  3  3  0  2  2  0  2  0  1  0  1  0  0  1  2  0  0  2  0  0  0
Plc  1  2  1  1  1  4  1  1  0  1  0  1  1  1  1  0  1  0  1  2  0  0  1  1  0  1  1  1
  75 77 78 82 83 86 87 95 96 101 102 107 116 124 125 132 135 181 184 199 209 250 n.Ptt
Met  0  2  2  0  0  0  1  0  0  1  0  2  1  0  1  0  1  1  1  1  1  1  1  1  1  1  157
Plc  1  0  0  1  1  1  0  1  1  0  1  0  0  1  0  1  0  0  0  0  0  0  0  0  0  0  0  156
n.Epi
Met  4347
Plc  3161
```

```
Met vs. Plc  2.5% 97.5%      P
RR (N events)      1.3726 1.3112 1.437 0.0000
OR (Any event)     1.0185 0.6444 1.610 0.9374
```

```
-----
total.sa
```

```
  0  1  2  3  4  9 12 n.Ptt n.Epi
Met 152 41 9 2 1 0 1  54  81
Plc 161 33 6 2 3 1 0  45  72
```

```
Met vs. Plc  2.5% 97.5%      P
RR (N events)      1.1146 0.8114 1.5312 0.5029
OR (Any event)     1.2627 0.7994 1.9943 0.3173
```

```
-----
sae.sevh
```

```
  0  1  2  3  4  6 10 12 n.Ptt n.Epi
Met 148 40 10 4 3 0 0 1  58  96
Plc 157 35  7 1 4 1 1 0  49  84
```

```
Met vs. Plc  2.5% 97.5%      P
RR (N events)      1.1338 0.8460 1.5196 0.4007
OR (Any event)     1.2472 0.7989 1.9473 0.3311
```

3.2 Analysis by Insulin group

```
> CM <- rbind( c(1,0), c(0,1), c(1,-1) )
> rownames( CM ) <- paste( levels( base$igr )[c(2,3,2)], "vs.",
+                           levels( base$igr )[c(1,1,3)] )
> CM

      [,1] [,2]
Detm vs. AspD      1      0
Biph vs. AspD      0      1
Detm vs. Biph      1     -1

> for( i in wh )
+   {
+     cat( "\n-----\n",
+         names(base)[i], "\n" )
+     tt <- table(base[,i], base[, "igr" ] )
+     tt <- rbind( tt, apply( tt[-1,], 2, sum ),
```

```
+      apply( tt*as.numeric(dimnames(tt)[[1]]), 2, sum ) )
+   rownames(tt)[nrow(tt)-1:0] <- c("n.Ptt","n.Epi")
+   print( t(tt) )
+   cat ("\n")
+   RR <- ci.lin( p1 <- glm( base[,i] ~ igr + pre.ins + over.65 + sdc,
+                         family=poisson, data=base ),
+             subset="igr", ctr.mat=CM, E=T )[,c(5:7,4),drop=FALSE]
+   OR <- ci.lin( b1 <- glm( (base[,i]>0) ~ igr + pre.ins + over.65 + sdc,
+                         family=binomial, data=base ),
+             subset="igr", ctr.mat=CM, E=T )[,c(5:7,4),drop=FALSE]
+   est <- rbind( RR,
+               "RR=1" = c(NA,NA,NA,anova(p1,update(p1,~.-igr),test="Chisq")[2,5]),
+               OR,
+               "OR=1" = c(NA,NA,NA,anova(b1,update(b1,~.-igr),test="Chisq")[2,5]) )
+   rownames( est ) <- paste( c("RR (N events) ",
+                             "OR (Any event) ",
+                             " " ) [c(1,3,3,3,2,3,3,3)],
+                          rownames(est) )
+   colnames( est )[1] <- "Estimate"
+   print( round( est, 4 ) )
+ }
```

```
-----
sevhypos
  0 1 2 4 6 n.Ptt n.Epi
AspD 133 2 0 2 1 5 16
Detm 131 5 1 0 0 6 7
Biph 134 2 1 0 0 3 4
```

		Estimate	2.5%	97.5%	P
RR (N events)	Detm vs. AspD	0.4408	0.1814	1.0715	0.0707
	Biph vs. AspD	0.2534	0.0847	0.7579	0.0141
	Detm vs. Biph	1.7397	0.5093	5.9431	0.3770
	RR=1	NA	NA	NA	0.0162
OR (Any event)	Detm vs. AspD	1.2178	0.3625	4.0905	0.7500
	Biph vs. AspD	0.5968	0.1397	2.5487	0.4859
	Detm vs. Biph	2.0405	0.4996	8.3347	0.3205
	OR=1	NA	NA	NA	0.5840

```
-----
nonsevhy
  0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29
AspD 30 9 9 14 5 4 2 3 4 2 3 2 1 1 3 1 1 2 1 3 0 2 0 3 2 1 3 1 1 0
Detm 42 11 7 7 8 2 0 6 5 0 4 2 3 1 2 1 1 1 1 2 1 0 1 0 0 1 1 0 0 0
Biph 27 10 8 5 5 6 4 4 2 5 4 3 2 1 1 3 2 2 0 2 2 0 2 1 2 0 0 3 2 1
  30 31 32 33 34 35 36 37 38 40 42 43 44 48 51 52 53 54 56 57 59 64 66 68 70 71 72 74
AspD 1 1 1 1 2 1 0 0 1 0 0 0 1 0 0 0 1 0 1 0 1 1 0 1 1 0 1 0 0 0
Detm 1 1 1 0 0 3 0 3 1 1 1 1 0 2 1 0 0 0 0 1 1 0 1 0 1 0 1 1 1 1
Biph 1 2 2 0 0 2 1 1 1 0 1 2 0 1 0 1 0 1 0 1 0 1 0 0 0 0 1 0 0 0
  75 77 78 82 83 86 87 95 96 101 102 107 116 124 125 132 135 181 184 199 209 250 n.Ptt
AspD 0 1 2 0 1 1 0 1 1 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 1 108
Detm 1 1 0 0 0 0 0 0 0 0 0 0 1 0 1 0 0 0 0 0 0 1 0 0 0 1 0 95
Biph 0 0 0 1 0 0 1 0 0 0 0 1 1 1 0 1 1 1 0 1 1 0 1 0 1 0 1 0 110
n.Epi
AspD 2570
Detm 2115
Biph 2823
```

		Estimate	2.5%	97.5%	P
RR (N events)	Detm vs. AspD	0.8328	0.7862	0.8821	0.0000
	Biph vs. AspD	1.1065	1.0489	1.1672	0.0002
	Detm vs. Biph	0.7526	0.7114	0.7963	0.0000
	RR=1	NA	NA	NA	0.0000
OR (Any event)	Detm vs. AspD	0.6233	0.3592	1.0815	0.0927
	Biph vs. AspD	1.1334	0.6278	2.0460	0.6778
	Detm vs. Biph	0.5499	0.3131	0.9661	0.0375
	OR=1	NA	NA	NA	0.0814

```

-----
total.sa
      0  1  2  3  4  9  12  n.Ptt  n.Epi
AspD 107 23 4 2 2 0 0    31    45
Detm 106 26 3 1 0 1 0    31    44
Biph 100 25 8 1 2 0 1    37    64

RR (N events)  Detm vs. AspD  Estimate  2.5%  97.5%  P
                Biph vs. AspD  0.9882  0.6522  1.4974  0.9555
                Detm vs. Biph  1.4309  0.9772  2.0951  0.0656
                RR=1           0.6907  0.4705  1.0139  0.0588
                RR=1           NA      NA      NA      0.0900
OR (Any event) Detm vs. AspD  1.0125  0.5725  1.7906  0.9658
                Biph vs. AspD  1.2801  0.7354  2.2280  0.3826
                Detm vs. Biph  0.7910  0.4544  1.3771  0.4072
                OR=1           NA      NA      NA      0.6137
-----

```

```

-----
sae.sevh
      0  1  2  3  4  6  10  12  n.Ptt  n.Epi
AspD 103 23 5 2 4 1 0 0    35    61
Detm 104 26 4 1 1 0 1 0    33    51
Biph  98 26 8 2 2 0 0 1    39    68

RR (N events)  Detm vs. AspD  Estimate  2.5%  97.5%  P
                Biph vs. AspD  0.8446  0.5823  1.2251  0.3735
                Detm vs. Biph  1.1230  0.7948  1.5867  0.5107
                RR=1           0.7521  0.5231  1.0814  0.1241
                RR=1           NA      NA      NA      0.3013
OR (Any event) Detm vs. AspD  0.9357  0.5383  1.6264  0.8137
                Biph vs. AspD  1.1729  0.6845  2.0096  0.5617
                Detm vs. Biph  0.7978  0.4629  1.3749  0.4159
                OR=1           NA      NA      NA      0.7026
-----

```

Chapter 4

Primary outcome (CIMT)

4.1 Analysis as repeated measures

We load the data and the two necessary packages from R, and convert the subject indicator to a factor as is needed for use in `lmer`:

```
> library( lme4 )
> library( Epi )
> load( file="./data/AD.Rda" )
> AD$subjid <- factor( AD$subjid )
```

4.1.1 Model with baseline difference

We analyze data with a random effects model, for the CIMT-mean y_{it} on individual i at time $t = 1, 7$ (`fimtavg`), randomized to treatment $m = \text{Met, Plc}$ using subject as random, and with a separate metformin by time (`visit`) interaction:

$$\begin{aligned} y_{it} &= \mu + \beta_t + \gamma_{mt} \\ &+ \alpha_1 \text{over.65} + \alpha_2 \text{pre.ins} + \alpha_3 \text{sdc} \\ &+ a_i + e_{it}, \quad t = 1, 7 \\ a_i &\sim \mathcal{N}(0, \tau^2), \quad e_{it} \sim \mathcal{N}(0, \sigma^2), \quad \text{all independent} \end{aligned} \tag{4.1}$$

The model states that persons have an average baseline level of CIMT depending on randomization and stratification group; the mean at baseline and follow-up are:

$$\begin{aligned} \text{baseline:} & \quad \mu + \beta_1 + \gamma_{m1} + \alpha_1 \text{over.65} + \alpha_2 \text{pre.ins} + \alpha_3 \text{sdc} \\ \text{follow-up:} & \quad \mu + \beta_7 + \gamma_{m7} + \alpha_1 \text{over.65} + \alpha_2 \text{pre.ins} + \alpha_3 \text{sdc} \\ \text{change:} & \quad \beta_7 - \beta_1 + (\gamma_{m7} - \gamma_{m1}) \end{aligned}$$

So in the changes in CIMT are:

$$\begin{aligned} \text{metformin:} & \quad \beta_7 - \beta_1 + (\gamma_{\text{Met},7} - \gamma_{\text{Met},1}) \\ \text{placebo:} & \quad \beta_7 - \beta_1 + (\gamma_{\text{Plc},7} - \gamma_{\text{Plc},1}) \end{aligned}$$

The model as stated here is overparametrized, it can be identified if all parameters relating to baseline (β_1, γ_{m1}) and placebo ($\gamma_{\text{Plc},7}$) were set to 0, the changes in CIMT over the

follow-up will then be

$$\begin{aligned} \text{Metformin: } & \beta_7 + \gamma_{\text{Met},v7} \\ \text{Placebo: } & \beta_7 \\ \text{difference (Met-Plc): } & \gamma_{\text{Met},v7} \end{aligned}$$

These three parameters are those of interest which should be extracted.

The model is a random effects model that is very close to using the baseline (y_{i1}) as covariate in an analysis of the follow-up (y_{i7}) as outcome, as we shall see below:

```
> m0 <- lmer( fimtavg ~ -1 + visit + visit:grp + over.65 + pre.ins + sdc +(1|subjid),
+           data = AD )
> summary( m0 )

Linear mixed model fit by REML ['lmerMod']
Formula: fimtavg ~ -1 + visit + visit:grp + over.65 + pre.ins + sdc +      (1 | subjid)
Data: AD

REML criterion at convergence: -1383.079

Random effects:
 Groups   Name                Variance Std.Dev.
 subjid   (Intercept) 0.014486 0.12036
 Residual                    0.002639 0.05137
Number of obs: 783, groups: subjid, 412

Fixed effects:
              Estimate Std. Error t value
visitv1      0.7651115  0.0122561  62.43
visitv7      0.7515577  0.0123754  60.73
over.65>65   0.0897483  0.0138468   6.48
pre.insnoIns 0.0061575  0.0138009   0.45
sdcnnotSDC   0.0140605  0.0127182   1.11
visitv1:grpMet -0.0120250 0.0128962  -0.93
visitv7:grpMet 0.0007237  0.0130987   0.06

Correlation of Fixed Effects:
          vistv1 vistv7 o.65>6 pr.nsnI sdcSDC vst1:M
visitv7      0.905
over.65>65  -0.355 -0.351
pre.insnoIns -0.267 -0.266  0.075
sdcnnotSDC  -0.462 -0.456  0.031 -0.204
vst1:grpMt  -0.520 -0.434 -0.015  0.005 -0.006
vstv7:grpMt -0.432 -0.526 -0.017  0.008 -0.007  0.833

> round( ee <- ci.lin( m0, subset="visit" ), 4 )

              Estimate StdErr      z      P    2.5% 97.5%
visitv1      0.7651 0.0123 62.4268 0.0000  0.7411 0.7891
visitv7      0.7516 0.0124 60.7298 0.0000  0.7273 0.7758
visitv1:grpMet -0.0120 0.0129 -0.9324 0.3511 -0.0373 0.0133
visitv7:grpMet  0.0007 0.0131  0.0552 0.9559 -0.0249 0.0264

> C0 <- rbind(rbind(cbind(diag(2),0,0),
+                  cbind(diag(2),diag(2))),
+            c(-1,1,-1,1),
+            c(-1,1, 0,0),
+            c( 0,0,-1,1) )
> row.names(C0) <- c( paste( gN[c(1,1,2,2,2,1)],
+                          c(c("v1","v7")[c(1,2,1,2)]),
+                          rep("18m - baseline",2) ) ),
+                   paste( gN[2], "vs.", gN[1] ) )
> colnames(C0) <- row.names(ee)
> C0
```



```

          visitv1 visitv7 visitv1:grpMet
Placebo+Insulin v1          1          0          0
Placebo+Insulin v7          0          1          0
Metformin+Insulin v1        1          0          1
Metformin+Insulin v7        0          1          0
Metformin+Insulin 18m - baseline -1          1          -1
Placebo+Insulin 18m - baseline -1          1          0
Metformin+Insulin vs. Placebo+Insulin 0          0          -1

          visitv7:grpMet
Placebo+Insulin v1          0
Placebo+Insulin v7          0
Metformin+Insulin v1        0
Metformin+Insulin v7        1
Metformin+Insulin 18m - baseline 1
Placebo+Insulin 18m - baseline 0
Metformin+Insulin vs. Placebo+Insulin 1

> e0 <- ci.lin( m0, subset="visit", ctr.mat=C0 )
> round( e0, 4 )

          Estimate StdErr      z      P    2.5%
Placebo+Insulin v1      0.7651 0.0123 62.4268 0.0000 0.7411
Placebo+Insulin v7      0.7516 0.0124 60.7298 0.0000 0.7273
Metformin+Insulin v1    0.7531 0.0123 61.0270 0.0000 0.7289
Metformin+Insulin v7    0.7523 0.0124 60.6012 0.0000 0.7280
Metformin+Insulin 18m - baseline -0.0008 0.0053 -0.1529 0.8785 -0.0111
Placebo+Insulin 18m - baseline -0.0136 0.0054 -2.5283 0.0115 -0.0241
Metformin+Insulin vs. Placebo+Insulin 0.0127 0.0075 1.6963 0.0898 -0.0020
          97.5%
Placebo+Insulin v1      0.7891
Placebo+Insulin v7      0.7758
Metformin+Insulin v1    0.7773
Metformin+Insulin v7    0.7766
Metformin+Insulin 18m - baseline 0.0095
Placebo+Insulin 18m - baseline -0.0030
Metformin+Insulin vs. Placebo+Insulin 0.0275

```

The model fitted here gives a separate mean CIMT value for each of the randomization groups at each of the two timepoints. This allows derivation of the group-specific changes and the difference between these changes as shown above.

The assumption introduced in order to get these baseline-values is that the between-person-variation in CIMT is the same in the two randomization groups. So only the population-*means* at baseline are assumed different between the two randomization groups.

Note that the between-person-SD is 0.0144 mm whereas the the mean difference between the groups at baseline is $0.7531 - 0.7651 = -0.0120$ mm, in the same order of magnitude as the between-person SD, but with a SE of the same order too (0.0129).

4.1.2 Assuming identical mean baseline

Since the study is randomized, we might argue that it would be equally sensible to assume the the population means were identical at baseline too¹.

If we want to fit this model, we must hand-code the interaction at the follow-up visit:

```

> mm <- model.matrix( ~ visit:grp-1, data = AD )
> m7 <- mm[,xx <- grep("v7",colnames(mm))]
> head( m7 )

```

¹This is a rare example of a model with group×visit interaction but no corresponding group intercept, violating the so-called “principle of marginality”. But in this case there is an explicit argument for the model, namely the randomization at baseline.

```

      visitv7:grpPlc visitv7:grpMet
1           0           0
2           0           0
3           0           0
4           0           0
5           0           0
6           0           0

```

The model matrix `m7` thus generated only has the indicators of randomization group at follow-up, so we need the intercept in this model to take care of the overall mean:

```

> m1 <- lmer( fimtavg ~ m7 + over.65 + pre.ins + sdc + (1/subject),
+           data = AD )
> summary( m1 )
Linear mixed model fit by REML ['lmerMod']
Formula: fimtavg ~ m7 + over.65 + pre.ins + sdc + (1 | subject)
Data: AD

REML criterion at convergence: -1389.073

Random effects:
 Groups   Name                Variance Std.Dev.
 subject (Intercept)  0.014482 0.12034
 Residual                    0.002639 0.05137
Number of obs: 783, groups: subject, 412

Fixed effects:
              Estimate Std. Error t value
(Intercept)   0.759174   0.010470  72.51
m7visitv7:grpPlc -0.012628  0.005268  -2.40
m7visitv7:grpMet -0.001732  0.005173  -0.33
over.65>65     0.089549   0.013843   6.47
pre.insnoIns   0.006222   0.013799   0.45
sdcnnotSDC     0.013985   0.012716   1.10

Correlation of Fixed Effects:
      (Intr) m7v7:P m7v7:M o.65>6 pr.nsl
m7vstv7:grP -0.119
m7vstv7:grM -0.120  0.036
over.65>65 -0.425  0.006 -0.005
pre.insnoIns -0.309 -0.007  0.004  0.075
sdcnnotSDC  -0.545  0.006  0.003  0.031 -0.204
> round( ee <- ci.lin( m1, subset=1:3 ), 4 )

              Estimate StdErr      z      P    2.5%  97.5%
(Intercept)   0.7592 0.0105 72.5063 0.0000  0.7387  0.7797
m7visitv7:grpPlc -0.0126 0.0053 -2.3971 0.0165 -0.0230 -0.0023
m7visitv7:grpMet -0.0017 0.0052 -0.3347 0.7378 -0.0119  0.0084
> C1 <- rbind( c(1,0,0),
+           c(1,1,0),
+           c(1,0,0),
+           c(1,0,1),
+           c(0,0,1),
+           c(0,1,0),
+           c(0,-1,1) )
> colnames(C1) <- row.names(ee)
> C1

      (Intercept) m7visitv7:grpPlc m7visitv7:grpMet
[1,]             1             0             0
[2,]             1             1             0
[3,]             1             0             0
[4,]             1             0             1
[5,]             0             0             1
[6,]             0             1             0
[7,]             0             -1            1

```

```
> round( e1 <- ci.lin( m1, subset=1:3, ctr.mat=C1 ), 4 )
      Estimate StdErr      z      P    2.5%  97.5%
[1,]  0.7592 0.0105 72.5063 0.0000  0.7387  0.7797
[2,]  0.7465 0.0111 66.9806 0.0000  0.7247  0.7684
[3,]  0.7592 0.0105 72.5063 0.0000  0.7387  0.7797
[4,]  0.7574 0.0111 68.1777 0.0000  0.7357  0.7792
[5,] -0.0017 0.0052 -0.3347 0.7378 -0.0119  0.0084
[6,] -0.0126 0.0053 -2.3971 0.0165 -0.0230 -0.0023
[7,]  0.0109 0.0072  1.5033 0.1328 -0.0033  0.0251

> rownames( e1 ) <- rownames( e0 )
> round( e1, 4 )

      Estimate StdErr      z      P    2.5%
Placebo+Insulin v1      0.7592 0.0105 72.5063 0.0000  0.7387
Placebo+Insulin v7      0.7465 0.0111 66.9806 0.0000  0.7247
Metformin+Insulin v1    0.7592 0.0105 72.5063 0.0000  0.7387
Metformin+Insulin v7    0.7574 0.0111 68.1777 0.0000  0.7357
Metformin+Insulin 18m - baseline -0.0017 0.0052 -0.3347 0.7378 -0.0119
Placebo+Insulin 18m - baseline -0.0126 0.0053 -2.3971 0.0165 -0.0230
Metformin+Insulin vs. Placebo+Insulin  0.0109 0.0072  1.5033 0.1328 -0.0033
      97.5%
Placebo+Insulin v1      0.7797
Placebo+Insulin v7      0.7684
Metformin+Insulin v1    0.7797
Metformin+Insulin v7    0.7792
Metformin+Insulin 18m - baseline  0.0084
Placebo+Insulin 18m - baseline -0.0023
Metformin+Insulin vs. Placebo+Insulin  0.0251
```

We can compare the estimated changes within groups under the two different assumptions:

```
> round( cbind( e0[,1:2], e1[,1:2] ), 4 )

      Estimate StdErr Estimate StdErr
Placebo+Insulin v1      0.7651 0.0123  0.7592 0.0105
Placebo+Insulin v7      0.7516 0.0124  0.7465 0.0111
Metformin+Insulin v1    0.7531 0.0123  0.7592 0.0105
Metformin+Insulin v7    0.7523 0.0124  0.7574 0.0111
Metformin+Insulin 18m - baseline -0.0008 0.0053 -0.0017 0.0052
Placebo+Insulin 18m - baseline -0.0136 0.0054 -0.0126 0.0053
Metformin+Insulin vs. Placebo+Insulin  0.0127 0.0075  0.0109 0.0072
```

If we are going to present the effect measure as derived from the conditional model (*i.e.* using baseline as covariate, then we should use the estimated changes from the model `m1` without allowance for baseline imbalance.

4.1.3 Plotting results

For plotting convenience we need the `cnr` function:

```
> source( "cnr.R" )
> cnr
function (xf, yf)
{
  cn <- par()$usr
  xf <- ifelse(xf > 1, xf/100, xf)
  yf <- ifelse(yf > 1, yf/100, yf)
  xx <- (1 - xf) * cn[1] + xf * cn[2]
  yy <- (1 - yf) * cn[3] + yf * cn[4]
  if (par()$xlog)
    xx <- 10^xx
}
```

```

    if (par()$ylog)
      yy <- 10^yy
    list(x = xx, y = yy)
  }
> ppclr <- rgb( t(col2rgb(clr)+255)/2, max=255 )

```

We first produce an overview of the estimates of the absolute levels (in this case in the reference group, which is the largest: under 65, previous insulin, from SDC):

Note that the dramatically looking differences are of the same magnitude as the between person variation. The two lines represent the between-person SD from the two different models.

From the figure ?? it is clear that the changes in each group (and hence the difference between the changes) are pretty similar under the two models, it is the absolute levels in the groups that differ.

```

> par( mar=c(3,1,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[5:7,c(1,5,6)], lwd=4, cex=1.5,
+         xlab="", col=ppclr, vref=0, y=3:1+0.1,
+         restore.par=FALSE )
> linesEst( e1[5:7,c(1,5,6)], lwd=4, lty=3, cex=1.5,
+          xlab="", col=clr, vref=0, y=3:1-0.1,
+          restore.par=FALSE )
> axis( side=1 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6, col=clr[4] )

```

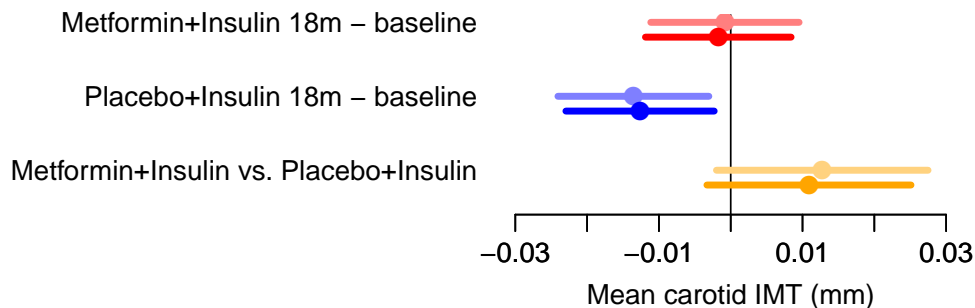


Figure 4.1: *Estimated changes and treatment effect on CIMT, full colors are from the model assuming common means at baseline, pale colors from the model allowing baseline imbalance.*

For the sake of showing the effects in slides we start out by defining the colors to be used for Metformin, Placebo, differences and the axes etc. on the transparent plots:

```

> win.metafile( "./results/forest1.emf", width=10, height=5, pointsize=24 )
> par( mar=c(3,1,1,1), mgp=c(3,1,0)/1.6,
+     bg="#black",
+     "transparent",
+     col.axis=clr[4], col.lab=clr[4] )
> plotEst( e0[5:7,c(1,5,6)], lwd=7, cex=1.5,
+         xlab="", col.txt="transparent", col=clr,
+         restore.par=FALSE )
> for( i in 1:3 ) axis( side=2, at=4-i, labels=rownames(e0)[4+i], col="transparent",
+                   col.axis= clr[i], las=1 )
> abline( v=0, col=clr[4] )
> axis( side=1, col=clr[4] )
> mtext( "Carotid intima-media thickness (mm)", side=1, line=3/1.6, col=clr[4] )
> dev.off()
null device
1

```

4.2 Analysis using baseline as covariate

Another way of looking at the analysis is to use the measurement at the second occasion using the baseline measurement as covariate. The regression on the baseline-value is effectively making an analysis *conditional* on this value for each person. This means that we are not making any assumptions about the population distribution of baseline-CIMT between the two randomization groups, that is, taking a step in the **opposite** direction from the initial model of the model assuming equal baseline means in the two groups.

But because of this lack of assumptions about the distribution of baseline CIMT measurements, the model does not address the change in CIMT in each treatment group, simply because the expected CIMT at baseline for a given person is not a parameter in the model.

4.2.1 Model

The main difference is that the absolute change in the response from baseline to follow-up in each of the groups does not appear as a parameter in this approach. The model is (for 7—follow-up and 1—baseline):

$$\begin{aligned}
 y_{i7} &= \mu + \theta y_{i1} + \gamma_m \\
 &\quad + \alpha_1 \text{o.65} + \alpha_2 \text{pre.ins} + \alpha_1 \text{SDC} \\
 &\quad + e_i, \\
 e_i &\sim \mathcal{N}(0, \sigma^2)
 \end{aligned}
 \tag{4.2}$$

The parameter of interest here is γ_m , the *difference* between the changes in the Met and the Plc groups.

In order to use this approach we restructure the data set so that we have only one row per person with follow-up and baseline as separate variables:

```

> names( AD )
  [1] "subjid"          "grp"           "igr"
  [4] "over.65"         "pre.ins"       "sdc"
  [7] "visit"           "weight"        "bmi"
 [10] "whr"             "hba1c"         "gluc"
 [13] "ins"             "idos"          "ipkg"
 [16] "cpep"           "chol"          "ldl"
 [19] "hdl"            "vldl"          "trig"
 [22] "sys"            "dia"           "pulse"
 [25] "vdate"          "dov"           "typ.mor"
 [28] "dos.mor"        "typ.lch"       "dos.lch"
 [31] "typ.din"        "dos.din"       "typ.bed"
 [34] "dos.bed"        "typ.ext"       "dos.ext"
 [37] "birthdat"       "visitdat"      "sex"
 [40] "diabetes"       "peri.neu"     "auto.neu"
 [43] "laserbeh"       "sys1.b0"       "dia1.b0"
 [46] "sys2.b0"        "dia2.b0"       "pulse.b0"
 [49] "microalb"       "macroalb"      "e.gfr"
 [52] "blbdat"         "smoking."      "alcohol."
 [55] "hba1c.b1"       "hba1c.b7"      "gluc.b1a"
 [58] "gluc.b7a"       "cpep.b1a"      "cpep.b7a"
 [61] "ins.b1a"        "ins.b7a"       "chol.b1a"
 [64] "chol.b7a"       "trig.b1a"      "trig.b7a"
 [67] "ldl.b1a"        "ldl.b7a"       "vldl.b1a"
 [70] "vldl.b7a"       "hdlc.b1a"      "hdlc.b7a"
 [73] "gad65.b1"       "weight.b"      "weight.2"

```

```

[76] "height.b"          "height.2"          "talje.b1"
[79] "talje.b7"          "hofte.b1"          "hofte.b7"
[82] "avgnatua"          "avgnatu2"          "metformi"
[85] "su"                 "statin"            "fibrat"
[88] "lipids"             "asa"                "thyre"
[91] "apurin"             "nsaid"              "painkill"
[94] "antidep"           "gaba"               "impo"
[97] "ntg"                "gastro"             "contrace"
[100] "antibiot"          "dvit"               "calc"
[103] "alendr"            "bvit"               "lung"
[106] "other"              "plataggr"          "iron"
[109] "fishoil"            "othernat"          "loop.ccb"
[112] "dvit.cal"           "bvit.iro"          "dob"
[115] "doV"                "dodm"               "dor"
[118] "caucas"             "gad.0"              "gad.pos"
[121] "retin"              "cvd"                 "ras"
[124] "oah"                "oad"                 "aav"
[127] "dmdurav"           "xdate"              "xtype"
[130] "total.sa"           "any.sae."           "allhypos"
[133] "sum.klar"           "sevhypos"           "any.hypo"
[136] "any.seve"           "nonsevhy"           "sae.sevh"
[139] "any.sae2"           "any.nons"           "pp"
[142] "datescanned"       "fimtavg"            "fimtmin"
[145] "fimtmax"            "minvesseldia"       "maxvesseldia"
[148] "vesselareal"        "lumenareal"         "imtareal"
[151] "systolicpressure"  "diastolicpressure" "ddpct"
[154] "csdpct"             "dc"                  "csc1"
[157] "csc2"               "iem"                 "fimtavg.R"
[160] "fimtmin.R"          "fimtmax.R"           "minvesseldia.R"
[163] "maxvesseldia.R"    "vesselareal.R"      "lumenareal.R"
[166] "imtareal.R"         "csc1.R"              "csc2.R"
[169] "iem.R"              "fimtavg.L"           "fimtmin.L"
[172] "fimtmax.L"          "minvesseldia.L"     "maxvesseldia.L"
[175] "vesselareal.L"     "lumenareal.L"       "imtareal.L"
[178] "csc1.L"             "csc2.L"              "iem.L"
[181] "BIF.L"              "BIF.R"               "CCA.L"
[184] "CCA.R"              "ICA.L"               "ICA.R"
[187] "n.pl"

> wimt <- reshape( AD[AD$visit %in% c("v1","v7"),
+                  c("fimtavg","visit","subjid","grp","over.65","pre.ins","sdc")],
+                  direction = "wide",
+                  v.names = "fimtavg",
+                  timevar = "visit",
+                  idvar = "subjid" )
> subset( AD[,c("fimtavg","visit","subjid","grp","over.65","pre.ins","sdc")],
+         subjid=="10002" )

  fimtavg visit subjid grp over.65 pre.ins  sdc
8    0.925   v1  10002 Plc    >65   noIns notSDC
9      NA    v2  10002 Plc    >65   noIns notSDC
10     NA    v3  10002 Plc    >65   noIns notSDC
11     NA    v4  10002 Plc    >65   noIns notSDC
12     NA    v5  10002 Plc    >65   noIns notSDC
13     NA    v6  10002 Plc    >65   noIns notSDC
14    0.760   v7  10002 Plc    >65   noIns notSDC

> subset( wimt, subjid=="10002" )

  subjid grp over.65 pre.ins  sdc fimtavg.v1 fimtavg.v7
8  10002 Plc    >65   noIns notSDC    0.925    0.76

```

We now have a dataset with the relevant variables, where we can estimate the difference in changes between the two groups:

```

> mf <- lm( fimtavg.v7 ~ fimtavg.v1 + grp + over.65 + pre.ins + sdc,
+          data = wimt )
> summary( mf )

```

```

Call:
lm(formula = fimtavg.v7 ~ fimtavg.v1 + grp + over.65 + pre.ins +
    sdc, data = wimt)

Residuals:
    Min       1Q   Median       3Q      Max
-0.246178 -0.039118  0.000996  0.042370  0.218314

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  0.105199   0.022289   4.720 3.37e-06
fimtavg.v1   0.839373   0.027631  30.378 < 2e-16
grpMet       0.010418   0.007252   1.437  0.1517
over.65>65  0.020962   0.008412   2.492  0.0132
pre.insnoIns -0.005352   0.008056  -0.664  0.5069
sdcnotSDC   0.011232   0.007432   1.511  0.1316

Residual standard error: 0.06966 on 365 degrees of freedom
(41 observations deleted due to missingness)
Multiple R-squared:  0.7439,    Adjusted R-squared:  0.7404
F-statistic:  212 on 5 and 365 DF,  p-value: < 2.2e-16
> mm <- lm( fimtavg.v7 ~ fimtavg.v1 + grp,
+          data = wimt )
> summary( mm )

Call:
lm(formula = fimtavg.v7 ~ fimtavg.v1 + grp, data = wimt)

Residuals:
    Min       1Q   Median       3Q      Max
-0.259533 -0.038533  0.000097  0.042784  0.218626

Coefficients:
            Estimate Std. Error t value Pr(>|t|)
(Intercept)  0.098472   0.021941   4.488 9.63e-06
fimtavg.v1   0.859657   0.026706  32.190 < 2e-16
grpMet       0.011424   0.007296   1.566  0.118

Residual standard error: 0.07018 on 368 degrees of freedom
(41 observations deleted due to missingness)
Multiple R-squared:  0.7379,    Adjusted R-squared:  0.7365
F-statistic:  518.1 on 2 and 368 DF,  p-value: < 2.2e-16
> round( cf <- ci.lin( mf, subset=c("fimt","Met") ), 4 )
            Estimate StdErr      z      P    2.5% 97.5%
fimtavg.v1  0.8394 0.0276 30.3782 0.0000  0.7852 0.8935
grpMet      0.0104 0.0073  1.4366 0.1508 -0.0038 0.0246
> round( cm <- ci.lin( mm, subset=c("fimt","Met") ), 4 )
            Estimate StdErr      z      P    2.5% 97.5%
fimtavg.v1  0.8597 0.0267 32.1899 0.0000  0.8073 0.9120
grpMet      0.0114 0.0073  1.5658 0.1174 -0.0029 0.0257

```

These estimates can now be compared with those from the random effects model, where the relevant quantities to compare are the additive effects of treatment:

```

> round( rbind( "Base-simple" = cm[2,],
+             "Base-contrl" = cf[2,],
+             "RanEff-dif" = e0[7,],
+             "RanEff-eql" = e1[7,] ), 4 )
            Estimate StdErr      z      P    2.5% 97.5%
Base-simple  0.0114 0.0073  1.5658 0.1174 -0.0029 0.0257
Base-contrl  0.0104 0.0073  1.4366 0.1508 -0.0038 0.0246
RanEff-dif   0.0127 0.0075  1.6963 0.0898 -0.0020 0.0275
RanEff-eql   0.0109 0.0072  1.5033 0.1328 -0.0033 0.0251

```

Clearly, the conclusion for the models are not substantially different; CIMT difference is some 0.01 mm larger between the groups at follow-up; in favor of the Placebo group.

```
> par( mar=c(3,1,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[5:7,c(1,5,6)], lwd=4, cex=1.5,
+         xlab="", col=ppclr, vref=0, y=3:1-0.1, ylim=c(0,3.5),
+         restore.par=FALSE )
> linesEst( e1[5:7,c(1,5,6)], lwd=4, lty=3, cex=1.5,
+          xlab="", col=clr, vref=0, y=3:1+0.1 )
> linesEst( cf[2,c(1,5,6),drop=FALSE], lwd=4, lty=3, cex=1.5,
+          xlab="", col=clr[4], vref=0, y=1+0.3 )
> axis( side=1 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6, col=clr[4] )
```

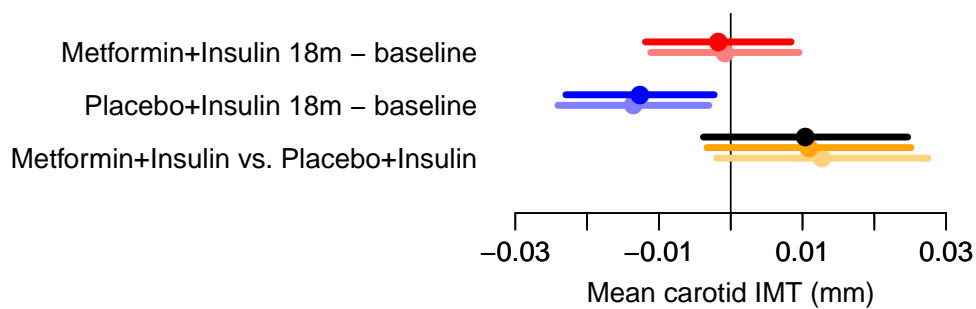


Figure 4.2: *Estimated changes and treatment effect on CIMT, full colors are from the model assuming common means at baseline, pale colors from the model allowing baseline imbalance. The top (black) estimate for the difference is the effect estimate from the conditional model using the baseline as covariate.*

4.3 Multiple imputation

```
> load( file="./data/AD.Rda" )
```

We see that there are some missing values in the follow-up values. Therefore we make a multiple imputation using a rich model to predict the outcome for additional analyses.

Hence we are using the multiple imputation on a wide dataset, expanded with the variables to be used in the imputation

```
> v.names <- c("fimtavg","hba1c","bmi","weight","sys","dia",
+             "chol","trig","ldl","hdl","idos","n.pl")
> wimt <- reshape( AD[,c("subjid","visit","grp","igr","over.65","pre.ins","sdc",
+             "sex","cvd","statin",
+             v.names)],
+               direction = "wide",
+               v.names = v.names,
+               timevar = "visit",
+               idvar = "subjid" )
> subset( AD[,c("fimtavg","visit","subjid","grp","igr","over.65","pre.ins","sdc","sex","cvd","statin",
+             "subjid=="10002" )
      fimtavg visit subjid grp igr over.65 pre.ins sdc sex cvd statin
8      0.925   v1 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
9      NA     v2 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
10     NA     v3 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
11     NA     v4 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
12     NA     v5 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
13     NA     v6 10002 Plc Biph >65 noIns notSDC 0 FALSE 1
14     0.760   v7 10002 Plc Biph >65 noIns notSDC 0 FALSE 1

> subset( wimt, subjid=="10002" )
      subjid grp igr over.65 pre.ins sdc sex cvd statin fimtavg.v1 hba1c.v1
8 10002 Plc Biph >65 noIns notSDC 0 FALSE 1 0.925 7.6
      bmi.v1 weight.v1 sys.v1 dia.v1 chol.v1 trig.v1 ldl.v1 hdl.v1 idos.v1
8 25.14208 66.8 128 75.5 3.8 1.03 1.7 1.66 14
      n.pl.v1 fimtavg.v2 hba1c.v2 bmi.v2 weight.v2 sys.v2 dia.v2 chol.v2 trig.v2
8 17 NA 7.5 25.44319 67.6 123 72.5 NA NA
      ldl.v2 hdl.v2 idos.v2 n.pl.v2 fimtavg.v3 hba1c.v3 bmi.v3 weight.v3 sys.v3
8 NA NA 38 NA NA 6.9 26.00775 69.1 115.5
      dia.v3 chol.v3 trig.v3 ldl.v3 hdl.v3 idos.v3 n.pl.v3 fimtavg.v4 hba1c.v4
8 65 4 0.9 2 1.6 40 NA NA 6.3
      bmi.v4 weight.v4 sys.v4 dia.v4 chol.v4 trig.v4 ldl.v4 hdl.v4 idos.v4
8 26.00775 69.1 131.5 71.5 NA NA NA NA 40
      n.pl.v4 fimtavg.v5 hba1c.v5 bmi.v5 weight.v5 sys.v5 dia.v5 chol.v5 trig.v5
8 NA NA 6.6 25.78193 68.5 133 68 4.7 0.6
      ldl.v5 hdl.v5 idos.v5 n.pl.v5 fimtavg.v6 hba1c.v6 bmi.v6 weight.v6 sys.v6
8 2.4 2 40 NA NA 6.4 26.23358 69.7 142.5
      dia.v6 chol.v6 trig.v6 ldl.v6 hdl.v6 idos.v6 n.pl.v6 fimtavg.v7 hba1c.v7
8 76 NA NA NA NA 40 NA 0.76 6.1
      bmi.v7 weight.v7 sys.v7 dia.v7 chol.v7 trig.v7 ldl.v7 hdl.v7 idos.v7
8 26.72287 71 107 66.5 4.2 1.05 1.6 2.08 NA
      n.pl.v7
8 23
```

Naturally, some of the generated variables in `ximt` have all missing values, so we exclude these from the dataset:

```
> wh.use <- names(wimt)[apply( wimt, 2, function(x) mean(is.na(x)) )<1]
> wimt <- wimt[,wh.use]
```

We then take a look at the missingness pattern of the outcome variable, since we will include this in the multiple imputation too:

```

> library( mice )
> library( foreign )
> mm <- cbind( 1:ncol(wimt),
+             t( apply( wimt, 2, function(x) c(sum(is.na(x)),
+                                             length(unique(x))) ) ) )
> colnames( mm ) <- c("no.", "N.miss", "N.values")
> mm

```

	no.	N.miss	N.values
subjid	1	0	412
grp	2	0	2
igr	3	0	3
over.65	4	0	2
pre.ins	5	0	2
sdsc	6	0	2
sex	7	0	2
cvd	8	0	2
statin	9	0	2
fimtag.v1	10	0	118
hba1c.v1	11	0	49
bmi.v1	12	0	404
weight.v1	13	0	299
sys.v1	14	5	119
dia.v1	15	5	88
chol.v1	16	0	46
trig.v1	17	0	228
ldl.v1	18	14	43
hdl.v1	19	0	129
idos.v1	20	2	79
n.pl.v1	21	118	18
hba1c.v2	22	32	61
bmi.v2	23	32	377
weight.v2	24	32	269
sys.v2	25	33	122
dia.v2	26	33	89
idos.v2	27	32	130
hba1c.v3	28	45	57
bmi.v3	29	42	370
weight.v3	30	42	273
sys.v3	31	42	124
dia.v3	32	42	87
chol.v3	33	66	49
trig.v3	34	69	179
ldl.v3	35	75	42
hdl.v3	36	66	95
idos.v3	37	45	142
hba1c.v4	38	53	55
bmi.v4	39	54	354
weight.v4	40	54	278
sys.v4	41	54	123
dia.v4	42	54	79
idos.v4	43	51	144
hba1c.v5	44	64	54
bmi.v5	45	65	344
weight.v5	46	65	263
sys.v5	47	64	112
dia.v5	48	64	80
chol.v5	49	74	44
trig.v5	50	75	187
ldl.v5	51	86	40
hdl.v5	52	75	107
idos.v5	53	63	146
hba1c.v6	54	83	46
bmi.v6	55	79	331
weight.v6	56	79	265
sys.v6	57	81	109
dia.v6	58	81	82

idos.v6	59	78	143
fimtavg.v7	60	41	105
hba1c.v7	61	39	56
bmi.v7	62	43	366
weight.v7	63	43	286
sys.v7	64	69	119
dia.v7	65	69	82
chol.v7	66	42	52
trig.v7	67	42	214
ldl.v7	68	55	40
hdl.v7	69	42	118
n.pl.v7	70	133	22

We must define the variables `sex`, `cvd` and `statin` as factors in order to get the imputation running properly:

```
> wimt <- transform( wimt, sex = factor(sex,labels=c("F","M")),
+                   cvd = factor(cvd,labels=c("No","Yes")),
+                   statin = factor(statin,labels=c("No","Yes")) )
> str( wimt )
'data.frame':      412 obs. of  70 variables:
 $ subjid      : int  10001 10002 10003 10004 10005 10006 10007 10008 10009 10010 ...
 $ grp         : Factor w/ 2 levels "Plc","Met": 2 1 1 1 1 1 1 1 1 2 ...
 $ igr         : Factor w/ 3 levels "Biph","AspD",...: 1 1 2 1 1 1 2 1 3 3 ...
 $ over.65    : Factor w/ 2 levels "<65",">65": 2 2 1 1 1 1 2 1 1 1 ...
 $ pre.ins    : Factor w/ 2 levels "preIns","noIns": 2 2 1 2 1 2 2 2 2 1 ...
 $ sdc        : Factor w/ 2 levels "SDC","notSDC": 2 2 2 2 2 2 2 2 2 2 ...
 $ sex        : Factor w/ 2 levels "F","M": 2 1 1 1 2 2 1 1 1 2 ...
 $ cvd        : Factor w/ 2 levels "No","Yes": 1 1 1 1 1 2 2 1 1 1 ...
 $ statin     : Factor w/ 2 levels "No","Yes": 1 2 2 2 2 2 2 2 2 2 ...
 $ fimtavg.v1 : num  0.825 0.925 0.94 1.02 0.71 0.805 0.78 0.96 0.585 0.7 ...
 $ hba1c.v1   : num  7.9 7.6 9.3 8.9 8.7 8.6 8.5 10.7 10.2 8.3 ...
 $ bmi.v1     : num  33 25.1 34.2 25.1 30.4 ...
 $ weight.v1  : num  121.7 66.8 98.8 77.8 96.4 ...
 $ sys.v1     : num  149 128 156 125 97.5 ...
 $ dia.v1     : num  86 75.5 93 83.5 60 70.5 79.5 89 93.5 76.5 ...
 $ chol.v1    : num  4.4 3.8 3.6 2.6 4.6 4.5 3.5 6.3 6.4 5.1 ...
 $ trig.v1    : num  1.82 1.03 1.61 3.31 2.28 1.93 1.74 4.36 2.48 4.29 ...
 $ ldl.v1     : num  2.3 1.7 1.9 0.6 2.8 2.1 1.2 3.4 4.2 2.2 ...
 $ hdl.v1     : num  1.3 1.66 1.01 0.5 0.81 1.5 1.55 0.95 1.03 0.95 ...
 $ idos.v1    : num  14 14 40 14 70 20 30 20 44 44 ...
 $ n.pl.v1    : int  4 17 NA 5 NA 3 5 NA 2 2 ...
 $ hba1c.v2   : num  7.1 7.5 10.5 10.6 9.2 8.2 8.6 9.4 11.1 7.7 ...
 $ bmi.v2     : num  33.1 25.4 34.7 27.2 31.6 ...
 $ weight.v2  : num  122.1 67.6 100.3 84.4 100 ...
 $ sys.v2     : num  136 123 145 128 136 ...
 $ dia.v2     : num  65.5 72.5 87 83.5 79 89.5 74.5 75.5 86 74.5 ...
 $ idos.v2    : num  54 38 86 146 156 66 52 170 90 66 ...
 $ hba1c.v3   : num  6.3 6.9 NA 8.7 8.1 6.8 6.9 7.3 10.7 8.2 ...
 $ bmi.v3     : num  32.8 26 NA 27.7 32 ...
 $ weight.v3  : num  120.8 69.1 NA 85.7 101.3 ...
 $ sys.v3     : num  136 116 NA 126 121 ...
 $ dia.v3     : num  69.5 65 NA 79 69.5 70 73.5 82 91.5 80 ...
 $ chol.v3    : num  4 4 NA 4.3 4.8 4.8 4.1 5.1 4.1 5 ...
 $ trig.v3    : num  1.1 0.9 NA 2.7 1.3 1.2 1.5 2.3 0.8 3.4 ...
 $ ldl.v3     : num  2.2 2 NA 2.3 3.3 2.9 2 3.1 2.6 2.5 ...
 $ hdl.v3     : num  1.3 1.6 NA 0.8 0.9 1.4 1.4 1 1.1 1 ...
 $ idos.v3    : num  64 40 NA 216 250 88 70 180 90 64 ...
 $ hba1c.v4   : num  5.9 6.3 NA 7.4 7.2 6.9 6.9 7.3 9.8 7.9 ...
 $ bmi.v4     : num  33.7 26 NA 28.3 32.5 ...
 $ weight.v4  : num  124.2 69.1 NA 87.8 102.9 ...
 $ sys.v4     : num  132 132 NA 120 130 ...
 $ dia.v4     : num  69 71.5 NA 79 77 77 71 81.5 93.5 82 ...
 $ idos.v4    : num  64 40 NA 292 306 88 70 160 146 62 ...
 $ hba1c.v5   : num  6.1 6.6 NA 6.6 6.8 6.8 6.9 7.1 10.3 8.3 ...
```


sd	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sex	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
cvd	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
statin	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimtavg.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
trig.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hdl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
dia.v1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
ldl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
hba1c.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
weight.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
idos.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
dia.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
hba1c.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimtavg.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v3	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
weight.v3	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
sys.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
trig.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
hdl.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
bmi.v7	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
weight.v7	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
hba1c.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v4	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1
bmi.v4	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
weight.v4	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
sys.v4	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
dia.v4	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
ldl.v7	1	0	0	0	1	1	1	1	1	1	1	1	1	1	0	0
idos.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v3	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
hdl.v3	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
trig.v3	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
sys.v7	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v7	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1
ldl.v3	1	1	1	1	1	1	1	1	1	1	1	0	1	1	0	1
trig.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	0	1	1
hdl.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1
idos.v6	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v6	1	1	1	1	1	1	0	1	1	0	1	1	1	1	1	1
ldl.v5	1	1	0	1	1	1	1	0	0	1	1	1	1	0	0	1
n.pl.v1	1	0	1	1	0	1	1	0	0	0	1	1	1	1	1	1
n.pl.v7	1	1	1	1	0	1	1	0	0	0	0	1	1	1	1	1
	2	2	2	2	2	3	3	3	3	3	3	4	4	4	4	4

	1	3	1	1	1	1	1	1	1	3	1	5	1	1	1	1	1
subjid	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
grp	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
igr	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
over.65	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
pre.ins	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sdsc	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sex	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
cvd	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
statin	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimtag.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
trig.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hdl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
dia.v1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
ldl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
weight.v2	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1
idos.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v2	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1
dia.v2	1	1	1	1	1	0	1	1	1	1	0	1	1	1	1	1	1
hba1c.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimtag.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v7	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
trig.v7	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
hdl.v7	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1
bmi.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v3	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v4	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
weight.v4	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
sys.v4	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
dia.v4	0	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1
ldl.v7	1	1	1	1	1	1	1	1	1	0	1	1	0	1	1	1	1
idos.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v5	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v5	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
weight.v5	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1
chol.v3	1	1	0	1	1	1	0	0	0	1	1	0	1	1	1	0	1
hdl.v3	1	1	0	1	1	1	0	0	0	1	1	0	1	1	1	0	1
trig.v3	1	1	0	1	1	0	0	0	0	1	1	0	1	1	1	0	1
sys.v7	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0
dia.v7	1	0	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0
chol.v5	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1
ldl.v3	1	1	0	1	1	1	0	0	0	1	0	0	1	1	1	0	1
trig.v5	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1
hdl.v5	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1
idos.v6	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0
bmi.v6	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	0
weight.v6	1	1	1	1	1	1	1	1	1	0	1	1	1	1	0	1	0
sys.v6	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	0

dia.v6	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	0
hba1c.v6	1	1	1	1	0	1	1	1	1	0	1	1	1	1	0	1	0
ldl.v5	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	0	1
n.pl.v1	0	0	1	0	1	0	1	1	1	1	1	0	0	0	0	1	1
n.pl.v7	0	0	1	1	1	0	0	1	1	1	1	0	0	0	0	1	1
	4	4	5	5	5	5	5	6	6	6	6	6	6	6	7	8	8
subjid	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5	1
grp	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
igr	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
over.65	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
pre.ins	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sdsc	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sex	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
cvd	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
statin	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimtag.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
trig.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hdl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ldl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
fimtag.v7	1	1	1	0	1	0	1	1	1	0	1	1	0	1	0	1	1
bmi.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
trig.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
hdl.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
bmi.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
weight.v7	1	1	1	1	1	0	1	1	1	0	1	1	0	1	0	1	1
hba1c.v3	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
idos.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v4	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v4	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
weight.v4	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
sys.v4	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
dia.v4	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1
ldl.v7	1	1	1	1	0	0	0	1	1	0	0	0	0	1	0	1	0
idos.v5	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	0	0
hba1c.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0
sys.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0
dia.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0
bmi.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0
weight.v5	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	0	0
chol.v3	1	0	1	1	1	1	1	1	1	1	0	0	1	1	0	1	1
hdl.v3	1	0	1	1	1	1	1	1	1	1	0	0	1	1	0	1	1
trig.v3	1	0	1	1	1	1	1	1	1	0	0	1	1	0	1	1	1
sys.v7	1	1	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1
dia.v7	1	1	1	1	1	1	1	0	0	0	0	0	0	0	0	1	1
chol.v5	1	0	1	1	1	1	0	0	1	1	1	1	1	0	1	0	0
ldl.v3	1	0	1	1	1	1	1	1	1	0	0	0	1	0	1	0	0

trig.v5	1	0	1	1	1	1	0	0	1	1	1	1	0	1	0	0
hdl.v5	1	0	1	1	1	1	0	0	1	1	1	1	0	1	0	0
idos.v6	0	1	0	0	0	1	1	0	0	1	1	1	0	1	0	0
bmi.v6	0	1	0	0	0	1	1	0	0	1	1	0	1	0	1	0
weight.v6	0	1	0	0	0	1	1	0	0	1	1	0	1	0	1	0
sys.v6	0	1	0	0	0	1	1	0	0	1	1	0	1	0	1	0
dia.v6	0	1	0	0	0	1	1	0	0	1	1	0	1	0	1	0
hba1c.v6	0	1	0	0	0	1	1	0	0	1	1	0	1	0	1	0
ldl.v5	1	0	1	1	1	1	0	0	1	1	1	1	0	1	0	0
n.pl.v1	0	0	1	0	0	1	1	0	0	1	1	1	0	1	1	1
n.pl.v7	0	1	1	0	0	0	1	1	0	0	1	1	0	0	0	1
	8	9	9	9	9	9	10	11	11	11	12	12	12	14	15	16
subjid	1	1	1	1	2	2	1	1	1	1	2	1	1	1	1	1
grp	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
igr	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
over.65	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
pre.ins	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sdsc	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sex	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
cvd	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
statin	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
fimavg.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
chol.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
trig.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hdl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
ldl.v1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
bmi.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
weight.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
idos.v2	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
sys.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
dia.v2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
hba1c.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
fimavg.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
bmi.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
weight.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
sys.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
dia.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
chol.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
trig.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
hdl.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
bmi.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
weight.v7	1	1	0	1	1	0	1	1	1	1	1	0	1	0	1	0
hba1c.v3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1
idos.v3	1	0	1	1	1	1	1	1	1	0	0	1	1	1	0	1
idos.v4	1	0	1	1	1	1	0	1	0	0	0	0	1	0	0	0
hba1c.v4	1	1	0	1	1	1	0	1	0	0	0	0	1	0	0	0
bmi.v4	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0
weight.v4	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0
sys.v4	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0
dia.v4	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0
ldl.v7	1	1	0	1	1	0	1	1	1	1	1	0	0	1	0	0
idos.v5	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0
hba1c.v5	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
sys.v5	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
dia.v5	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
bmi.v5	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
weight.v5	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
chol.v3	1	1	1	0	1	1	1	0	1	1	1	1	0	1	0	1

hba1c.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	64
sys.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	64
dia.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	64
bmi.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	65
weight.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	65
chol.v3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	66
hdl.v3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	66
trig.v3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	69
sys.v7	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	69
dia.v7	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	69
chol.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	74
ldl.v3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	75
trig.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	75
hdl.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	75
idos.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	78
bmi.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	79
weight.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	79
sys.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	81
dia.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	81
hba1c.v6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	83
ldl.v5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	86
n.pl.v1	0	0	0	1	0	1	1	1	1	0	0	1	1	1	0	118
n.pl.v7	1	0	0	1	0	0	0	0	1	0	0	0	0	0	0	133
	35	36	36	40	42	43	44	44	46	47	47	48	49	50	50	2986

```
> pairs( wimt[,8:22], gap=0, pch=16, cex=0.2 )
```

```
> pairs( wimt[,23:37], gap=0, pch=16, cex=0.2 )
```

```
> pairs( wimt[,38:53], gap=0, pch=16, cex=0.2 )
```

```
> pairs( wimt[,54:69], gap=0, pch=16, cex=0.2 )
```

With this in place we can now make a multiple imputation of the missing values, including those on the outcome variable:

```
> set.seed( 876528358 )
> mi.time <- system.time( imp <- mice( wimt[,-1], m=50 ) )
```

```
> mi.time
```

```
      user  system elapsed
873.70    0.70  892.36
```

```
> save( imp, file="./data/imp" )
```

4.4 Analysis of multiply imputed data

Once we have done the imputation we can make the analyses based on the imputed data one with the Metformin / Placebo comparison, and one with the comparisons between the insulin groups.

```
> library( mice )
> load( file="./data/imp" )
> class( imp )
[1] "mids"
```

```

> mf <- with( imp, lm( fimtavg.v7 ~ fimtavg.v1 + grp + over.65 + pre.ins + sdc ) )
> round( summary( pool( mf ) ), 4 )

              est      se      t      df Pr(>|t|)   lo 95   hi 95  nmis    fmi
(Intercept)  0.1016 0.0230  4.4093 332.6742  0.0000  0.0563 0.1469   NA 0.1124
fimtavg.v1   0.8431 0.0287 29.4023 325.2795  0.0000  0.7867 0.8995    0 0.1213
grp2         0.0118 0.0074  1.5958 339.5838  0.1115 -0.0028 0.0264   NA 0.1039
over.652    0.0214 0.0089  2.4067 291.5830  0.0167  0.0039 0.0389   NA 0.1618
pre.ins2    -0.0045 0.0083 -0.5377 323.6307  0.5911 -0.0208 0.0119   NA 0.1233
sdc2        0.0098 0.0077  1.2762 316.8374  0.2028 -0.0053 0.0250   NA 0.1315

              lambda
(Intercept)  0.1071
fimtavg.v1   0.1160
grp2         0.0987
over.652    0.1560
pre.ins2    0.1179
sdc2        0.1260

> round( smf <- ci.lin( pool( mf ), subset="grp" ), 4 )

              Estimate StdErr      z      P    2.5%  97.5%
grp2         0.0118 0.0074  1.5958 0.1105 -0.0027 0.0264

> rownames( smf ) <- paste( gN[2], "vs.", gN[1] )

```

With the estimate for the metformin effect in `smm` (which is the relevant one) we can now re-do the forest plot using the “old” estimates of the corrected changes estimated from the random-effects model:

```

> round( rbind( e1[5:6,c(1,5,6)],
+             smf[ ,c(1,5,6)] ), 3 )

              Estimate    2.5%  97.5%
Metformin+Insulin 18m - baseline  -0.002 -0.012  0.008
Placebo+Insulin 18m - baseline   -0.013 -0.023 -0.002
                                0.012 -0.003  0.026

> tmpl <-
+ function()
+ {
+ par( mar=c(3,1,1,1), mgp=c(3,1,0)/1.6 )
+ plotEst( rbind(e1[5:6,c(1,5,6)],smf[,c(1,5,6)]),
+         ylim=c(0,3.5),
+         txt=rownames(e0)[5:7], lwd=3, cex=1.5, col=clr,
+         restore.par=FALSE )
+ abline( v=0 )
+ axis( side=1 )
+ text( -0.03, 0.2, "Improvement" , adj=0, col=clr[4], cex=0.8 )
+ text( 0.03, 0.2, "Deterioration", adj=1, col=clr[4], cex=0.8 )
+ mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )
+ }
> tmpl()

> win.metafile( "./results/forest-met-imp.emf", width=10, height=6, pointsize=20 )
> tmpl()
> dev.off()

null device
1

```

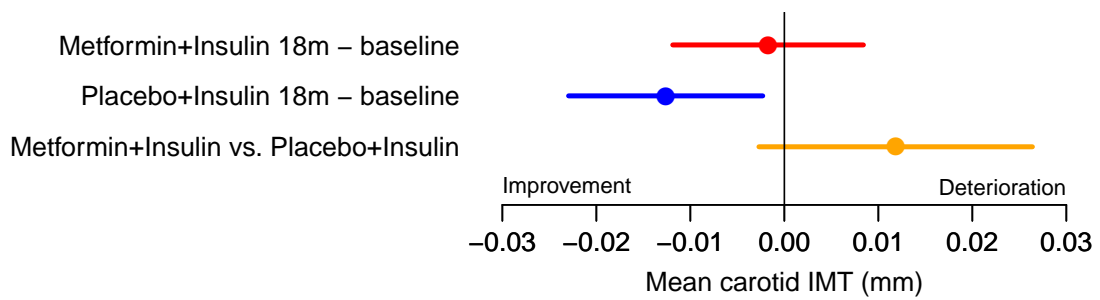


Figure 4.3: *Estimated changes in each treatment group from the random effects model with identical baseline. The difference in changes between treatments is the estimate from the model with baseline as covariate, using multiply imputed data, adjusted for stratification variables. Bars indicate 95% c.i.*

Chapter 5

Primary outcome (CIMT) by insulin type

5.1 Analysis of CIMT by insulin group

We now do the analysis of CIMT by insulin group, first by a random effects model *with* baseline differences between groups: First we fit the random effects model that allows different baseline means between the randomization groups, and from that model extract both the individual changes in each of the three groups, and the differences in changes between them:

```
> m0 <- lmer( fimtavg ~ -1 + visit + visit:igr + over.65 + pre.ins + sdc +(1|subjid),
+           data = AD )
> summary( m0 )

Linear mixed model fit by REML ['lmerMod']
Formula: fimtavg ~ -1 + visit + visit:igr + over.65 + pre.ins + sdc +      (1 | subjid)
Data: AD

REML criterion at convergence: -1369.156

Random effects:
Groups   Name                Variance Std.Dev.
subjid   (Intercept) 0.014475 0.12031
Residual                    0.002654 0.05152
Number of obs: 783, groups: subjid, 412

Fixed effects:
              Estimate Std. Error t value
visitv1      0.750871   0.013932  53.90
visitv7      0.742022   0.014021  52.92
over.65>65   0.089815   0.013845   6.49
pre.insnoIns 0.006249   0.013800   0.45
sdcnnotSDC   0.013905   0.012717   1.09
visitv1:igrAspD 0.011096   0.015786   0.70
visitv7:igrAspD 0.019900   0.016000   1.24
visitv1:igrDetm 0.013664   0.015815   0.86
visitv7:igrDetm 0.010015   0.016073   0.62

Correlation of Fixed Effects:
              vistv1 vistv7 o.65>6 pr.nsl sdcSDC vs1:AD vs7:AD vst1:D
visitv7      0.893
over.65>65  -0.328 -0.326
pre.insnoIns -0.239 -0.238 0.075
sdcnnotSDC  -0.405 -0.399 0.031 -0.204
vstv1:grAsD -0.572 -0.481 0.009 0.010 -0.004
```

```

vstv7:grAsD -0.476 -0.573 0.008 0.009 -0.007 0.834
vstv1:grDetm -0.571 -0.480 0.013 0.009 -0.007 0.501 0.418
vstv7:grDetm -0.474 -0.571 0.014 0.007 -0.009 0.417 0.499 0.832
> round( ee <- ci.lin( m0, subset="visit" ), 4 )

      Estimate StdErr      z      P    2.5% 97.5%
visitv1      0.7509 0.0139 53.8958 0.0000  0.7236 0.7782
visitv7      0.7420 0.0140 52.9232 0.0000  0.7145 0.7695
visitv1:igrAspD 0.0111 0.0158  0.7029 0.4821 -0.0198 0.0420
visitv7:igrAspD 0.0199 0.0160  1.2437 0.2136 -0.0115 0.0513
visitv1:igrDetm 0.0137 0.0158  0.8640 0.3876 -0.0173 0.0447
visitv7:igrDetm 0.0100 0.0161  0.6231 0.5332 -0.0215 0.0415
> CO <- rbind( cbind(diag(2), 0,0, 0,0 ),
+             cbind(diag(2),diag(2), 0,0 ),
+             cbind(diag(2), 0,0,diag(2)) )
> CO <- rbind( CO, CO[2,]-CO[1,],
+             CO[4,]-CO[3,],
+             CO[6,]-CO[5,] )
> CO <- rbind( CO, CO[8,]-CO[7,],
+             CO[9,]-CO[7,],
+             CO[9,]-CO[8,] )
> row.names(CO) <- c(
+ as.vector( outer( c("v1","v7"), levels(AD$igr), function(x,y) paste(y,x) ) ),
+ paste( levels(AD$igr), "v7-v1" ),
+ paste( "d", levels(AD$igr)[c(2,3,3)],
+       "- d", levels(AD$igr)[c(1,1,2)] ) )
> colnames(CO) <- row.names(ee)
> CO

      visitv1 visitv7 visitv1:igrAspD visitv7:igrAspD visitv1:igrDetm
Biph v1          1          0              0              0              0
Biph v7          0          1              0              0              0
AspD v1          1          0              1              0              0
AspD v7          0          1              0              1              0
Detm v1          1          0              0              0              1
Detm v7          0          1              0              0              0
Biph v7-v1      -1          1              0              0              0
AspD v7-v1     -1          1             -1              1              0
Detm v7-v1     -1          1              0              0             -1
d AspD - d Biph  0          0             -1              1              0
d Detm - d Biph  0          0              0              0             -1
d Detm - d AspD  0          0              1             -1             -1
      visitv7:igrDetm
Biph v1          0
Biph v7          0
AspD v1          0
AspD v7          0
Detm v1          0
Detm v7          1
Biph v7-v1       0
AspD v7-v1       0
Detm v7-v1       1
d AspD - d Biph  0
d Detm - d Biph  1
d Detm - d AspD  1
> e0 <- ci.lin( m0, subset="visit", ctr.mat=CO )
> inames <- c("Biphasic","Asp+Det","Detemir")
> cbind( levels( AD$igr ), inames )

      inames
[1,] "Biph" "Biphasic"
[2,] "AspD" "Asp+Det"
[3,] "Detm" "Detemir"
> elab <- c( paste(inames,"18m - baseline"),
+           paste(inames[c(2,3,3)], "vs.",
+           inames[c(1,1,2)], "change" ) )

```

```
> rownames( e0 )[7:12] <- elab
> round( e0[7:12,c(1,5,6,4)], 4 )

      Estimate    2.5%  97.5%    P
Biphasic 18m - baseline -0.0088 -0.0215 0.0038 0.1715
Asp+Det 18m - baseline  0.0000 -0.0128 0.0127 0.9945
Detemir 18m - baseline -0.0125 -0.0255 0.0005 0.0590
Asp+Det vs. Biphasic change 0.0088 -0.0092 0.0268 0.3369
Detemir vs. Biphasic change -0.0036 -0.0218 0.0145 0.6934
Detemir vs. Asp+Det change -0.0125 -0.0306 0.0057 0.1793
```

We can make a plot of this:

```
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[7:12,c(1,5,6)], lwd=3, vref=0, y=rev(c(1:3,5:7))+1,
+         xlab="", ylim=c(0,8), xlim=c(-0.03,0.03),
+         col.lines =iclr[c(1:3,1,1,2)],
+         col.points=iclr[c(1:3,2,3,3)], cex=1.5 )
> axis( side=1 )
> text( -0.03, 0.2, "Improvement" , adj=0, col=clr[4], cex=0.8 )
> text( 0.03, 0.2, "Deterioration", adj=1, col=clr[4], cex=0.8 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )
```

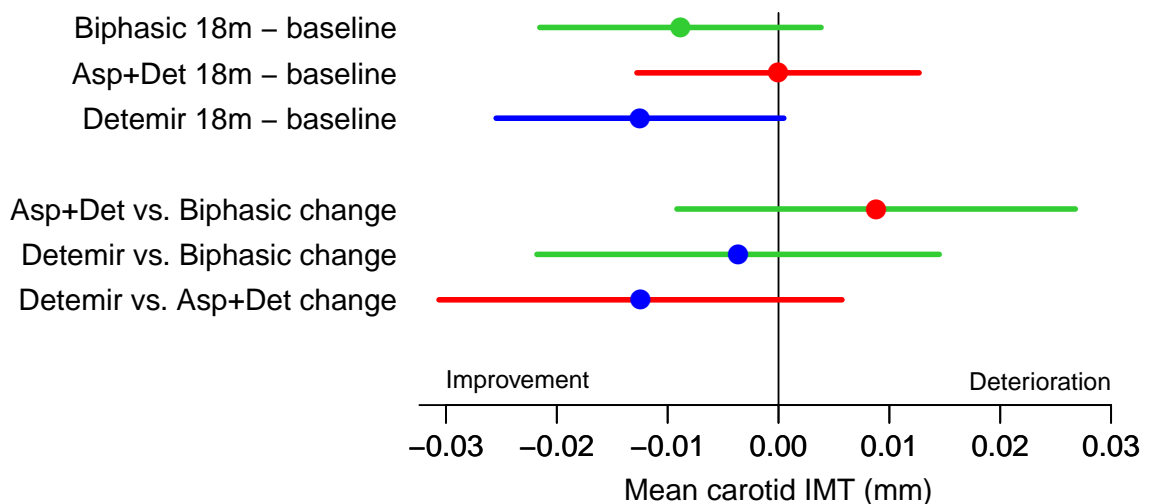


Figure 5.1: Estimates of insulin regimen effects from a random effects model with baseline differences for complete ITT data, adjusted for stratification variables.

Analysis with identical baseline values

We also fit a model with identical baselines for the three groups; and again it is necessary to hand-code the effects:

```
> mm <- model.matrix( ~ visit:igr-1, data = AD )
> m7 <- mm[,xx <- grep("v7",colnames(mm))]
> head( m7 )

      visitv7:igrBiph visitv7:igrAspD visitv7:igrDetm
1              0              0              0
2              0              0              0
3              0              0              0
4              0              0              0
5              0              0              0
6              0              0              0
```


The model matrix `m7` thus generated only has the indicators of randomization group at follow-up, so we need the intercept in this model to take care of the overall mean:

```
> m1 <- lmer( fimtavg ~ m7 + over.65 + pre.ins + sdc + (1|subjid),
+           data = AD )
> summary( m1 )
Linear mixed model fit by REML ['lmerMod']
Formula: fimtavg ~ m7 + over.65 + pre.ins + sdc + (1 | subjid)
Data: AD

REML criterion at convergence: -1381.517

Random effects:
  Groups   Name                Variance Std.Dev.
  subjid   (Intercept)  0.014433 0.12014
  Residual                    0.002654 0.05152
Number of obs: 783, groups: subjid, 412

Fixed effects:
              Estimate Std. Error t value
(Intercept)    0.7591776  0.0104583   72.59
m7visitv7:igrBiph -0.0101292  0.0063133   -1.60
m7visitv7:igrAspD  0.0003949  0.0063375    0.06
m7visitv7:igrDetm -0.0116614  0.0064651   -1.80
over.65>65      0.0896469  0.0138254    6.48
pre.insnoIns     0.0061213  0.0137808    0.44
sdcnnotSDC      0.0139843  0.0127003    1.10

Correlation of Fixed Effects:
      (Intr) m7v7:B m77:AD m7v7:D o.65>6 pr.nsI
m7vstv7:grB -0.101
m7vstv7:gAD -0.098  0.025
m7vstv7:grD -0.097  0.024  0.024
over.65>65 -0.425 -0.003 -0.001  0.006
pre.insnoIns -0.309 -0.003  0.001 -0.002  0.075
sdcnnotSDC  -0.545  0.010  0.001  0.000  0.031 -0.204

> round( ee <- ci.lin( m1, subset=1:4 ), 4 )

              Estimate StdErr      z      P    2.5% 97.5%
(Intercept)    0.7592 0.0105 72.5906 0.0000  0.7387 0.7797
m7visitv7:igrBiph -0.0101 0.0063 -1.6044 0.1086 -0.0225 0.0022
m7visitv7:igrAspD  0.0004 0.0063  0.0623 0.9503 -0.0120 0.0128
m7visitv7:igrDetm -0.0117 0.0065 -1.8037 0.0713 -0.0243 0.0010

> C1 <- rbind( c(1,0,0,0),
+           c(1,1,0,0),
+           c(1,0,0,0),
+           c(1,0,1,0),
+           c(1,0,0,0),
+           c(1,0,0,1) )
> C1 <- rbind( C1, C1[2,]-C1[1,],
+           C1[4,]-C1[3,],
+           C1[6,]-C1[5,] )
> C1 <- rbind( C1, C1[8,]-C1[7,],
+           C1[9,]-C1[7,],
+           C1[9,]-C1[8,] )
> rownames(C1) <- row.names(C0)
> colnames(C1) <- row.names(ee)
> C1

              (Intercept) m7visitv7:igrBiph m7visitv7:igrAspD
Biph v1                1                0                0
Biph v7                1                1                0
AspD v1                1                0                0
AspD v7                1                0                1
Detm v1                1                0                0
Detm v7                1                0                0
```

```

Biph v7-v1          0          1          0
AspD v7-v1         0          0          1
Detm v7-v1         0          0          0
d AspD - d Biph    0          -1         1
d Detm - d Biph    0          -1         0
d Detm - d AspD    0          0         -1
m7visitv7:igrDetm
Biph v1            0
Biph v7            0
AspD v1            0
AspD v7            0
Detm v1            0
Detm v7            1
Biph v7-v1         0
AspD v7-v1         0
Detm v7-v1         1
d AspD - d Biph    0
d Detm - d Biph    1
d Detm - d AspD    1
> round( e1 <- ci.lin( m1, subset=1:4, ctr.mat=C1 ), 4 )

```

	Estimate	StdErr	z	P	2.5%	97.5%
Biph v1	0.7592	0.0105	72.5906	0.0000	0.7387	0.7797
Biph v7	0.7490	0.0117	64.2646	0.0000	0.7262	0.7719
AspD v1	0.7592	0.0105	72.5906	0.0000	0.7387	0.7797
AspD v7	0.7596	0.0117	64.9889	0.0000	0.7367	0.7825
Detm v1	0.7592	0.0105	72.5906	0.0000	0.7387	0.7797
Detm v7	0.7475	0.0118	63.6095	0.0000	0.7245	0.7705
Biph v7-v1	-0.0101	0.0063	-1.6044	0.1086	-0.0225	0.0022
AspD v7-v1	0.0004	0.0063	0.0623	0.9503	-0.0120	0.0128
Detm v7-v1	-0.0117	0.0065	-1.8037	0.0713	-0.0243	0.0010
d AspD - d Biph	0.0105	0.0088	1.1915	0.2335	-0.0068	0.0278
d Detm - d Biph	-0.0015	0.0089	-0.1717	0.8637	-0.0190	0.0160
d Detm - d AspD	-0.0121	0.0089	-1.3483	0.1776	-0.0296	0.0055

```

> rownames( e1 ) <- rownames( e0 )

```

We can compare the estimated changes within groups under the two different assumptions:

```

> round( cbind( e0[,1:2], e1[,1:2] ), 4 )

```

	Estimate	StdErr	Estimate	StdErr
Biph v1	0.7509	0.0139	0.7592	0.0105
Biph v7	0.7420	0.0140	0.7490	0.0117
AspD v1	0.7620	0.0138	0.7592	0.0105
AspD v7	0.7619	0.0140	0.7596	0.0117
Detm v1	0.7645	0.0139	0.7592	0.0105
Detm v7	0.7520	0.0141	0.7475	0.0118
Biphasic 18m - baseline	-0.0088	0.0065	-0.0101	0.0063
Asp+Det 18m - baseline	0.0000	0.0065	0.0004	0.0063
Detemir 18m - baseline	-0.0125	0.0066	-0.0117	0.0065
Asp+Det vs. Biphasic change	0.0088	0.0092	0.0105	0.0088
Detemir vs. Biphasic change	-0.0036	0.0093	-0.0015	0.0089
Detemir vs. Asp+Det change	-0.0125	0.0093	-0.0121	0.0089

If we are going to present the effect measure as derived from the conditional model (*i.e.* using baseline as covariate, then we should use the estimated changes from the model `m1` without allowance for baseline imbalance.

5.1.1 Multiple imputation analysis

Once we have done the imputation we can make the analyses based on the imputed data with the insulin comparisons too.

```

> library( mice )
> load( file="./data/imp" )
> class( imp )
[1] "mids"
> mif <- with( imp, lm( fimtavg.v7 ~ fimtavg.v1 + igr + over.65 + pre.ins + sdc ) )
> round( smif <- summary( pool( mif ) ), 4 )

      est      se      t      df Pr(>|t|)   lo 95   hi 95 nmis   fmi
(Intercept) 0.1066 0.0231  4.6244 329.5136  0.0000  0.0613 0.1520  NA 0.1153
fimtavg.v1   0.8407 0.0286 29.3856 330.5100  0.0000  0.7844 0.8970   0 0.1141
igr2         0.0100 0.0091  1.0984 343.2165  0.2728 -0.0079 0.0278  NA 0.0984
igr3        -0.0021 0.0092 -0.2311 319.0870  0.8174 -0.0203 0.0160  NA 0.1279
over.652     0.0218 0.0089  2.4554 294.1692  0.0146  0.0043 0.0393  NA 0.1579
pre.ins2    -0.0045 0.0083 -0.5356 323.0410  0.5926 -0.0209 0.0119  NA 0.1232
sdc2         0.0099 0.0077  1.2877 316.6005  0.1988 -0.0052 0.0251  NA 0.1309
lambda
(Intercept) 0.1100
fimtavg.v1  0.1088
igr2        0.0932
igr3        0.1225
over.652    0.1522
pre.ins2    0.1178
sdc2        0.1255
> mim <- with( imp, lm( fimtavg.v7 ~ fimtavg.v1 + igr ) )
> round( smim <- summary( pool( mim ) ), 4 )

      est      se      t      df Pr(>|t|)   lo 95   hi 95 nmis   fmi
(Intercept) 0.0999 0.0226  4.4279 339.3884  0.0000  0.0555 0.1443  NA 0.1061
fimtavg.v1   0.8619 0.0273 31.5819 350.6084  0.0000  0.8082 0.9156   0 0.0922
igr2         0.0096 0.0091  1.0534 346.8200  0.2929 -0.0083 0.0276  NA 0.0969
igr3        -0.0026 0.0093 -0.2807 321.6481  0.7792 -0.0209 0.0157  NA 0.1274
lambda
(Intercept) 0.1008
fimtavg.v1  0.0870
igr2        0.0917
igr3        0.1220
> CI <- rbind( c(1,0), c(0,1), c(-1,1) )
> rownames( CI ) <- elab[4:6]
> CI

      [,1] [,2]
Asp+Det vs. Biphasic change  1  0
Detemir vs. Biphasic change  0  1
Detemir vs. Asp+Det change  -1  1
> round( i0 <- ci.lin( pool( mif ) , subset="igr", ctr.mat=CI ), 4 )

      Estimate StdErr      z      P    2.5% 97.5%
Asp+Det vs. Biphasic change  0.0100 0.0091  1.0984 0.2720 -0.0078 0.0277
Detemir vs. Biphasic change -0.0021 0.0092 -0.2311 0.8173 -0.0202 0.0160
Detemir vs. Asp+Det change  -0.0121 0.0092 -1.3193 0.1871 -0.0301 0.0059

```

With the estimate for the insulin effects in `smif` (which is the relevant one) we can now re-do the forest plot using the “old” estimates of the corrected changes estimated from the random-effects model:

```

> round( rbind( el[7:9,c(1,5,6)],
+             i0[ ,c(1,5,6)] ), 3 )

      Estimate  2.5% 97.5%
Biphasic 18m - baseline  -0.010 -0.023 0.002
Asp+Det 18m - baseline   0.000 -0.012 0.013
Detemir 18m - baseline  -0.012 -0.024 0.001
Asp+Det vs. Biphasic change  0.010 -0.008 0.028
Detemir vs. Biphasic change -0.002 -0.020 0.016
Detemir vs. Asp+Det change  -0.012 -0.030 0.006

```

```

> tmp1 <-
+ function(xtra=FALSE)
+ {
+ par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6 )
+ piclr <- rgb(t(col2rgb( iclr ))/3 + 255*2/3,max=255)
+ plotEst( rbind( e1[7:9,c(1,5,6)],
+               i0[ ,c(1,5,6)] ),
+         xlab="", ylim=c(0.3,8), xlim=c(-0.03,0.03),
+         lwd=3, vref=0, y=c(8:6,4:2),
+         col.lines =c(iclr[c(1:3,1,1,2)]),
+         col.points=c(iclr[c(1:3,2,3,3)]),
+         cex=1.5 )
+ if( xtra )
+ {
+ linesEst( e0[10:12,c(1,5,6)],
+          lwd=3, vref=0, y=c(4:2-0.1),
+          col.lines =piclr[c(1,1,2)],
+          col.points=piclr[c(2,3,3)],
+          cex=1.5 )
+ linesEst( i0[,c(1,5,6)],
+          lwd=3, vref=0, y=c(4:2),
+          col.lines =iclr[c(1,1,2)],
+          col.points=iclr[c(2,3,3)],
+          cex=1.5 )
+ }
+ axis( side=1 )
+ text( -0.03, 0.4, "Improvement" , adj=0, col=clr[4], cex=0.8 )
+ text( 0.03, 0.4, "Deterioration", adj=1, col=clr[4], cex=0.8 )
+ mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )
+ }
> tmp1(TRUE)

```

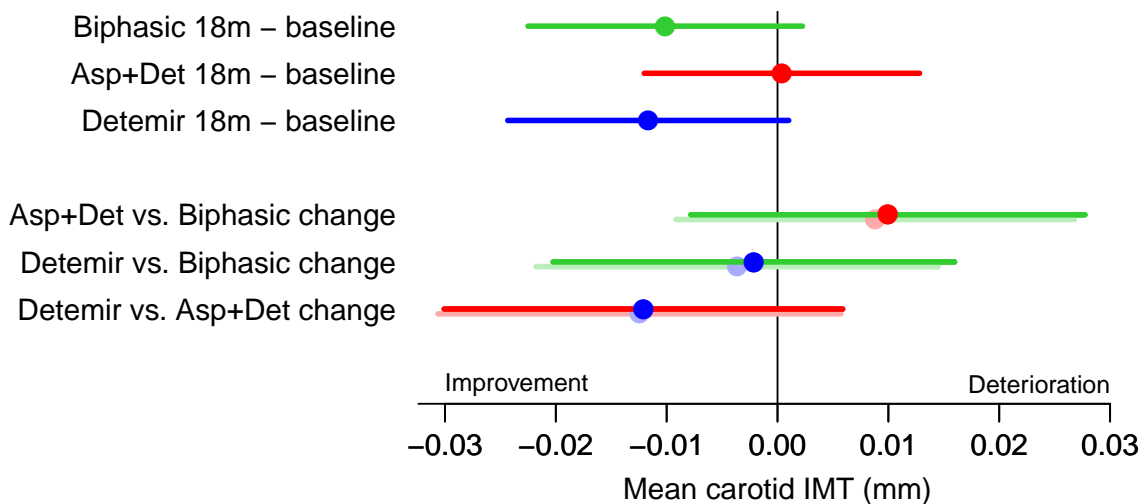


Figure 5.2: Estimated changes in each treatment group from the random effects model with identical baseline. The difference in changes between treatments are from the model with baseline as covariate, using multiply imputed data, adjusted for stratification variables. Pale colors indicate the contrasts from the random effects model. Bars indicate 95% c.i.

```

> tmp1(FALSE)

```

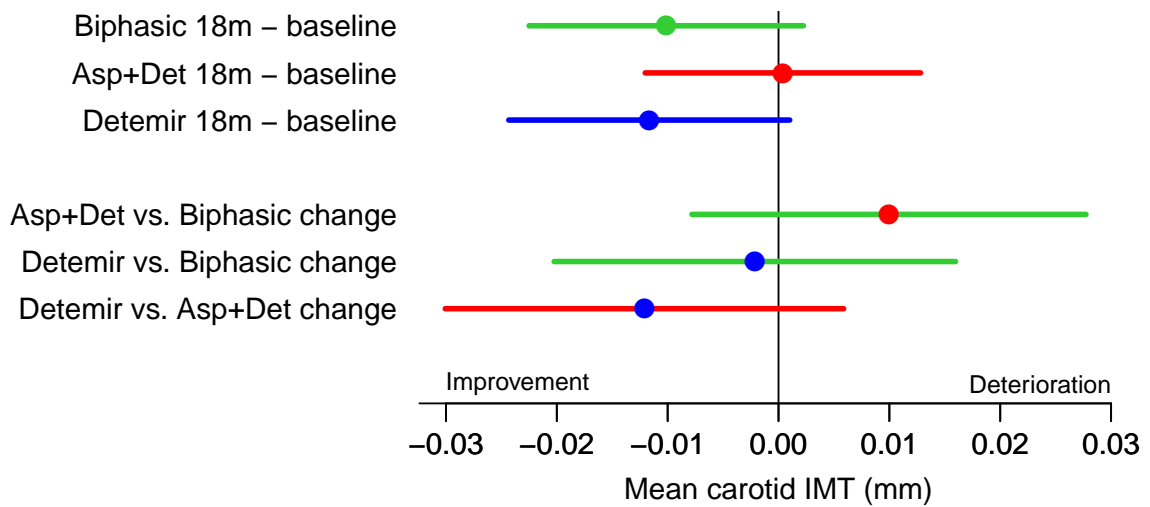


Figure 5.3: *Estimated changes in each treatment group from the random effects model with identical baseline. The difference in changes between treatments are from the model with baseline as covariate, using multiply imputed data, adjusted for stratification variables. Bars indicate 95% c.i.*

```
> win.metafile( "./results/forest-ins-imp.emf", width=7, height=4, pointsize=20 )
> tml(FALSE)
> dev.off()

null device
      1
```

Chapter 6

Interaction analyses of primary outcome (CIMT)

First we fit the random effects model that allows different baseline means between the (six) randomization groups, and from that model extract both the individual changes in each of the three groups, and the differences in changes between them. Also we make tests comparing the different models, testing whether there are

```
> AD$subjid <- factor( AD$subjid )
> m0 <- lmer( fimtavg ~ -1 + visit +
+           + over.65 + pre.ins + sdc +(1/subjid), data = AD )
> mM <- lmer( fimtavg ~ -1 + visit + visit:grp
+           + over.65 + pre.ins + sdc +(1/subjid), data = AD )
> mI <- lmer( fimtavg ~ -1 + visit + visit:igr
+           + over.65 + pre.ins + sdc +(1/subjid), data = AD )
> mA <- lmer( fimtavg ~ -1 + visit + visit:grp + visit:igr
+           + over.65 + pre.ins + sdc +(1/subjid), data = AD )
> mi <- lmer( fimtavg ~ -1 + visit + visit:interaction(igr,grp)
+           + over.65 + pre.ins + sdc +(1/subjid), data = AD )
> round( ci.lin( m0 ), 3 )

      Estimate StdErr      z      P   2.5% 97.5%
visitv1      0.759  0.010 72.567 0.000  0.739 0.780
visitv7      0.752  0.011 71.543 0.000  0.731 0.773
over.65>65   0.090  0.014  6.486 0.000  0.063 0.117
pre.insnoIns 0.006  0.014  0.440 0.660 -0.021 0.033
sdcnnotSDC   0.014  0.013  1.105 0.269 -0.011 0.039

> round( ci.lin( mi ), 3 )

      Estimate StdErr      z      P   2.5% 97.5%
visitv1      0.754  0.018 42.116 0.000  0.719 0.789
visitv7      0.724  0.018 40.062 0.000  0.689 0.760
over.65>65   0.089  0.014  6.395 0.000  0.062 0.116
pre.insnoIns 0.007  0.014  0.490 0.624 -0.020 0.034
sdcnnotSDC   0.013  0.013  1.051 0.293 -0.012 0.038
visitv1:interaction(igr, grp)AspD.Plc 0.020  0.022  0.898 0.369 -0.024 0.063
visitv7:interaction(igr, grp)AspD.Plc 0.050  0.023  2.215 0.027  0.006 0.094
visitv1:interaction(igr, grp)Detm.Plc 0.014  0.023  0.636 0.525 -0.030 0.059
visitv7:interaction(igr, grp)Detm.Plc 0.031  0.023  1.354 0.176 -0.014 0.077
visitv1:interaction(igr, grp)Biph.Met -0.005  0.022 -0.224 0.823 -0.049 0.039
visitv7:interaction(igr, grp)Biph.Met 0.035  0.023  1.541 0.123 -0.010 0.080
visitv1:interaction(igr, grp)AspD.Met -0.004  0.023 -0.187 0.851 -0.049 0.040
visitv7:interaction(igr, grp)AspD.Met 0.025  0.023  1.069 0.285 -0.021 0.070
visitv1:interaction(igr, grp)Detm.Met 0.008  0.022  0.356 0.722 -0.036 0.052
visitv7:interaction(igr, grp)Detm.Met 0.025  0.023  1.110 0.267 -0.019 0.069

> mod <- rbind( anova( m0, mM, mA )[-1,],
+             anova( m0, mI, mA, mi )[-1,] )
```

```
> rownames( mod ) <- c("Met|0", "Ins|Met", "Ins|0", "Met|Ins", "Interact")
> attr( mod, "heading" ) <- NULL
> round( mod, 4 )[c(1,3,4,2,5),]
```

	Df	AIC	BIC	logLik	deviance	Chisq	Chi	Df	Pr(>Chisq)
Met 0	9	-1418.0	-1376.1	718.02	-1436.0	3.1344		2	0.2086
Ins 0	11	-1414.0	-1362.7	717.98	-1436.0	3.0489		4	0.5497
Met Ins	13	-1413.4	-1352.7	719.68	-1439.4	3.4016		2	0.1825
Ins Met	13	-1413.4	-1352.7	719.68	-1439.4	3.3161		4	0.5064
Interact	17	-1413.5	-1334.3	723.77	-1447.5	8.1830		4	0.0851

Comparing the models with each of the randomization variables and with interaction between these show that there is no effect of any of the interventions separately, and no interaction either. However the interaction test, even if quite unspecific has a somewhat smaller p-value than the other tests.

We therefore look at the estimated effects in the interaction model:

```
> round( ee <- ci.lin( mi, subset="visit" ), 4 )
```

	Estimate	StdErr	z	P	2.5%	97.5%
visitv1	0.7538	0.0179	42.1160	0.0000	0.7187	0.7889
visitv7	0.7243	0.0181	40.0620	0.0000	0.6889	0.7597
visitv1:interaction(igr, grp)AspD.Plc	0.0199	0.0222	0.8977	0.3693	-0.0236	0.0634
visitv7:interaction(igr, grp)AspD.Plc	0.0498	0.0225	2.2145	0.0268	0.0057	0.0939
visitv1:interaction(igr, grp)Detm.Plc	0.0145	0.0227	0.6360	0.5248	-0.0301	0.0590
visitv7:interaction(igr, grp)Detm.Plc	0.0314	0.0232	1.3543	0.1757	-0.0141	0.0769
visitv1:interaction(igr, grp)Biph.Met	-0.0050	0.0224	-0.2243	0.8226	-0.0490	0.0390
visitv7:interaction(igr, grp)Biph.Met	0.0350	0.0227	1.5412	0.1233	-0.0095	0.0795
visitv1:interaction(igr, grp)AspD.Met	-0.0043	0.0228	-0.1872	0.8515	-0.0490	0.0404
visitv7:interaction(igr, grp)AspD.Met	0.0247	0.0231	1.0692	0.2850	-0.0206	0.0700
visitv1:interaction(igr, grp)Detm.Met	0.0080	0.0223	0.3564	0.7216	-0.0358	0.0517
visitv7:interaction(igr, grp)Detm.Met	0.0251	0.0226	1.1099	0.2670	-0.0192	0.0694

```
> C0 <- diag(12)
> C0[,1] <- rep(1:0,6)
> C0[,2] <- rep(0:1,6)
> igrps <- as.vector( outer( iN, gN, FUN=function(x,y) paste(x,y,sep="," ) ) )
> for( i in 1:6 ) C0 <- rbind( C0, C0[2*i,]-C0[2*i-1,] )
> rownames( C0 ) <- c( as.vector( outer( levels( AD$visit ) [c(1,7)],
+                               igrps,
+                               paste ) ),
+
+                               paste( igrps, "18m - baseline" ) )
> C0
```

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]	[,8]
v1 Biphasic, Placebo+Insulin	1	0	0	0	0	0	0	0
v7 Biphasic, Placebo+Insulin	0	1	0	0	0	0	0	0
v1 Aspart+Detemir, Placebo+Insulin	1	0	1	0	0	0	0	0
v7 Aspart+Detemir, Placebo+Insulin	0	1	0	1	0	0	0	0
v1 Detemir, Placebo+Insulin	1	0	0	0	1	0	0	0
v7 Detemir, Placebo+Insulin	0	1	0	0	0	1	0	0
v1 Biphasic, Metformin+Insulin	1	0	0	0	0	0	1	0
v7 Biphasic, Metformin+Insulin	0	1	0	0	0	0	0	1
v1 Aspart+Detemir, Metformin+Insulin	1	0	0	0	0	0	0	0
v7 Aspart+Detemir, Metformin+Insulin	0	1	0	0	0	0	0	0
v1 Detemir, Metformin+Insulin	1	0	0	0	0	0	0	0
v7 Detemir, Metformin+Insulin	0	1	0	0	0	0	0	0
Biphasic, Placebo+Insulin 18m - baseline	-1	1	0	0	0	0	0	0
Aspart+Detemir, Placebo+Insulin 18m - baseline	-1	1	-1	1	0	0	0	0
Detemir, Placebo+Insulin 18m - baseline	-1	1	0	0	-1	1	0	0
Biphasic, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	-1	1
Aspart+Detemir, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	0	0
Detemir, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	0	0

```
[,9] [,10] [,11] [,12]
```

	[,9]	[,10]	[,11]	[,12]
v1 Biphasic, Placebo+Insulin	0	0	0	0
v7 Biphasic, Placebo+Insulin	0	0	0	0

```

v1 Aspart+Detemir, Placebo+Insulin      0    0    0    0
v7 Aspart+Detemir, Placebo+Insulin      0    0    0    0
v1 Detemir, Placebo+Insulin              0    0    0    0
v7 Detemir, Placebo+Insulin              0    0    0    0
v1 Biphasic, Metformin+Insulin           0    0    0    0
v7 Biphasic, Metformin+Insulin           0    0    0    0
v1 Aspart+Detemir, Metformin+Insulin     1    0    0    0
v7 Aspart+Detemir, Metformin+Insulin     0    1    0    0
v1 Detemir, Metformin+Insulin            0    0    1    0
v7 Detemir, Metformin+Insulin            0    0    0    1
Biphasic, Placebo+Insulin 18m - baseline 0    0    0    0
Aspart+Detemir, Placebo+Insulin 18m - baseline 0    0    0    0
Detemir, Placebo+Insulin 18m - baseline  0    0    0    0
Biphasic, Metformin+Insulin 18m - baseline 0    0    0    0
Aspart+Detemir, Metformin+Insulin 18m - baseline -1    1    0    0
Detemir, Metformin+Insulin 18m - baseline 0    0   -1    1

```

```

> dim( CO )
[1] 18 12

```

```

> CO <- rbind( CO, CO[15+1:3      ,]-CO[12+1:3      ,],
+            CO[12+c(2,3,3),]-CO[12+c(1,1,2),],
+            CO[15+c(2,3,3),]-CO[15+c(1,1,2),] )
> rownames( CO )[18+1:9] <- c( paste( iN, ":", gN[2], "vs", gN[1] ),
+                             paste( rep(gN,each=3), ":",
+                                   iN[c(2,3,3)], "vs", iN[c(1,1,2)] ) )
> CO

```

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]
v1 Biphasic, Placebo+Insulin	1	0	0	0	0	0	0
v7 Biphasic, Placebo+Insulin	0	1	0	0	0	0	0
v1 Aspart+Detemir, Placebo+Insulin	1	0	1	0	0	0	0
v7 Aspart+Detemir, Placebo+Insulin	0	1	0	1	0	0	0
v1 Detemir, Placebo+Insulin	1	0	0	0	1	0	0
v7 Detemir, Placebo+Insulin	0	1	0	0	0	1	0
v1 Biphasic, Metformin+Insulin	1	0	0	0	0	0	1
v7 Biphasic, Metformin+Insulin	0	1	0	0	0	0	0
v1 Aspart+Detemir, Metformin+Insulin	1	0	0	0	0	0	0
v7 Aspart+Detemir, Metformin+Insulin	0	1	0	0	0	0	0
v1 Detemir, Metformin+Insulin	1	0	0	0	0	0	0
v7 Detemir, Metformin+Insulin	0	1	0	0	0	0	0
Biphasic, Placebo+Insulin 18m - baseline	-1	1	0	0	0	0	0
Aspart+Detemir, Placebo+Insulin 18m - baseline	-1	1	-1	1	0	0	0
Detemir, Placebo+Insulin 18m - baseline	-1	1	0	0	-1	1	0
Biphasic, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	-1
Aspart+Detemir, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	0
Detemir, Metformin+Insulin 18m - baseline	-1	1	0	0	0	0	0
Biphasic : Metformin+Insulin vs Placebo+Insulin	0	0	0	0	0	0	-1
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin	0	0	1	-1	0	0	0
Detemir : Metformin+Insulin vs Placebo+Insulin	0	0	0	0	1	-1	0
Placebo+Insulin : Aspart+Detemir vs Biphasic	0	0	-1	1	0	0	0
Placebo+Insulin : Detemir vs Biphasic	0	0	0	0	-1	1	0
Placebo+Insulin : Detemir vs Aspart+Detemir	0	0	1	-1	-1	1	0
Metformin+Insulin : Aspart+Detemir vs Biphasic	0	0	0	0	0	0	1
Metformin+Insulin : Detemir vs Biphasic	0	0	0	0	0	0	1
Metformin+Insulin : Detemir vs Aspart+Detemir	0	0	0	0	0	0	0
	[,8]	[,9]	[,10]	[,11]	[,12]		
v1 Biphasic, Placebo+Insulin	0	0	0	0	0		
v7 Biphasic, Placebo+Insulin	0	0	0	0	0		
v1 Aspart+Detemir, Placebo+Insulin	0	0	0	0	0		
v7 Aspart+Detemir, Placebo+Insulin	0	0	0	0	0		
v1 Detemir, Placebo+Insulin	0	0	0	0	0		
v7 Detemir, Placebo+Insulin	0	0	0	0	0		
v1 Biphasic, Metformin+Insulin	0	0	0	0	0		
v7 Biphasic, Metformin+Insulin	1	0	0	0	0		
v1 Aspart+Detemir, Metformin+Insulin	0	1	0	0	0		
v7 Aspart+Detemir, Metformin+Insulin	0	0	1	0	0		


```

v1 Detemir, Metformin+Insulin          0    0    0    1    0
v7 Detemir, Metformin+Insulin          0    0    0    0    1
Biphasic, Placebo+Insulin 18m - baseline 0    0    0    0    0
Aspart+Detemir, Placebo+Insulin 18m - baseline 0    0    0    0    0
Detemir, Placebo+Insulin 18m - baseline 0    0    0    0    0
Biphasic, Metformin+Insulin 18m - baseline 1    0    0    0    0
Aspart+Detemir, Metformin+Insulin 18m - baseline 0   -1    1    0    0
Detemir, Metformin+Insulin 18m - baseline 0    0    0   -1    1
Biphasic : Metformin+Insulin vs Placebo+Insulin 1    0    0    0    0
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin 0   -1    1    0    0
Detemir : Metformin+Insulin vs Placebo+Insulin 0    0    0   -1    1
Placebo+Insulin : Aspart+Detemir vs Biphasic 0    0    0    0    0
Placebo+Insulin : Detemir vs Biphasic 0    0    0    0    0
Placebo+Insulin : Detemir vs Aspart+Detemir 0    0    0    0    0
Metformin+Insulin : Aspart+Detemir vs Biphasic -1   -1    1    0    0
Metformin+Insulin : Detemir vs Biphasic -1    0    0   -1    1
Metformin+Insulin : Detemir vs Aspart+Detemir 0    1   -1   -1    1
> e0 <- ci.lin( mi, subset="visit", ctr.mat=C0 )
> round( e0, 4 )

                                Estimate StdErr      z      P
v1 Biphasic, Placebo+Insulin      0.7538 0.0179 42.1160 0.0000
v7 Biphasic, Placebo+Insulin      0.7243 0.0181 40.0620 0.0000
v1 Aspart+Detemir, Placebo+Insulin 0.7737 0.0175 44.1682 0.0000
v7 Aspart+Detemir, Placebo+Insulin 0.7741 0.0177 43.6408 0.0000
v1 Detemir, Placebo+Insulin        0.7683 0.0181 42.5581 0.0000
v7 Detemir, Placebo+Insulin        0.7557 0.0184 41.0094 0.0000
v1 Biphasic, Metformin+Insulin     0.7488 0.0179 41.8297 0.0000
v7 Biphasic, Metformin+Insulin     0.7593 0.0180 42.1173 0.0000
v1 Aspart+Detemir, Metformin+Insulin 0.7495 0.0181 41.4297 0.0000
v7 Aspart+Detemir, Metformin+Insulin 0.7490 0.0183 40.9793 0.0000
v1 Detemir, Metformin+Insulin      0.7618 0.0176 43.1682 0.0000
v7 Detemir, Metformin+Insulin      0.7494 0.0178 42.0145 0.0000
Biphasic, Placebo+Insulin 18m - baseline -0.0295 0.0092 -3.2026 0.0014
Aspart+Detemir, Placebo+Insulin 18m - baseline 0.0004 0.0089 0.0449 0.9642
Detemir, Placebo+Insulin 18m - baseline -0.0126 0.0097 -1.2973 0.1945
Biphasic, Metformin+Insulin 18m - baseline 0.0105 0.0089 1.1783 0.2387
Aspart+Detemir, Metformin+Insulin 18m - baseline -0.0005 0.0094 -0.0557 0.9556
Detemir, Metformin+Insulin 18m - baseline -0.0124 0.0089 -1.3853 0.1659
Biphasic : Metformin+Insulin vs Placebo+Insulin 0.0400 0.0128 3.1197 0.0018
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin -0.0009 0.0129 -0.0713 0.9431
Detemir : Metformin+Insulin vs Placebo+Insulin 0.0002 0.0132 0.0139 0.9889
Placebo+Insulin : Aspart+Detemir vs Biphasic 0.0299 0.0128 2.3401 0.0193
Placebo+Insulin : Detemir vs Biphasic 0.0170 0.0134 1.2692 0.2044
Placebo+Insulin : Detemir vs Aspart+Detemir -0.0130 0.0131 -0.9872 0.3235
Metformin+Insulin : Aspart+Detemir vs Biphasic -0.0110 0.0129 -0.8534 0.3934
Metformin+Insulin : Detemir vs Biphasic -0.0229 0.0126 -1.8127 0.0699
Metformin+Insulin : Detemir vs Aspart+Detemir -0.0118 0.0129 -0.9154 0.3600
                                2.5%   97.5%
v1 Biphasic, Placebo+Insulin      0.7187 0.7889
v7 Biphasic, Placebo+Insulin      0.6889 0.7597
v1 Aspart+Detemir, Placebo+Insulin 0.7394 0.8081
v7 Aspart+Detemir, Placebo+Insulin 0.7394 0.8089
v1 Detemir, Placebo+Insulin        0.7329 0.8037
v7 Detemir, Placebo+Insulin        0.7196 0.7918
v1 Biphasic, Metformin+Insulin     0.7137 0.7839
v7 Biphasic, Metformin+Insulin     0.7240 0.7946
v1 Aspart+Detemir, Metformin+Insulin 0.7141 0.7850
v7 Aspart+Detemir, Metformin+Insulin 0.7132 0.7848
v1 Detemir, Metformin+Insulin      0.7272 0.7963
v7 Detemir, Metformin+Insulin      0.7144 0.7844
Biphasic, Placebo+Insulin 18m - baseline -0.0476 -0.0115
Aspart+Detemir, Placebo+Insulin 18m - baseline -0.0170 0.0178
Detemir, Placebo+Insulin 18m - baseline -0.0315 0.0064
Biphasic, Metformin+Insulin 18m - baseline -0.0070 0.0280
Aspart+Detemir, Metformin+Insulin 18m - baseline -0.0189 0.0178
Detemir, Metformin+Insulin 18m - baseline -0.0299 0.0051

```

Biphasic : Metformin+Insulin vs Placebo+Insulin	0.0149	0.0652
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin	-0.0262	0.0244
Detemir : Metformin+Insulin vs Placebo+Insulin	-0.0256	0.0260
Placebo+Insulin : Aspart+Detemir vs Biphasic	0.0049	0.0550
Placebo+Insulin : Detemir vs Biphasic	-0.0092	0.0432
Placebo+Insulin : Detemir vs Aspart+Detemir	-0.0387	0.0128
Metformin+Insulin : Aspart+Detemir vs Biphasic	-0.0364	0.0143
Metformin+Insulin : Detemir vs Biphasic	-0.0477	0.0019
Metformin+Insulin : Detemir vs Aspart+Detemir	-0.0372	0.0135

We can make a plot of this:

```
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[13:27,c(1,5,6)], lwd=3, vref=0,
+         y = 18-c(1:3,
+                 1:3+3.5,
+                 1:3+7.5,
+                 1:3+11.1,
+                 1:3+14.5),
+         xlab="", ylim=c(0,17), xlim=c(-0.06,0.06) )
> abline( h=18-7.5, col=gray(0.7), lty=2 )
> axis( side=1 )
> text( -0.06, -0.2, "Improvement" , adj=0, cex=0.8 )
> text( 0.06, -0.2, "Deterioration", adj=1, cex=0.8 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )
```

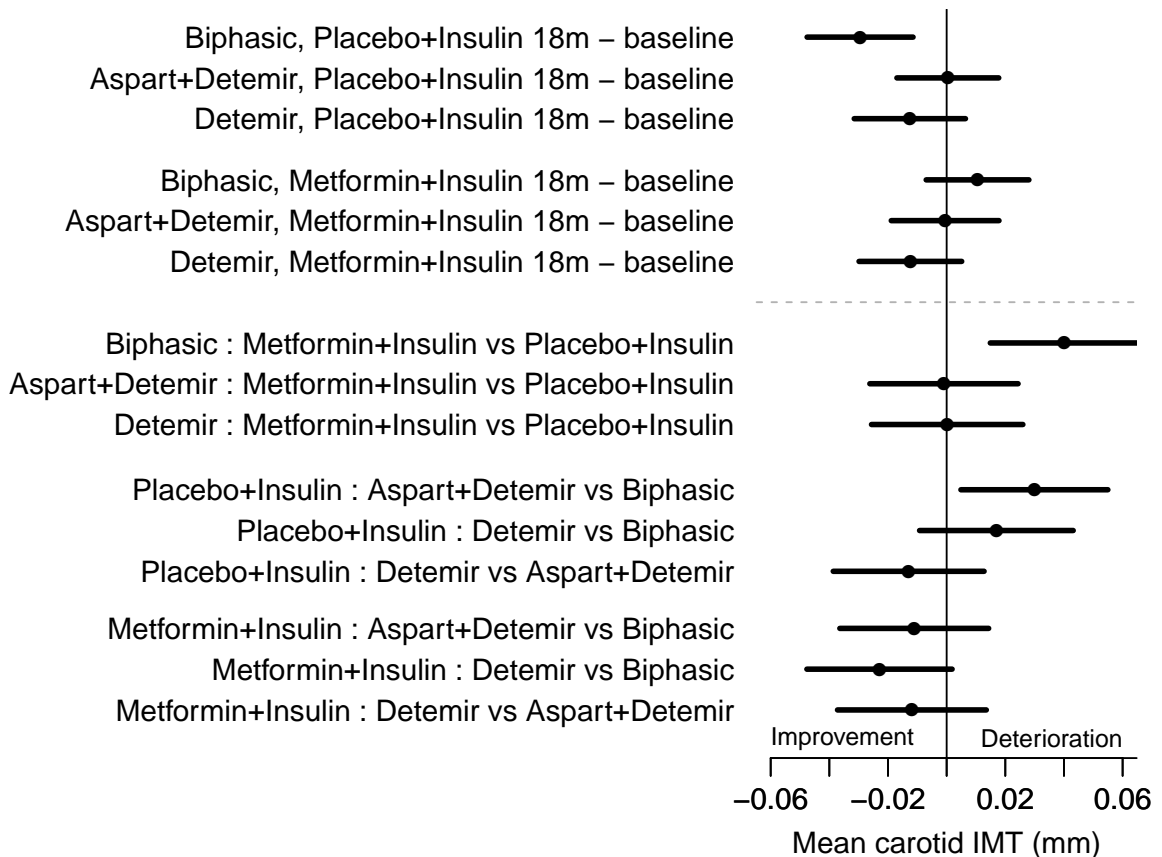


Figure 6.1: Estimates of insulin regimen effects from a random effects model for complete ITT data, adjusted for stratification variables.

6.0.2 Multiple imputation analysis

We can make the same analysis in the model with baseline as covariate, using multiply imputed data:

```
> library( mice )
> load( file="./data/imp" )
> class( imp )
[1] "mids"
> mii <- with( imp, lm( fimtavg.v7 ~ fimtavg.v1 + interaction(igr,grp) + over.65 + pre.ins + sdc ) )
> round( smii <- summary( pool( mii ) ), 4 )
```

	est	se	t	df	Pr(> t)	lo 95	hi 95
(Intercept)	0.0875	0.0238	3.6729	329.1274	0.0003	0.0406	0.1343
fimtavg.v1	0.8413	0.0285	29.5248	323.9575	0.0000	0.7852	0.8973
interaction(igr, grp)AspD.Plc	0.0306	0.0128	2.3967	326.7959	0.0171	0.0055	0.0557
interaction(igr, grp)Detm.Plc	0.0159	0.0133	1.1964	303.3143	0.2325	-0.0102	0.0420
interaction(igr, grp)Biph.Met	0.0376	0.0128	2.9385	336.3923	0.0035	0.0124	0.0628
interaction(igr, grp)AspD.Met	0.0276	0.0130	2.1242	337.6848	0.0344	0.0020	0.0532
interaction(igr, grp)Detm.Met	0.0182	0.0128	1.4213	329.7788	0.1562	-0.0070	0.0433
over.652	0.0202	0.0088	2.2879	293.4225	0.0229	0.0028	0.0376
pre.ins2	-0.0037	0.0083	-0.4422	320.5923	0.6586	-0.0199	0.0126
sdc2	0.0094	0.0077	1.2256	312.3481	0.2213	-0.0057	0.0245

```

nmis      fmi lambda
(Intercept)      NA 0.1131 0.1077
fimtavg.v1        0 0.1194 0.1140
interaction(igr, grp)AspD.Plc  NA 0.1159 0.1105
interaction(igr, grp)Detm.Plc  NA 0.1445 0.1389
interaction(igr, grp)Biph.Met  NA 0.1040 0.0987
interaction(igr, grp)AspD.Met  NA 0.1024 0.0971
interaction(igr, grp)Detm.Met  NA 0.1123 0.1069
over.652          NA 0.1565 0.1508
pre.ins2          NA 0.1235 0.1181
sdc2              NA 0.1336 0.1280

```

```
> ci.lin( pool( mii ), subset="igr" )
```

	Estimate	StdErr	z	P	2.5%
interaction(igr, grp)AspD.Plc	0.03057046	0.01275524	2.396699	0.016543528	0.005570654
interaction(igr, grp)Detm.Plc	0.01588586	0.01327765	1.196436	0.231526529	-0.010137861
interaction(igr, grp)Biph.Met	0.03763734	0.01280832	2.938507	0.003297972	0.012533492
interaction(igr, grp)AspD.Met	0.02761767	0.01300126	2.124230	0.033650926	0.002135664
interaction(igr, grp)Detm.Met	0.01818059	0.01279166	1.421285	0.155233880	-0.006890594

```

97.5%
interaction(igr, grp)AspD.Plc 0.05557027
interaction(igr, grp)Detm.Plc 0.04190958
interaction(igr, grp)Biph.Met 0.06274118
interaction(igr, grp)AspD.Met 0.05309967
interaction(igr, grp)Detm.Met 0.04325177

```

```
> ( CI <- -C0[19:27,1:5*2+1] )
```

	[,1]	[,2]	[,3]	[,4]	[,5]
Biphasic : Metformin+Insulin vs Placebo+Insulin	0	0	1	0	0
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin	-1	0	0	1	0
Detemir : Metformin+Insulin vs Placebo+Insulin	0	-1	0	0	1
Placebo+Insulin : Aspart+Detemir vs Biphasic	1	0	0	0	0
Placebo+Insulin : Detemir vs Biphasic	0	1	0	0	0
Placebo+Insulin : Detemir vs Aspart+Detemir	-1	1	0	0	0
Metformin+Insulin : Aspart+Detemir vs Biphasic	0	0	-1	1	0
Metformin+Insulin : Detemir vs Biphasic	0	0	-1	0	1
Metformin+Insulin : Detemir vs Aspart+Detemir	0	0	0	-1	1

```
> round( i0 <- ci.lin( pool( mii ), subset="igr", ctr.mat=CI ), 4 )
```

	Estimate	StdErr	z	P
Biphasic : Metformin+Insulin vs Placebo+Insulin	0.0376	0.0128	2.9385	0.0033
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin	-0.0030	0.0129	-0.2292	0.8187

Detemir : Metformin+Insulin vs Placebo+Insulin	0.0023	0.0130	0.1768	0.8597
Placebo+Insulin : Aspart+Detemir vs Biphasic	0.0306	0.0128	2.3967	0.0165
Placebo+Insulin : Detemir vs Biphasic	0.0159	0.0133	1.1964	0.2315
Placebo+Insulin : Detemir vs Aspart+Detemir	-0.0147	0.0130	-1.1253	0.2605
Metformin+Insulin : Aspart+Detemir vs Biphasic	-0.0100	0.0129	-0.7740	0.4389
Metformin+Insulin : Detemir vs Biphasic	-0.0195	0.0126	-1.5411	0.1233
Metformin+Insulin : Detemir vs Aspart+Detemir	-0.0094	0.0128	-0.7395	0.4596
	2.5%	97.5%		
Biphasic : Metformin+Insulin vs Placebo+Insulin	0.0125	0.0627		
Aspart+Detemir : Metformin+Insulin vs Placebo+Insulin	-0.0282	0.0223		
Detemir : Metformin+Insulin vs Placebo+Insulin	-0.0231	0.0277		
Placebo+Insulin : Aspart+Detemir vs Biphasic	0.0056	0.0556		
Placebo+Insulin : Detemir vs Biphasic	-0.0101	0.0419		
Placebo+Insulin : Detemir vs Aspart+Detemir	-0.0403	0.0109		
Metformin+Insulin : Aspart+Detemir vs Biphasic	-0.0354	0.0154		
Metformin+Insulin : Detemir vs Biphasic	-0.0442	0.0053		
Metformin+Insulin : Detemir vs Aspart+Detemir	-0.0345	0.0156		

With the estimate for the insulin effects in `smif` (which is the relevant one) we can now re-do the forest plot using the “old” estimates of the corrected changes estimated from the random-effects model:

```
> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[13:27,c(1,5,6)], lwd=3, vref=0,
+         y = 18-c(1:3,
+               1:3+ 3.5,
+               1:3+ 7.5-0.1,
+               1:3+11.1-0.1,
+               1:3+14.5-0.1),
+         xlab="", ylim=c(0,17), xlim=c(-0.06,0.06) )
> linesEst( i0[,c(1,5,6)], lwd=3, vref=0,
+          y = 18-c(1:3+ 7.5+0.1,
+                1:3+11.1+0.1,
+                1:3+14.5+0.1),
+          col=gray(0.6) )
> abline( h=18-7.5, col=gray(0.7), lty=2 )
> axis( side=1 )
> text( -0.06, -0.2, "Improvement" , adj=0, cex=0.8 )
> text( 0.06, -0.2, "Deterioration", adj=1, cex=0.8 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )

> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6 )
> plotEst( e0[13:27,c(1,5,6)], lwd=3, vref=0,
+         y = 18-c(1:3,
+               1:3+ 3.5,
+               1:3+ 7.5,
+               1:3+11.1,
+               1:3+14.5), col=rep(c("black","transparent"),
+                               c(6,9) ),
+         xlab="", ylim=c(0,17), xlim=c(-0.06,0.06) )
> linesEst( i0[,c(1,5,6)], lwd=3, vref=0,
+          y = 18-c(1:3+ 7.5,
+                1:3+11.1,
+                1:3+14.5),
+          col=gray(0.0) )
> abline( h=18-7.5, col=gray(0.0), lty=2 )
> axis( side=1 )
> text( -0.06, -0.2, "Improvement" , adj=0, cex=0.8 )
> text( 0.06, -0.2, "Deterioration", adj=1, cex=0.8 )
> mtext( "Mean carotid IMT (mm)", side=1, line=3/1.6 )
```

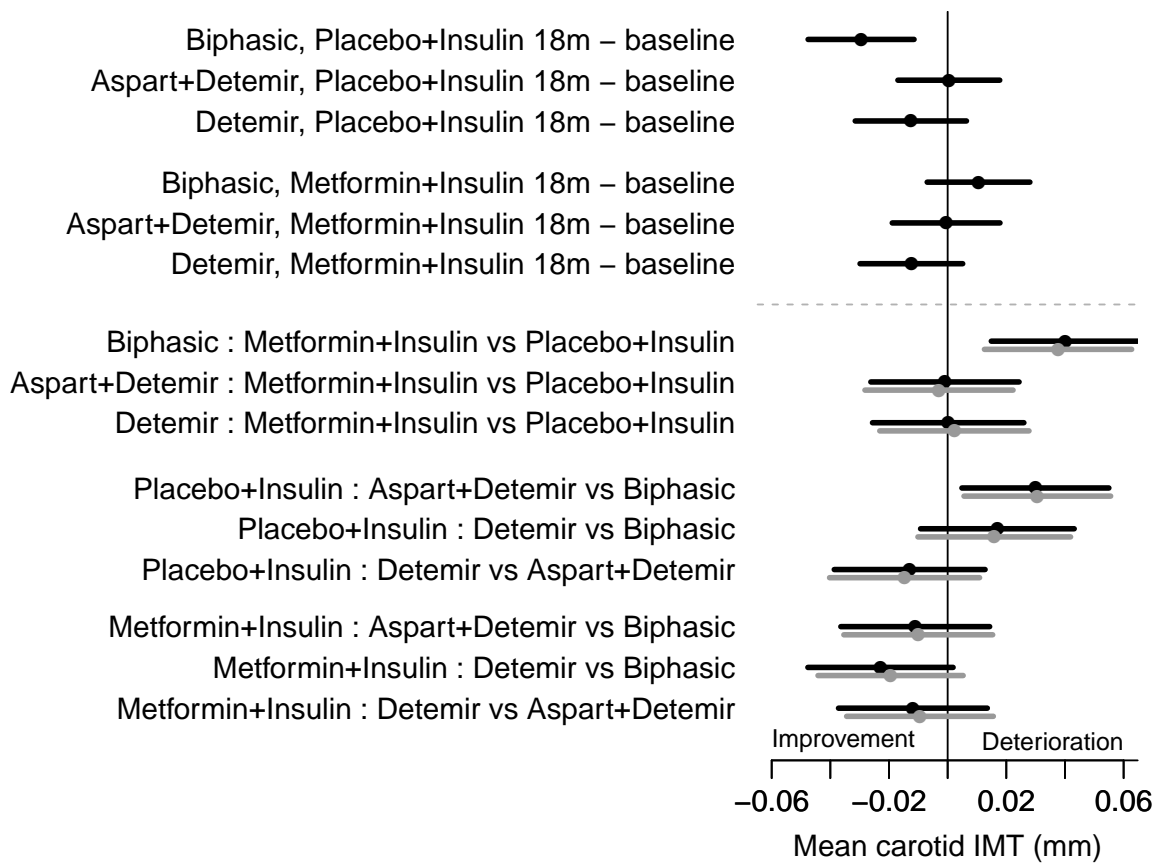


Figure 6.2: *Estimated changes in each treatment group from the random effects model, adjusted for stratification variables. Pale colors indicate the difference in changes between treatments from the model with baseline as covariate, using multiply imputed data. Bars indicate 95% c.i.*

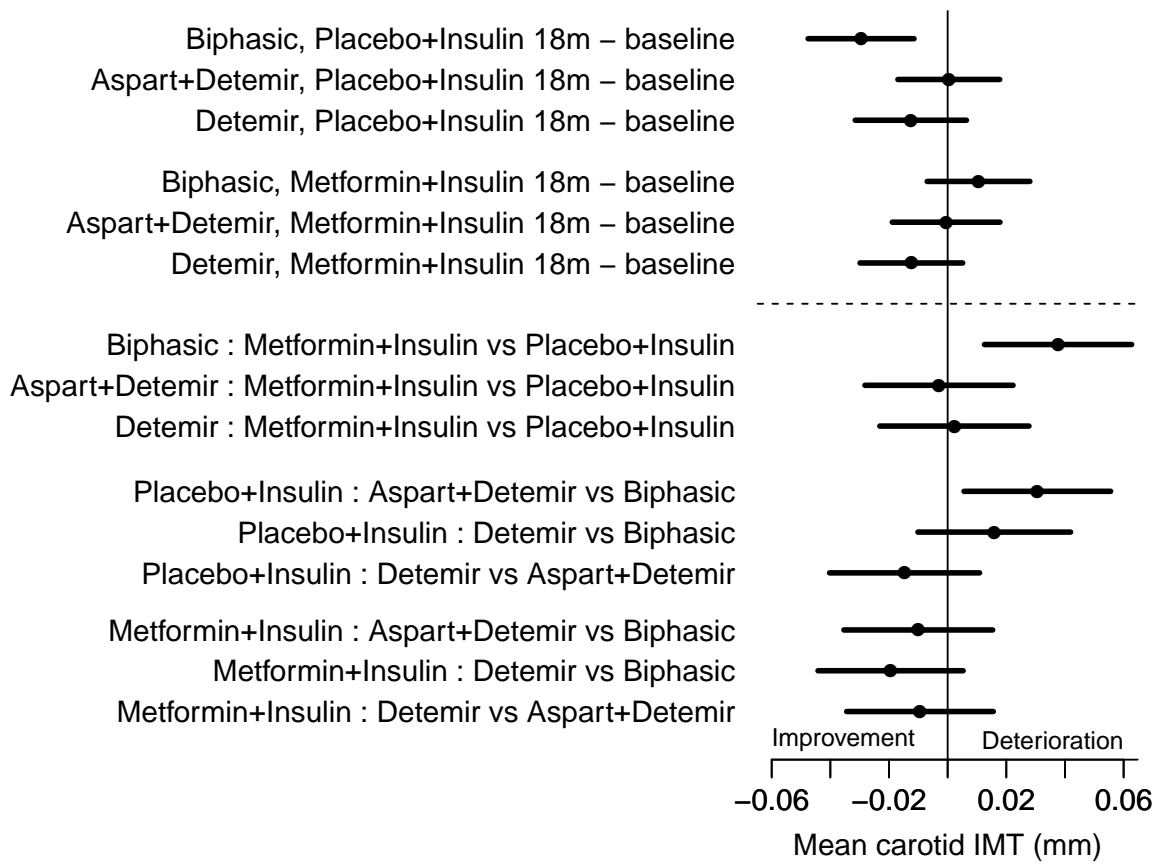


Figure 6.3: Estimated changes in each treatment group from the random effects model. The difference in changes between treatments are from the model with baseline as covariate, using multiply imputed data, adjusted for stratification variables. Bars indicate 95% c.i.

Chapter 7

Secondary outcome: Met/Plc

Initially we load the collected analysis dataset, and tabulate records and persons by randomization status and per protocol status:

```
> library( Epi )
> library( lme4 )
> library( abind )
> load( file="./data/AD.Rda" )
> with( AD, ftable( addmargins( table(grp,igr,PP=pp),
+                               2:3 ) ) )
```

	PP	FALSE	TRUE	Sum
grp igr				
Plc Biph		7	425	432
AspD		7	448	455
Detm		17	355	372
Sum		31	1228	1259
Met Biph		4	465	469
AspD		8	403	411
Detm		10	438	448
Sum		22	1306	1328

```
> with( AD, ftable( addmargins( tapply( subjid,
+                                       list(grp,igr,PP=pp),
+                                       function(x) length(unique(x)) ),
+                               2:3 ) ) )
```

	PP	FALSE	TRUE	Sum
Plc Biph		5	62	67
AspD		5	68	73
Detm		12	54	66
Sum		22	184	206
Met Biph		3	67	70
AspD		5	60	65
Detm		7	64	71
Sum		15	191	206

7.1 HbA_{1c}

7.1.1 HbA_{1c} at end of study

Initially we make a simple tabulation of the patients that achieve a HbA_{1c} ≤ 7.0%:

```
> load( file="./data/base.Rda" )
> tt <- addmargins( with( base, table( grp, hba1c.b7>7.0 )[2:1,] ) )
> cbind( tt, round( 100*tt/tt[,3], 1 ) )[, -6]
```

```

      FALSE TRUE Sum FALSE TRUE
Met    53  137 190  27.9 72.1
Plc    28  155 183  15.3 84.7
Sum    81  292 373  21.7 78.3

> twoby2( tt )

2 by 2 table analysis:
-----
Outcome   : FALSE
Comparing  : Met vs. Plc

      FALSE TRUE      P(FALSE) 95% conf. interval
Met    53  137      0.2789    0.2198  0.3469
Plc    28  155      0.1530    0.1078  0.2127

                                95% conf. interval
                                Relative Risk: 1.8231    1.2094  2.7483
                                Sample Odds Ratio: 2.1416    1.2830  3.5747
Conditional MLE Odds Ratio: 2.1372    1.2486  3.7190
Probability difference: 0.1259    0.0424  0.2072

                                Exact P-value: 0.0038
                                Asymptotic P-value: 0.0036
-----

```

We see that 12% more patients on Metformin achieve an HbA_{1c} of 7.0% or less.

A more formal test which also generalizes to three groups is achieved by using a binomial model, in this case with a log-link:

```

> m1 <- glm( hba1c.b7<=7.0 ~ grp -1, family=binomial(link="log"), data=base )
> round( 100*ci.exp( m1 ), 1 )
      exp(Est.) 2.5% 97.5%
grpPlc    15.3 10.9 21.5
grpMet    27.9 22.2 35.1

> anova( m1, update( m1, . ~ 1 ), test="Chisq" )

Analysis of Deviance Table

Model 1: hba1c.b7 <= 7 ~ grp - 1
Model 2: hba1c.b7 <= 7 ~ 1
  Resid. Df Resid. Dev Df Deviance Pr(>Chi)
1         371      381.55
2         372      390.37 -1  -8.8224 0.002976

```

So we can choose to give the p-value as 0.003 or 0.004, depending on what test we use.

The effect is also present if we control for insulin group:

```

> mi <- update( m1, . ~ . + 1 )
> mx <- update( mi, . ~ . + igr )
> round( rbind( ci.exp( mi ),
+           ci.exp( mx ) ), 2 )
      exp(Est.) 2.5% 97.5%
(Intercept)    0.15 0.11 0.22
grpMet         1.82 1.21 2.75
(Intercept)    0.21 0.14 0.31
grpMet         1.88 1.26 2.81
igrAspD        0.83 0.56 1.23
igrDetm        0.32 0.18 0.59

```

So without control for insulin, 82% more on Metformin achieve the goal, and controlling for insulin it is 88% — in both cases with quite large confidence intervals.

7.1.2 HbA_{1c} trajectories

We shall use the analysis of HbA_{1c} to set up the model for analyzing the other glucose related outcomes.

We set up a random effects model using `lmer`, first fitted to the entire dataset (intention to treat) and then to the restricted (per protocol) — analysis I.

```
> ITa <- lmer( hba1c ~ grp + grp:factor(visit) - 1 +
+             sdc + over.65 + pre.ins +
+             (1|subjid),
+             data = AD )
> round( ci.lin( ITa ), 3 )
```

	Estimate	StdErr	z	P	2.5%	97.5%
grpPlc	8.631	0.097	89.225	0.000	8.441	8.820
grpMet	8.750	0.097	89.950	0.000	8.559	8.941
sdcnotSDC	0.116	0.091	1.264	0.206	-0.064	0.295
over.65>65	-0.337	0.099	-3.389	0.001	-0.532	-0.142
pre.insnoIns	-0.335	0.099	-3.376	0.001	-0.529	-0.141
grpPlc:factor(visit)v2	0.240	0.071	3.358	0.001	0.100	0.380
grpMet:factor(visit)v2	-0.585	0.071	-8.302	0.000	-0.724	-0.447
grpPlc:factor(visit)v3	-0.252	0.073	-3.470	0.001	-0.395	-0.110
grpMet:factor(visit)v3	-0.886	0.071	-12.504	0.000	-1.025	-0.747
grpPlc:factor(visit)v4	-0.267	0.073	-3.648	0.000	-0.411	-0.124
grpMet:factor(visit)v4	-0.876	0.071	-12.278	0.000	-1.016	-0.736
grpPlc:factor(visit)v5	-0.269	0.074	-3.623	0.000	-0.414	-0.123
grpMet:factor(visit)v5	-0.841	0.072	-11.706	0.000	-0.982	-0.700
grpPlc:factor(visit)v6	-0.371	0.076	-4.882	0.000	-0.520	-0.222
grpMet:factor(visit)v6	-0.858	0.073	-11.808	0.000	-1.001	-0.716
grpPlc:factor(visit)v7	-0.356	0.072	-4.956	0.000	-0.497	-0.215
grpMet:factor(visit)v7	-0.781	0.071	-11.027	0.000	-0.920	-0.642

```
> # Per protocol analysis
> PPa <- update( ITa, data = subset( AD, pp ) )
```

We do the parallel analyses not adjusted for the stratification variables (II)

```
> ITr <- update( ITa, . ~ grp + grp:factor(visit) - 1 + (1|subjid) )
> PPr <- update( ITr, data = subset( AD, pp ) )
```

Finally we expand the first analysis by including further potential confounders (III):

```
> ITc <- update( ITa, . ~ . + sex + statin + gad.pos + cvd )
> P Pc <- update( ITc, data = subset( AD, pp ) )
```

So now we have 6 different models for the same outcome, which either will show approximately the same, or in the case they show slightly different results, enables us to pick the results that suits or prejudices best.

7.1.3 Extraction of estimated effects

From this model we want to extract first the average level of HbA_{1c} at each visit, and additionally the estimated change from visit 1 to visit 7, so we set up the corresponding contrast matrix, which will extract these from the models

```
> eM <- rbind( cbind(1,rbind(0,diag(6))), rep(0:1,c(6,1)) )
> rownames( eM ) <- c( paste( "Vis", 1:7, sep="" ), "v7-v1" )
> eM
```

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]
Vis1	1	0	0	0	0	0	0
Vis2	1	1	0	0	0	0	0
Vis3	1	0	1	0	0	0	0

```

Vis4      1    0    0    1    0    0    0
Vis5      1    0    0    0    1    0    0
Vis6      1    0    0    0    0    1    0
Vis7      1    0    0    0    0    0    1
v7-v1     0    0    0    0    0    0    1

```

With a first look at the entire parameter vector for the model we can see what subset to extract to get the desired estimates:

```

> round( ci.exp( ITa, Exp=F ), 3 )
              Estimate  2.5%  97.5%
grpPlc          8.631  8.441  8.820
grpMet          8.750  8.559  8.941
sdcnnotSDC      0.116 -0.064  0.295
over.65>65     -0.337 -0.532 -0.142
pre.insnoIns   -0.335 -0.529 -0.141
grpPlc:factor(visit)v2  0.240  0.100  0.380
grpMet:factor(visit)v2 -0.585 -0.724 -0.447
grpPlc:factor(visit)v3 -0.252 -0.395 -0.110
grpMet:factor(visit)v3 -0.886 -1.025 -0.747
grpPlc:factor(visit)v4 -0.267 -0.411 -0.124
grpMet:factor(visit)v4 -0.876 -1.016 -0.736
grpPlc:factor(visit)v5 -0.269 -0.414 -0.123
grpMet:factor(visit)v5 -0.841 -0.982 -0.700
grpPlc:factor(visit)v6 -0.371 -0.520 -0.222
grpMet:factor(visit)v6 -0.858 -1.001 -0.716
grpPlc:factor(visit)v7 -0.356 -0.497 -0.215
grpMet:factor(visit)v7 -0.781 -0.920 -0.642
> round( ci.exp( ITa, subset="Met", Exp=F ), 3 )
              Estimate  2.5%  97.5%
grpMet          8.750  8.559  8.941
grpMet:factor(visit)v2 -0.585 -0.724 -0.447
grpMet:factor(visit)v3 -0.886 -1.025 -0.747
grpMet:factor(visit)v4 -0.876 -1.016 -0.736
grpMet:factor(visit)v5 -0.841 -0.982 -0.700
grpMet:factor(visit)v6 -0.858 -1.001 -0.716
grpMet:factor(visit)v7 -0.781 -0.920 -0.642
> round( ci.exp( ITa, subset="Plc", Exp=F ), 3 )
              Estimate  2.5%  97.5%
grpPlc          8.631  8.441  8.820
grpPlc:factor(visit)v2  0.240  0.100  0.380
grpPlc:factor(visit)v3 -0.252 -0.395 -0.110
grpPlc:factor(visit)v4 -0.267 -0.411 -0.124
grpPlc:factor(visit)v5 -0.269 -0.414 -0.123
grpPlc:factor(visit)v6 -0.371 -0.520 -0.222
grpPlc:factor(visit)v7 -0.356 -0.497 -0.215
> round( ci.lin( ITa, subint=c("Met","v7"), Exp=F ), 3 )
              Estimate StdErr      z P  2.5%  97.5%
grpMet:factor(visit)v7 -0.781  0.071 -11.027 0 -0.92 -0.642
> c.plc <- ci.exp( ITa, ctr.mat=eM, subset="Plc", Exp=F )
> c.met <- ci.exp( ITa, ctr.mat=eM, subset="Met", Exp=F )
> c.dif <- ci.exp( ITa, ctr.mat=cbind(eM,-eM),
+               subset=c("Met","Plc"), Exp=F )
> round( cbind( c.met, c.plc, c.dif ), 3 )
              Estimate  2.5%  97.5% Estimate  2.5%  97.5% Estimate  2.5%  97.5%
Vis1          8.750  8.559  8.941    8.631  8.441  8.820    0.119 -0.094  0.332
Vis2          8.164  7.971  8.358    8.871  8.677  9.064   -0.706 -0.924 -0.488
Vis3          7.864  7.670  8.057    8.378  8.184  8.573   -0.515 -0.735 -0.294
Vis4          7.874  7.679  8.068    8.363  8.168  8.559   -0.490 -0.712 -0.268
Vis5          7.909  7.714  8.104    8.362  8.165  8.559   -0.453 -0.676 -0.229
Vis6          7.892  7.695  8.088    8.260  8.060  8.460   -0.368 -0.595 -0.141
Vis7          7.969  7.776  8.162    8.275  8.081  8.468   -0.306 -0.525 -0.086
v7-v1        -0.781 -0.920 -0.642   -0.356 -0.497 -0.215   -0.425 -0.623 -0.227

```

We also want to test whether the trajectories of the outcome (HbA_{1c}) is the same in the two randomization groups, whether the values at the last visit is the same, and whether the change from first to last visit is the same. These three tests are accomplished by using the same contrasts matrix that we just set up:

```
> test <- rbind( Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[-8,] ),
+               Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+               Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+               Wald( ITa, subint=c("Met", "v7" ) ),
+               Wald( ITa, subint=c("Plc", "v7" ) ) )
> rownames( test ) <- c(" All equal",
+                       "Visit 7 equal",
+                       " Change equal",
+                       " Met chg = 0",
+                       " Plc chg = 0")
> round( test, 4 )
```

	Chisq	d.f.	P
All equal	94.8066	7	0.0000
Visit 7 equal	7.4532	1	0.0063
Change equal	17.7260	1	0.0000
Met chg = 0	121.5922	1	0.0000
Plc chg = 0	24.5619	1	0.0000

For convenience we pack these extractors and tests in a function, that takes a particular model as argument:

```
> resfun <-
+ function( ITa )
+ {
+   c.plc <- ci.exp( ITa, ctr.mat=eM, subset="Plc", Exp=F )
+   c.met <- ci.exp( ITa, ctr.mat=eM, subset="Met", Exp=F )
+   c.dif <- ci.exp( ITa, subset=c("Met", "Plc"), Exp=F, ctr.mat=cbind(eM,-eM) )
+   test <- rbind( Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[-8,] ),
+                 Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+                 Wald( ITa, subset=c("Met", "Plc"), ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+                 Wald( ITa, subint=c("Met", "v7" ) ),
+                 Wald( ITa, subint=c("Plc", "v7" ) ) )
+   rownames( test ) <- c(" All equal",
+                         "Visit 7 equal",
+                         " Change equal",
+                         " Met chg = 0",
+                         " Plc chg = 0")
+   eff <- cbind( c.met, c.plc, c.dif )
+   colnames( eff )[1+0:2*3] <- c("Met", "Plc", "M-P")
+   print( round( eff, 3 ) )
+   print( round( test, 4 ) )
+   invisible( list( eff=eff, test=test ) )
+ }
```

This can now be applied to all fitted models

```
> cat( "\nIntention to treat, stratum variables:\n-----\n" )
Intention to treat, stratum variables:
-----
> hbr <- resfun( ITa )
```

	Met	2.5%	97.5%	Plc	2.5%	97.5%	M-P	2.5%	97.5%
Vis1	8.750	8.559	8.941	8.631	8.441	8.820	0.119	-0.094	0.332
Vis2	8.164	7.971	8.358	8.871	8.677	9.064	-0.706	-0.924	-0.488
Vis3	7.864	7.670	8.057	8.378	8.184	8.573	-0.515	-0.735	-0.294
Vis4	7.874	7.679	8.068	8.363	8.168	8.559	-0.490	-0.712	-0.268
Vis5	7.909	7.714	8.104	8.362	8.165	8.559	-0.453	-0.676	-0.229
Vis6	7.892	7.695	8.088	8.260	8.060	8.460	-0.368	-0.595	-0.141

```

Vis7  7.969  7.776  8.162  8.275  8.081  8.468 -0.306 -0.525 -0.086
v7-v1 -0.781 -0.920 -0.642 -0.356 -0.497 -0.215 -0.425 -0.623 -0.227
      Chisq d.f.      P
All equal  94.8066    7 0.0000
Visit 7 equal  7.4532    1 0.0063
Change equal  17.7260    1 0.0000
Met chg = 0 121.5922    1 0.0000
Plc chg = 0  24.5619    1 0.0000
> cat( "\nIntention to treat, no stratum variables:\n-----\n" )
Intention to treat, no stratum variables:
-----
> resfun( ITr )
      Met  2.5% 97.5%   Plc  2.5% 97.5%   M-P  2.5% 97.5%
Vis1  8.608 8.455 8.761 8.492 8.339 8.645 0.117 -0.100 0.333
Vis2  8.021 7.865 8.177 8.730 8.573 8.888 -0.709 -0.931 -0.487
Vis3  7.720 7.564 7.877 8.239 8.080 8.399 -0.519 -0.743 -0.295
Vis4  7.731 7.573 7.888 8.225 8.064 8.385 -0.494 -0.719 -0.269
Vis5  7.766 7.607 7.924 8.223 8.060 8.385 -0.457 -0.684 -0.230
Vis6  7.749 7.589 7.908 8.121 7.956 8.287 -0.373 -0.603 -0.143
Vis7  7.826 7.670 7.983 8.135 7.977 8.293 -0.309 -0.532 -0.086
v7-v1 -0.782 -0.921 -0.643 -0.357 -0.498 -0.216 -0.425 -0.623 -0.228
      Chisq d.f.      P
All equal  94.5153    7 0.0000
Visit 7 equal  7.3928    1 0.0065
Change equal  17.7738    1 0.0000
Met chg = 0 121.9614    1 0.0000
Plc chg = 0  24.6403    1 0.0000
> cat( "\nIntention to treat, stratum variables + confounders:\n-----\n" )
Intention to treat, stratum variables + confounders:
-----
> resfun( ITc )
      Met  2.5% 97.5%   Plc  2.5% 97.5%   M-P  2.5% 97.5%
Vis1  8.901 8.588 9.214 8.790 8.469 9.111 0.111 -0.104 0.325
Vis2  8.316 8.001 8.631 9.030 8.707 9.354 -0.715 -0.934 -0.495
Vis3  8.015 7.700 8.330 8.538 8.213 8.863 -0.524 -0.745 -0.302
Vis4  8.025 7.709 8.340 8.523 8.198 8.849 -0.499 -0.722 -0.275
Vis5  8.060 7.744 8.376 8.522 8.195 8.848 -0.462 -0.686 -0.237
Vis6  8.043 7.726 8.360 8.420 8.092 8.748 -0.377 -0.605 -0.149
Vis7  8.120 7.805 8.436 8.435 8.110 8.759 -0.314 -0.535 -0.094
v7-v1 -0.781 -0.919 -0.642 -0.355 -0.496 -0.214 -0.425 -0.623 -0.227
      Chisq d.f.      P
All equal  95.3386    7 0.0000
Visit 7 equal  7.7967    1 0.0052
Change equal  17.7458    1 0.0000
Met chg = 0 121.4348    1 0.0000
Plc chg = 0  24.4352    1 0.0000
> cat( "\nPer protocol, stratum variables:\n-----\n" )
Per protocol, stratum variables:
-----
> resfun( PPa )
      Met  2.5% 97.5%   Plc  2.5% 97.5%   M-P  2.5% 97.5%
Vis1  8.807 8.609 9.005 8.650 8.454 8.847 0.157 -0.067 0.380
Vis2  8.179 7.982 8.377 8.841 8.644 9.038 -0.661 -0.885 -0.438
Vis3  7.889 7.692 8.087 8.373 8.175 8.571 -0.483 -0.708 -0.259
Vis4  7.900 7.701 8.098 8.358 8.159 8.557 -0.458 -0.684 -0.233
Vis5  7.935 7.736 8.134 8.357 8.156 8.557 -0.421 -0.649 -0.194
Vis6  7.918 7.717 8.118 8.255 8.052 8.458 -0.337 -0.568 -0.106
Vis7  7.980 7.781 8.178 8.253 8.055 8.450 -0.273 -0.498 -0.048
v7-v1 -0.827 -0.967 -0.687 -0.398 -0.541 -0.255 -0.429 -0.629 -0.229
      Chisq d.f.      P

```

```

      All equal  90.6987    7 0.0000
Visit 7 equal   5.6615    1 0.0173
Change equal   17.6808    1 0.0000
Met chg = 0  133.8320    1 0.0000
Plc chg = 0   29.8134    1 0.0000

> cat( "\nPer protocol, no stratum variables:\n-----\n" )
Per protocol, no stratum variables:
-----

> resfun( PPr )
      Met  2.5% 97.5%   Plc  2.5% 97.5%   M-P  2.5% 97.5%
Vis1  8.643 8.484 8.802  8.494 8.332 8.656 0.149 -0.078 0.376
Vis2  8.015 7.856 8.174  8.684 8.522 8.846 -0.669 -0.896 -0.442
Vis3  7.725 7.566 7.885  8.217 8.053 8.380 -0.491 -0.720 -0.263
Vis4  7.736 7.576 7.896  8.202 8.037 8.366 -0.466 -0.695 -0.236
Vis5  7.771 7.610 7.932  8.200 8.034 8.366 -0.429 -0.661 -0.198
Vis6  7.754 7.592 7.916  8.099 7.930 8.268 -0.345 -0.579 -0.110
Vis7  7.816 7.656 7.976  8.096 7.933 8.259 -0.280 -0.508 -0.051
v7-v1 -0.827 -0.967 -0.687 -0.398 -0.541 -0.255 -0.429 -0.629 -0.229
      Chisq d.f.      P
All equal  90.5797    7 0.0000
Visit 7 equal   5.7585    1 0.0164
Change equal   17.6339    1 0.0000
Met chg = 0  133.7395    1 0.0000
Plc chg = 0   29.8560    1 0.0000

> cat( "\nPer protocol, stratum variables + confounders:\n-----\n" )
Per protocol, stratum variables + confounders:
-----

> resfun( PPc )
      Met  2.5% 97.5%   Plc  2.5% 97.5%   M-P  2.5% 97.5%
Vis1  8.931 8.604 9.257  8.784 8.446 9.123 0.146 -0.078 0.371
Vis2  8.303 7.976 8.629  8.974 8.636 9.313 -0.671 -0.896 -0.447
Vis3  8.013 7.687 8.340  8.507 8.168 8.846 -0.494 -0.719 -0.268
Vis4  8.023 7.696 8.350  8.492 8.153 8.831 -0.468 -0.696 -0.241
Vis5  8.059 7.731 8.387  8.490 8.150 8.831 -0.431 -0.660 -0.203
Vis6  8.042 7.713 8.370  8.388 8.047 8.730 -0.347 -0.579 -0.115
Vis7  8.103 7.776 8.431  8.386 8.048 8.725 -0.283 -0.509 -0.057
v7-v1 -0.827 -0.967 -0.687 -0.398 -0.541 -0.255 -0.429 -0.629 -0.229
      Chisq d.f.      P
All equal  91.2269    7 0.0000
Visit 7 equal   6.0132    1 0.0142
Change equal   17.6734    1 0.0000
Met chg = 0  133.8161    1 0.0000
Plc chg = 0   29.8196    1 0.0000

```

We now have the results from all 6 analyses analysis, so we can plot the estimated trajectories of the HbA_{1c} over the seven visits:

```

> plt <-
+ function()
+ {
+   matplot( 0:6*3, hbr$eff[1:7,],
+           xlab="Months since trial entry", xaxt="n", xlim=c(0,19.5),
+           ylim=c(7,9.5), yaxs="i", yaxt="n",
+           ylab=expression( "Hb"*A[1][c]*" (%) [Mean (95% CI)]" ),
+           type="n", lwd=c(4,1,1), lty=1, col=rep(cnr[1:2],each=3) )
+ abline( h=seq(7,9.5,0.2), col=gray(0.8) )
+ matlines( 0:6*3, hbr$eff[1:7,],
+           type="l", lwd=c(5,1,1), lty=1, col=rep(cnr[1:2],each=3) )
+ axis( side=1, at=0:6*3, col=cnr[4] )
+ axis( side=2, at=7:9, col=cnr[4] )
+ text( c(20,20), c(9.3,9.1), c("Metformin","Placebo"), col=cnr[1:2],

```

```

+ font=2, adj=1, cex=1 )
+ text( 20, 8.9, substitute( "Equal change in Hb"*A[1][c]*" 0-18 mth: P ="*pval,
+ list(pval = formatC( hbr$test[3,3], format="f", digits=4 ) ) ),
+ col=clr[4], adj=1 )
+ text( 19.9, 8.7, "HbA1c change\n from baseline", col=clr[4], adj=c(1,0.5) )
+ text( c(20,20), hbr$eff[7,c(1,4)],
+ paste( formatC( hbr$eff[8,c(1,4)],
+ format="f", digits=1 ), "%", sep="" ),
+ col=clr[1:2], adj=1 )
+ }
> oldpar <- par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1, bty="n" )
> plt()

```

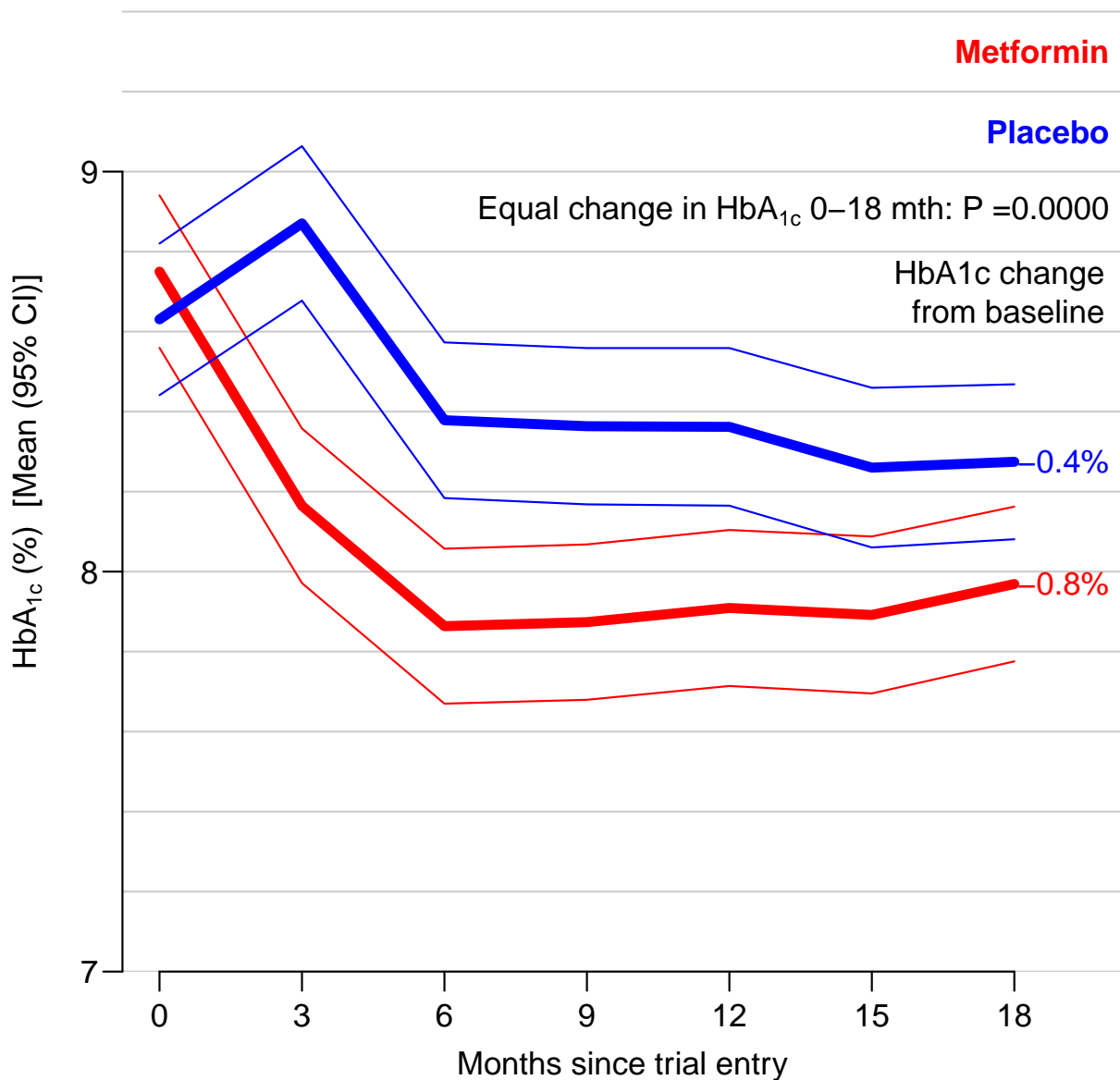


Figure 7.1: Fitted mean HbA_{1c} from a mixed model with 95% c.i.

7.2 A general lay-out of the analysis

The above analysis of HbA_{1c} can be groomed into a single function that does all analyses, shows the tables and ultimately give a result that can be used as input for a graph.

Some computer programs produce means corresponding to population means for a population with the same stratum composition as the study population. If we were to produce estimates (essentially just adding some fixed quantity, namely a suitably weighted sum of the stratum effects) corresponding to some population composition we would have to argue *a priori* exactly which population composition would be of interest. This would of course be totally arbitray, so we have chosen the largest group of patients as reference group, that is we report the estimated means in a population of patients from Steno Diabetes Center, under 65 with previous insulin use — a particular, yet still totally arbitray choice.

First the analysis function, that basically only takes the name of the variable as input. It should return a list of 3 arrays, one with mean estimates, one with standard deviation estimates and one with tests:

```
> var <- "hba1c"
```

First we define a few useful structures

```
> # Names of tests performed
> ( tnames <- rownames( test ) )
[1] " All equal" "Visit 7 equal" " Change equal" " Met chg = 0" " Plc chg = 0"
```

Then a function to generate a contrast matrix to *either* get the effects or the test statistics. This is called from eFUN and tFUN:

```
> CM <-
+ function( mod, eff )
+ {
+ # Contrast matrix to fish out the estimates, resp tests
+ cM <- cbind(1, rbind(0, diag(6)))
+ rownames( cM ) <- paste( "Vis", 1:7 )
+ # Find missing visits for the variable, make two versions of the matrix
+ tp <- sapply( strsplit(rownames(ci.exp(mod, subset="Met")), "" ),
+             function(x) x[length(x)] )
+ tp[1] <- 1
+ tp <- as.numeric( tp )
+ # The contrast row should be between the last existing measurement and
+ # the first:
+ cM <- rbind( cM, cM[tp[length(tp)],]-cM[1,] )
+ # Are there any missing timepoints in this analysis?
+ mv <- setdiff(1:7, tp)
+ if( length(mv) > 0 )
+ {
+ # If used to extract effects keep rows for all timepoints, but
+ # return NAs for timepoints with no measurements:
+ cM[mv,] <- NA
+ cM <- if(eff) cM[,-mv] else cM[-mv,-mv]
+ }
+ cM
+ }
```

Then we need a function to get the mean value estimates from a model


```

> eFUN <-
+ function( mod )
+ {
+ eM <- CM( mod, eff=TRUE )
+ # Insert some NA-rows to get results in right dimension
+ met <- ci.exp( mod, ctr.mat= eM, subset= "Met", Exp=F )
+ plc <- ci.exp( mod, ctr.mat= eM, subset= "Plc", Exp=F )
+ dif <- ci.exp( mod, ctr.mat=cbind(eM,-eM), subset=c("Met","Plc"), Exp=F )
+ abind( list(Met=met, Plc=plc, Dif=dif), rev.along=0 )
+ }

```

A function to get the between person and the residual sd from a model:

```

> sFUN <-
+ function( mod )
+ {
+ res <- c( attr( VarCorr( mod )$subjid, "stddev" ),
+ attr( VarCorr( mod ), "sc" ) )
+ names( res ) <- c("Btw","Res")
+ res
+ }

```

A function to compute the relevant tests from a fitted model

```

> tFUN <-
+ function( mod )
+ {
+ eX <- CM( mod, eff=FALSE )
+ np <- nrow( eX )
+ lastM <- grep( "Met", rownames(ci.exp(mod)) ) ; lastM <- lastM[length(lastM)]
+ lastP <- grep( "Plc", rownames(ci.exp(mod)) ) ; lastP <- lastP[length(lastP)]
+ test <- rbind( Wald( mod, subset=c("Met","Plc"), ctr.mat=cbind(-eX,eX)[-np,] ),
+ Wald( mod, subset=c("Met","Plc"), ctr.mat=cbind(-eX,eX)[ np-1,,drop=F] ),
+ Wald( mod, subset=c("Met","Plc"), ctr.mat=cbind(-eX,eX)[ np ,,drop=F] ),
+ Wald( mod, subset=lastM ),
+ Wald( mod, subset=lastP ) )
+ rownames( test ) <- tnames
+ test
+ }

```

Then we can define the function to use, including a few useful arrays that will be filled out:

```

> # Names of variable to be used in repeated measures analyses
> vnam <- c("hba1c","weight","bmi","whr","gluc","ins","cpep",
+ "idos","ipkg","sys","dia","pulse",
+ "chol","ldl","hdl","vldl","trig",
+ "fimtavg","fimtmax","iem","csc2","imtareal","n.pl")
> match( vnam, names(AD) )
      [1] 11  8  9 10 12 13 16 14 15 22 23 24 17 18 19 20 21 143 145 158 157
      [22] 150 187

```

We then produce an overview of the pairwise distribution of the variables in order to see if some of them are very strongly correlated and thus will give the same results:

```

> pairs( AD[,c("visit",vnam)], gap=0, pch=16, cex=0.3 )

```

This gives a very large plot in terms of space, so we will not include it in this document. Moreover, we also want to inspect the marginal distributions of each, as a preliminary guide to which of the variables to log-transform:


```
> par( mfrow=c(6,4), mar=c(2,1,1,1), mgp=c(3,1,0)/1.6 )
> for( vv in vnam ) hist( AD[,vv], breaks=50, border="black",
+                         col="black", main=vv, xlab="",ylab="",yaxt="n" )
> hist( log10(AD[,"ins"]), breaks=50, border="black",
+       col="black", main="log10(ins)", xlab="",ylab="",yaxt="n" )
```

It looks as if the insulin variables and vldl, trig and the no. of plaques need a log transform, so that will be the initial approach. For overview we also tabulate how many non-missing values there are for each visit:

```
> ltrf <- rep( FALSE, length(vnam) )
> ltrf[c(6:9,16,17,23)] <- TRUE
> cbind( vnam, ltrf )
```

	vnam	ltrf
[1,]	"hba1c"	"FALSE"
[2,]	"weight"	"FALSE"
[3,]	"bmi"	"FALSE"
[4,]	"whr"	"FALSE"
[5,]	"gluc"	"FALSE"
[6,]	"ins"	"TRUE"
[7,]	"cpep"	"TRUE"
[8,]	"idos"	"TRUE"
[9,]	"ipkg"	"TRUE"
[10,]	"sys"	"FALSE"
[11,]	"dia"	"FALSE"
[12,]	"pulse"	"FALSE"
[13,]	"chol"	"FALSE"
[14,]	"ldl"	"FALSE"
[15,]	"hdl"	"FALSE"
[16,]	"vldl"	"TRUE"
[17,]	"trig"	"TRUE"
[18,]	"fimtavg"	"FALSE"
[19,]	"fimtmax"	"FALSE"
[20,]	"iem"	"FALSE"
[21,]	"csc2"	"FALSE"
[22,]	"imtareal"	"FALSE"
[23,]	"n.pl"	"TRUE"

```
> for( vv in vnam )
+ {
+ cat( "-----\n",vv )
+ print( table( !is.na(AD[,vv]), AD$visit ) )
+ }
```

```
-----
hba1c
      v1 v2 v3 v4 v5 v6 v7
FALSE  0  3  4  3  2  6  1
TRUE  412 380 367 359 348 329 373
-----
```

```
weight
      v1 v2 v3 v4 v5 v6 v7
FALSE  0  3  1  4  3  2  5
TRUE  412 380 370 358 347 333 369
-----
```

```
bmi
      v1 v2 v3 v4 v5 v6 v7
FALSE  0  3  1  4  3  2  5
TRUE  412 380 370 358 347 333 369
-----
```

```
whr
      v1 v2 v3 v4 v5 v6 v7
FALSE  7  9  6  6  6  8  12
TRUE  405 374 365 356 344 327 362
-----
```

```
gluc
```

	v1	v2	v3	v4	v5	v6	v7
FALSE	1	25	30	24	15	20	1
TRUE	411	358	341	338	335	315	373

ins							
	v1	v2	v3	v4	v5	v6	v7
FALSE	0	383	371	362	350	335	5
TRUE	412	0	0	0	0	0	369

cpep							
	v1	v2	v3	v4	v5	v6	v7
FALSE	0	383	371	362	350	335	5
TRUE	412	0	0	0	0	0	369

idos							
	v1	v2	v3	v4	v5	v6	v7
FALSE	2	3	4	1	1	1	374
TRUE	410	380	367	361	349	334	0

ipkg							
	v1	v2	v3	v4	v5	v6	v7
FALSE	2	6	5	5	4	3	374
TRUE	410	377	366	357	346	332	0

sys							
	v1	v2	v3	v4	v5	v6	v7
FALSE	5	4	1	4	2	4	31
TRUE	407	379	370	358	348	331	343

dia							
	v1	v2	v3	v4	v5	v6	v7
FALSE	5	4	1	4	2	4	31
TRUE	407	379	370	358	348	331	343

pulse							
	v1	v2	v3	v4	v5	v6	v7
FALSE	8	8	8	6	5	6	39
TRUE	404	375	363	356	345	329	335

chol							
	v1	v2	v3	v4	v5	v6	v7
FALSE	0	383	25	362	12	335	4
TRUE	412	0	346	0	338	0	370

ldl							
	v1	v2	v3	v4	v5	v6	v7
FALSE	14	383	34	362	24	335	17
TRUE	398	0	337	0	326	0	357

hdl							
	v1	v2	v3	v4	v5	v6	v7
FALSE	0	383	25	362	13	335	4
TRUE	412	0	346	0	337	0	370

vldl							
	v1	v2	v3	v4	v5	v6	v7
FALSE	13	383	77	362	74	335	14
TRUE	399	0	294	0	276	0	360

trig							
	v1	v2	v3	v4	v5	v6	v7
FALSE	0	383	28	362	13	335	4
TRUE	412	0	343	0	337	0	370

fimtavg							
	v1	v2	v3	v4	v5	v6	v7

```

FALSE  0 383 371 362 350 335  3
TRUE   412  0  0  0  0  0 371
-----
fimtmax
      v1 v2 v3 v4 v5 v6 v7
FALSE  0 383 371 362 350 335  3
TRUE   412  0  0  0  0  0 371
-----
iem
      v1 v2 v3 v4 v5 v6 v7
FALSE  36 383 371 362 350 335  54
TRUE   376  0  0  0  0  0 320
-----
csc2
      v1 v2 v3 v4 v5 v6 v7
FALSE  36 383 371 362 350 335  54
TRUE   376  0  0  0  0  0 320
-----
imtareal
      v1 v2 v3 v4 v5 v6 v7
FALSE  36 383 371 362 350 335  54
TRUE   376  0  0  0  0  0 320
-----
n.pl
      v1 v2 v3 v4 v5 v6 v7
FALSE 118 383 371 362 350 335  95
TRUE  294  0  0  0  0  0 279

```

Now we can set up arrays to hold the results from the analyses — for each variable we do 6 analyses in order to 1) make the confusion complete 2) be able to choose the results that fits our prejudices better 3) and make the p-values smaller.

First, we set up a couple of arrays to hold the results from the analyses:

```

> # Arrays to hold results over variables
> # Variance components
> Std <- NArray( list( var = paste( vnam, ifelse(ltrf,"(1)",""), sep="" ),
+                       ana = c("IT","PP"),
+                       mod = c("Prim","Rest","Conf"),
+                       std = c("Btw","Res") ) )
> # Estimates
> Eff <- NArray( c( dimnames(Std)[-4],
+                  list( par = c(paste("Vis",1:7),"V7-V1"),
+                            c("Est","lo","hi"),
+                            c("Met","Plc","Dif") ) ) )
> # Tests
> Tst <- NArray( c( dimnames(Std)[-4],
+                  list( test = tnames,
+                        what = c("Chisq","df","Pval") ) ) )
> # Smaller versions of the arrys to be used inside the function that
> # does the calculations for each response variable
> std <- NArray( dimnames(Std)[-1] )
> eff <- NArray( dimnames(Eff)[-1] )
> tst <- NArray( dimnames(Tst)[-1] )

```

With these structures in place we can set up a function that fits the relevant models and extracts the results. The only argument is the name of the response variable, and an indicator of whether it should be log-transformed before analysis. We first define a log-function that returns NA instead of $-\text{Inf}$, since the variables we want to log-transform logically cannot have a 0 value.

```

> # Function to do PPplots for residuals
> PPplot <-
+ function( x, xl )

```

```

+ {
+ n <- length(x)
+ plot( pnorm( sort(x/sd(x)) ), (1:n-0.5)/n,
+       pch=16, cex=0.4,
+       xlim=0:1, ylim=0:1,
+       xlab="", ylab="",
+       xaxt="n", yaxt="n" )
+ text( 0, 1, xl, adj=c(0,1) )
+ abline( 0, 1 )
+ }
> # A function that returns NA instead of -Inf for 0 argument
> logI <- function(x) ifelse(x>0,log(x),NA)
> # Function that makes all analyses for one response variable
> ana.fun <-
+ function( var, log.tr=FALSE, respl=FALSE )
+ {
+ # We need a single name of the response variable
+ AD$Y <- if(log.tr) logI(AD[,var]) else AD[,var]
+ # Fit models to total and PP part of dataset:
+ # r: Reduced model
+ # a: Primary model
+ # c: Confounder-expanded model
+ ITr <- lmer( Y ~ grp + grp:factor(visit) - 1 + (1|subjid), data = AD )
+ ITa <- lmer( Y ~ grp + grp:factor(visit) - 1 + sdc + over.65 + pre.ins
+           + (1|subjid), data = AD )
+ ITc <- lmer( Y ~ grp + grp:factor(visit) - 1 + sdc + over.65 + pre.ins
+           + sex + statin + gad.pos + cvd
+           + (1|subjid), data = AD )
+ # ITa <- update( ITr, . ~ . + sdc + over.65 + pre.ins )
+ # ITc <- update( ITa, . ~ . + sex + statin + gad.pos + cvd )
+ PPa <- update( ITa, data = subset( AD, pp ) )
+ PPr <- update( ITr, data = subset( AD, pp ) )
+ PPc <- update( ITc, data = subset( AD, pp ) )
+
+ # Plots if specified - but only for ITa analysis - note the S4 way of
+ # extracting slots from the objects, does not work for medMod objects
+ # if( respl )
+ # {
+ # PPplot( ITa@ranef, paste(var,if(log.tr)"(log-tr)","nptt") )
+ # PPplot( ITa@resid, paste(var,if(log.tr)"(log-tr)","nres") )
+ # }
+
+ # Fixed effects
+ eff["IT","Prim",,,] <- eFUN( ITa )
+ eff["IT","Rest",,,] <- eFUN( ITr )
+ eff["IT","Conf",,,] <- eFUN( ITc )
+ eff["PP","Prim",,,] <- eFUN( PPa )
+ eff["PP","Rest",,,] <- eFUN( PPr )
+ eff["PP","Conf",,,] <- eFUN( PPc )
+ if( log.tr ) eff <- exp( eff )
+ # Variance components
+ std["IT","Prim",] <- sFUN( ITa )
+ std["IT","Rest",] <- sFUN( ITr )
+ std["IT","Conf",] <- sFUN( ITc )
+ std["PP","Prim",] <- sFUN( PPa )
+ std["PP","Rest",] <- sFUN( PPr )
+ std["PP","Conf",] <- sFUN( PPc )
+ # Tests
+ tst["IT","Prim",,,] <- tFUN( ITa )
+ tst["IT","Rest",,,] <- tFUN( ITr )
+ tst["IT","Conf",,,] <- tFUN( ITc )
+ tst["PP","Prim",,,] <- tFUN( PPa )
+ tst["PP","Rest",,,] <- tFUN( PPr )
+ tst["PP","Conf",,,] <- tFUN( PPc )
+ # Return all in a list
+ list( eff=eff, std=std, tst=tst )

```

```
+ }
```

With this specification of models we can now fill in the arrays and also show the residual plots:

```
> par( mfrow=c(8,6), mar=c(0,0,0,0), omi=c(3,3,1,1)/4 )
> for( i in 1:length(vnam) )
+ {
+   cat( vnam[i], "\n" )
+   res <- ana.fun( vnam[i], ltrf[i], respl=TRUE )
+   Eff[i,,,,] <- res$eff
+   Std[i,,,] <- res$std
+   Tst[i,,,,] <- res$tst
+   #   mtext( expression(Phi^-1*" [sort(std. res.) ]"),
+   #         side=1, line=2, outer=TRUE )
+   #   mtext( "Uniform[0,1]", side=2, line=2, outer=TRUE )
+ }
hba1c
weight
bmi
whr
gluc
ins
cpep
idos
ipkg
sys
dia
pulse
chol
ldl
hdl
vldl
trig
fimtavg
fimtmax
iem
csc2
imtareal
n.pl
> apply( Eff, 1:2, FUN=function(x) mean(is.na(x)) )
      ana
var    IT  PP
hba1c  0.000 0.000
weight 0.000 0.000
bmi     0.000 0.000
whr     0.000 0.000
gluc    0.000 0.000
ins(1)  0.625 0.625
cpep(1) 0.625 0.625
idos(1) 0.125 0.125
ipkg(1) 0.125 0.125
sys     0.000 0.000
dia     0.000 0.000
pulse   0.000 0.000
chol    0.375 0.375
ldl     0.375 0.375
hdl     0.375 0.375
vldl(1) 0.375 0.375
trig(1) 0.375 0.375
fimtavg 0.625 0.625
fimtmax 0.625 0.625
iem     0.625 0.625
csc2    0.625 0.625
imtareal 0.625 0.625
n.pl(1) 0.625 0.625
```


	Vis 7	1.128	1.064	1.191	1.116	1.053	1.180	0.011	-0.057	0.080
	V7-V1	0.011	-0.018	0.041	-0.005	-0.035	0.025	0.016	-0.026	0.058
vldl(1)	Vis 1	0.751	0.690	0.818	0.702	0.646	0.763	1.070	0.976	1.174
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.731	0.670	0.798	0.706	0.647	0.771	1.035	0.936	1.145
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	0.780	0.714	0.852	0.694	0.635	0.759	1.123	1.014	1.244
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.765	0.702	0.833	0.684	0.628	0.745	1.118	1.016	1.229
	V7-V1	1.018	0.960	1.079	0.975	0.920	1.033	1.044	0.962	1.134
trig(1)	Vis 1	1.737	1.584	1.906	1.577	1.439	1.730	1.101	0.996	1.218
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.667	1.516	1.832	1.575	1.432	1.731	1.058	0.953	1.176
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.728	1.572	1.900	1.598	1.452	1.758	1.082	0.973	1.203
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.759	1.602	1.933	1.549	1.411	1.702	1.136	1.024	1.259
	V7-V1	1.013	0.955	1.074	0.982	0.926	1.042	1.031	0.948	1.121
fimtavg	Vis 1	0.753	0.729	0.777	0.765	0.741	0.789	-0.012	-0.037	0.013
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.752	0.728	0.777	0.752	0.727	0.776	0.001	-0.025	0.026
	V7-V1	-0.001	-0.011	0.010	-0.014	-0.024	-0.003	0.013	-0.002	0.027
fimtmax	Vis 1	0.915	0.887	0.942	0.923	0.895	0.950	-0.008	-0.037	0.021
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.912	0.884	0.940	0.908	0.881	0.936	0.003	-0.026	0.033
	V7-V1	-0.003	-0.015	0.010	-0.014	-0.026	-0.002	0.011	-0.006	0.029
iem	Vis 1	2075.153	1901.945	2248.361	2029.019	1859.321	2198.717	46.134	-138.828	231.096
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2028.121	1850.602	2205.640	1858.558	1682.232	2034.885	169.563	-25.472	364.598
	V7-V1	-47.032	-173.147	79.083	-170.461	-296.495	-44.426	123.429	-54.875	301.733
csc2	Vis 1	2.852	2.675	3.030	2.887	2.712	3.061	-0.034	-0.223	0.155
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.866	2.684	3.048	2.966	2.785	3.146	-0.100	-0.299	0.098
	V7-V1	0.013	-0.109	0.135	0.079	-0.043	0.201	-0.066	-0.239	0.107
imtareal	Vis 1	17.671	16.815	18.528	18.278	17.436	19.120	-0.607	-1.497	0.283
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	17.834	16.969	18.699	18.033	17.179	18.887	-0.199	-1.108	0.711
	V7-V1	0.163	-0.197	0.523	-0.245	-0.605	0.114	0.408	-0.101	0.917
n.pl(1)	Vis 1	2.093	1.782	2.457	2.427	2.055	2.867	0.862	0.728	1.021
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.524	2.149	2.966	2.701	2.285	3.194	0.935	0.788	1.108
	V7-V1	1.206	1.131	1.287	1.113	1.037	1.194	1.084	0.985	1.193

```
> round( ftable( Eff[, "IT", "Rest",,,], col.vars=4:3 ), 3 )
```

var	par	Met Est	lo	hi	Plc Est	lo	hi	Dif Est	lo	hi
hba1c	Vis 1	8.608	8.455	8.761	8.492	8.339	8.645	0.117	-0.100	0.333
	Vis 2	8.021	7.865	8.177	8.730	8.573	8.888	-0.709	-0.931	-0.487
	Vis 3	7.720	7.564	7.877	8.239	8.080	8.399	-0.519	-0.743	-0.295
	Vis 4	7.731	7.573	7.888	8.225	8.064	8.385	-0.494	-0.719	-0.269
	Vis 5	7.766	7.607	7.924	8.223	8.060	8.385	-0.457	-0.684	-0.230
	Vis 6	7.749	7.589	7.908	8.121	7.956	8.287	-0.373	-0.603	-0.143
	Vis 7	7.826	7.670	7.983	8.135	7.977	8.293	-0.309	-0.532	-0.086
weight	V7-V1	-0.782	-0.921	-0.643	-0.357	-0.498	-0.216	-0.425	-0.623	-0.228
	Vis 1	97.183	95.026	99.339	97.149	94.992	99.305	0.034	-3.015	3.083
	Vis 2	97.552	95.392	99.712	98.466	96.304	100.627	-0.914	-3.969	2.142
	Vis 3	98.123	95.962	100.283	99.703	97.539	101.866	-1.580	-4.638	1.477
	Vis 4	98.626	96.464	100.787	100.510	98.345	102.676	-1.885	-4.944	1.175
	Vis 5	98.496	96.334	100.658	100.972	98.805	103.139	-2.476	-5.537	0.585
	Vis 6	98.739	96.575	100.902	101.368	99.198	103.537	-2.629	-5.692	0.435
bmi	Vis 7	98.766	96.604	100.927	101.297	99.135	103.459	-2.531	-5.589	0.526
	V7-V1	1.583	1.059	2.107	4.149	3.620	4.677	-2.565	-3.310	-1.821
	Vis 1	32.258	31.648	32.868	32.061	31.451	32.671	0.197	-0.666	1.060
	Vis 2	32.390	31.778	33.001	32.489	31.877	33.101	-0.099	-0.964	0.766
	Vis 3	32.576	31.964	33.188	32.895	32.282	33.507	-0.318	-1.184	0.547
	Vis 4	32.735	32.123	33.347	33.167	32.554	33.781	-0.432	-1.299	0.434
	Vis 5	32.693	32.080	33.305	33.321	32.706	33.935	-0.628	-1.495	0.240
whr	Vis 6	32.763	32.151	33.376	33.458	32.843	34.073	-0.694	-1.563	0.174
	Vis 7	32.710	32.098	33.322	33.425	32.813	34.038	-0.715	-1.581	0.151
	V7-V1	0.452	0.279	0.626	1.364	1.189	1.540	-0.912	-1.159	-0.665
	Vis 1	0.995	0.984	1.006	1.010	1.000	1.021	-0.015	-0.031	0.000
	Vis 2	0.995	0.984	1.006	0.999	0.988	1.010	-0.004	-0.019	0.012
	Vis 3	0.996	0.985	1.007	1.005	0.993	1.016	-0.009	-0.024	0.007
	Vis 4	0.995	0.984	1.006	1.002	0.991	1.014	-0.008	-0.024	0.008
gluc	Vis 5	1.003	0.992	1.014	1.003	0.991	1.014	0.000	-0.016	0.016
	Vis 6	0.997	0.986	1.008	1.005	0.993	1.016	-0.008	-0.024	0.009
	Vis 7	1.004	0.992	1.015	1.012	1.001	1.024	-0.009	-0.025	0.007
	V7-V1	0.008	0.000	0.016	0.002	-0.006	0.010	0.006	-0.005	0.018
	Vis 1	10.513	10.100	10.926	10.081	9.669	10.493	0.432	-0.151	1.016
	Vis 2	8.511	8.078	8.944	8.952	8.508	9.396	-0.441	-1.061	0.178
	Vis 3	8.069	7.631	8.508	8.888	8.432	9.344	-0.819	-1.452	-0.186
ins(1)	Vis 4	7.967	7.526	8.408	8.514	8.057	8.972	-0.547	-1.183	0.088
	Vis 5	8.073	7.630	8.515	8.771	8.311	9.231	-0.698	-1.336	-0.060
	Vis 6	8.239	7.788	8.689	8.377	7.902	8.852	-0.138	-0.793	0.516
	Vis 7	8.365	7.937	8.792	8.404	7.970	8.839	-0.040	-0.649	0.570
	V7-V1	-2.149	-2.652	-1.645	-1.677	-2.186	-1.167	-0.472	-1.188	0.244
	Vis 1	60.962	53.422	69.567	71.436	62.636	81.472	0.853	0.708	1.028
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
cpep(1)	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	40.857	35.585	46.909	44.923	39.068	51.655	0.909	0.747	1.107
	V7-V1	0.670	0.581	0.773	0.629	0.545	0.726	1.066	0.870	1.305
	Vis 1	645.505	572.334	728.030	718.305	637.068	809.901	0.899	0.758	1.065
idos(1)	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	471.955	417.412	533.626	496.210	438.595	561.394	0.951	0.799	1.132
	V7-V1	0.731	0.669	0.799	0.691	0.632	0.755	1.058	0.933	1.200
idos(1)	Vis 1	38.051	34.794	41.614	37.710	34.482	41.241	1.009	0.889	1.145
	Vis 2	68.297	62.381	74.775	88.058	80.381	96.468	0.776	0.682	0.882
	Vis 3	75.726	69.149	82.928	102.072	93.091	111.919	0.742	0.652	0.844
	Vis 4	78.702	71.850	86.206	107.778	98.271	118.206	0.730	0.641	0.831
	Vis 5	80.419	73.397	88.113	110.059	100.281	120.791	0.731	0.641	0.832
	Vis 6	81.898	74.708	89.781	111.060	101.120	121.977	0.737	0.647	0.841

	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.152	2.019	2.294	2.945	2.756	3.147	0.731	0.667	0.801
ipkg(1)	Vis 1	0.396	0.365	0.430	0.393	0.362	0.426	1.009	0.898	1.132
	Vis 2	0.708	0.651	0.769	0.905	0.832	0.984	0.782	0.695	0.880
	Vis 3	0.782	0.720	0.850	1.036	0.952	1.128	0.755	0.670	0.850
	Vis 4	0.809	0.744	0.880	1.086	0.997	1.182	0.745	0.662	0.840
	Vis 5	0.829	0.763	0.902	1.098	1.008	1.196	0.755	0.670	0.852
	Vis 6	0.842	0.774	0.916	1.107	1.016	1.207	0.761	0.674	0.858
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.127	1.998	2.263	2.820	2.642	3.009	0.754	0.689	0.825
sys	Vis 1	140.488	138.385	142.590	138.185	136.073	140.297	2.302	-0.678	5.283
	Vis 2	134.802	132.649	136.954	136.884	134.701	139.067	-2.083	-5.149	0.984
	Vis 3	136.759	134.598	138.920	134.203	131.990	136.417	2.556	-0.538	5.649
	Vis 4	135.375	133.195	137.555	134.197	131.954	136.440	1.178	-1.950	4.306
	Vis 5	134.091	131.896	136.286	133.724	131.455	135.993	0.367	-2.790	3.524
	Vis 6	134.063	131.845	136.282	132.909	130.589	135.230	1.154	-2.056	4.364
	Vis 7	134.790	132.568	137.012	132.794	130.534	135.054	1.996	-1.173	5.166
	V7-V1	-5.698	-7.972	-3.423	-5.392	-7.713	-3.070	-0.306	-3.556	2.944
dia	Vis 1	82.267	81.009	83.525	82.019	80.756	83.282	0.248	-1.534	2.031
	Vis 2	79.841	78.557	81.126	81.644	80.343	82.944	-1.802	-3.630	0.026
	Vis 3	80.627	79.338	81.916	80.086	78.770	81.403	0.541	-1.301	2.383
	Vis 4	80.351	79.053	81.650	80.399	79.067	81.730	-0.047	-1.907	1.813
	Vis 5	79.220	77.914	80.526	79.925	78.580	81.270	-0.705	-2.580	1.170
	Vis 6	79.532	78.213	80.850	79.975	78.604	81.346	-0.443	-2.345	1.459
	Vis 7	78.714	77.394	80.034	79.051	77.711	80.391	-0.337	-2.218	1.544
	V7-V1	-3.553	-4.800	-2.306	-2.968	-4.242	-1.694	-0.585	-2.368	1.198
pulse	Vis 1	75.954	74.323	77.586	76.654	75.013	78.295	-0.700	-3.014	1.614
	Vis 2	75.532	73.868	77.196	74.732	73.054	76.410	0.800	-1.564	3.163
	Vis 3	74.830	73.165	76.496	74.111	72.407	75.815	0.720	-1.663	3.102
	Vis 4	75.446	73.773	77.119	74.304	72.592	76.015	1.142	-1.251	3.536
	Vis 5	75.164	73.479	76.848	72.969	71.246	74.692	2.195	-0.214	4.604
	Vis 6	74.674	72.979	76.368	73.044	71.295	74.793	1.630	-0.806	4.065
	Vis 7	75.630	73.923	77.336	73.687	71.967	75.407	1.943	-0.481	4.366
	V7-V1	-0.325	-1.745	1.095	-2.967	-4.416	-1.518	2.642	0.613	4.671
chol	Vis 1	4.208	4.079	4.337	4.121	3.992	4.250	0.087	-0.095	0.270
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	4.286	4.153	4.420	4.294	4.157	4.431	-0.008	-0.199	0.184
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	4.236	4.102	4.370	4.326	4.188	4.464	-0.090	-0.282	0.102
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	4.278	4.146	4.411	4.323	4.190	4.456	-0.045	-0.233	0.143
	V7-V1	0.070	-0.043	0.184	0.202	0.088	0.317	-0.132	-0.293	0.029
ldl	Vis 1	2.169	2.057	2.281	2.164	2.053	2.275	0.005	-0.153	0.163
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	2.238	2.123	2.354	2.329	2.212	2.445	-0.090	-0.255	0.074
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	2.143	2.027	2.259	2.334	2.215	2.452	-0.191	-0.357	-0.025
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.206	2.091	2.320	2.378	2.264	2.493	-0.173	-0.335	-0.011
	V7-V1	0.037	-0.059	0.132	0.214	0.119	0.310	-0.178	-0.313	-0.043
hdl	Vis 1	1.164	1.116	1.212	1.166	1.119	1.214	-0.002	-0.070	0.065
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.206	1.157	1.255	1.209	1.159	1.258	-0.003	-0.072	0.067
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.228	1.179	1.277	1.180	1.130	1.230	0.048	-0.022	0.118
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.175	1.127	1.224	1.161	1.113	1.210	0.014	-0.055	0.083
	V7-V1	0.011	-0.018	0.041	-0.005	-0.035	0.025	0.016	-0.026	0.058
vldl(1)	Vis 1	0.730	0.683	0.780	0.685	0.641	0.732	1.066	0.971	1.171
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.710	0.661	0.763	0.689	0.641	0.741	1.030	0.930	1.140
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	0.757	0.704	0.813	0.678	0.630	0.730	1.116	1.006	1.238
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.743	0.694	0.795	0.668	0.624	0.715	1.112	1.010	1.224
	V7-V1	1.018	0.960	1.079	0.975	0.920	1.034	1.043	0.961	1.133

trig(l)	Vis 1	1.690	1.573	1.816	1.539	1.432	1.654	1.098	0.992	1.216
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.620	1.503	1.745	1.538	1.425	1.659	1.053	0.947	1.172
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.680	1.559	1.810	1.560	1.445	1.684	1.077	0.968	1.199
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.711	1.590	1.842	1.513	1.404	1.629	1.131	1.019	1.256
	V7-V1	1.013	0.955	1.074	0.983	0.926	1.043	1.030	0.948	1.120
fimtavg	Vis 1	0.788	0.770	0.807	0.799	0.780	0.818	-0.011	-0.037	0.016
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.788	0.769	0.806	0.785	0.766	0.804	0.002	-0.025	0.029
	V7-V1	-0.001	-0.011	0.010	-0.014	-0.024	-0.003	0.013	-0.002	0.028
fimtmax	Vis 1	0.953	0.931	0.974	0.959	0.938	0.980	-0.007	-0.036	0.023
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.950	0.929	0.972	0.945	0.923	0.967	0.005	-0.025	0.036
	V7-V1	-0.003	-0.015	0.010	-0.014	-0.027	-0.002	0.012	-0.006	0.029
iem	Vis 1	2380.505	2240.531	2520.480	2313.666	2174.403	2452.928	66.839	-130.612	264.291
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2332.882	2187.003	2478.762	2142.933	1995.801	2290.066	189.949	-17.244	397.142
	V7-V1	-47.623	-174.233	78.987	-170.732	-297.213	-44.251	123.110	-55.853	302.072
csc2	Vis 1	2.541	2.398	2.684	2.597	2.454	2.739	-0.055	-0.257	0.147
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.555	2.407	2.704	2.676	2.527	2.826	-0.121	-0.332	0.090
	V7-V1	0.014	-0.109	0.136	0.080	-0.042	0.202	-0.066	-0.239	0.107
imtareal	Vis 1	18.795	18.139	19.452	19.332	18.676	19.988	-0.536	-1.464	0.391
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	18.960	18.292	19.627	19.090	18.419	19.761	-0.130	-1.077	0.816
	V7-V1	0.164	-0.196	0.525	-0.242	-0.602	0.117	0.406	-0.103	0.915
n.pl(l)	Vis 1	2.433	2.164	2.735	2.844	2.512	3.221	0.855	0.721	1.015
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.937	2.611	3.303	3.165	2.792	3.589	0.928	0.781	1.102
	V7-V1	1.207	1.131	1.288	1.113	1.037	1.194	1.085	0.986	1.193

> round(ftable(Eff[, "IT", "Rest",,,], col.vars=4:3), 3)

var	par	Met			Plc			Dif		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
hba1c	Vis 1	8.608	8.455	8.761	8.492	8.339	8.645	0.117	-0.100	0.333
	Vis 2	8.021	7.865	8.177	8.730	8.573	8.888	-0.709	-0.931	-0.487
	Vis 3	7.720	7.564	7.877	8.239	8.080	8.399	-0.519	-0.743	-0.295
	Vis 4	7.731	7.573	7.888	8.225	8.064	8.385	-0.494	-0.719	-0.269
	Vis 5	7.766	7.607	7.924	8.223	8.060	8.385	-0.457	-0.684	-0.230
	Vis 6	7.749	7.589	7.908	8.121	7.956	8.287	-0.373	-0.603	-0.143

	Vis 7	7.826	7.670	7.983	8.135	7.977	8.293	-0.309	-0.532	-0.086
	V7-V1	-0.782	-0.921	-0.643	-0.357	-0.498	-0.216	-0.425	-0.623	-0.228
weight	Vis 1	97.183	95.026	99.339	97.149	94.992	99.305	0.034	-3.015	3.083
	Vis 2	97.552	95.392	99.712	98.466	96.304	100.627	-0.914	-3.969	2.142
	Vis 3	98.123	95.962	100.283	99.703	97.539	101.866	-1.580	-4.638	1.477
	Vis 4	98.626	96.464	100.787	100.510	98.345	102.676	-1.885	-4.944	1.175
	Vis 5	98.496	96.334	100.658	100.972	98.805	103.139	-2.476	-5.537	0.585
	Vis 6	98.739	96.575	100.902	101.368	99.198	103.537	-2.629	-5.692	0.435
	Vis 7	98.766	96.604	100.927	101.297	99.135	103.459	-2.531	-5.589	0.526
	V7-V1	1.583	1.059	2.107	4.149	3.620	4.677	-2.565	-3.310	-1.821
bmi	Vis 1	32.258	31.648	32.868	32.061	31.451	32.671	0.197	-0.666	1.060
	Vis 2	32.390	31.778	33.001	32.489	31.877	33.101	-0.099	-0.964	0.766
	Vis 3	32.576	31.964	33.188	32.895	32.282	33.507	-0.318	-1.184	0.547
	Vis 4	32.735	32.123	33.347	33.167	32.554	33.781	-0.432	-1.299	0.434
	Vis 5	32.693	32.080	33.305	33.321	32.706	33.935	-0.628	-1.495	0.240
	Vis 6	32.763	32.151	33.376	33.458	32.843	34.073	-0.694	-1.563	0.174
	Vis 7	32.710	32.098	33.322	33.425	32.813	34.038	-0.715	-1.581	0.151
	V7-V1	0.452	0.279	0.626	1.364	1.189	1.540	-0.912	-1.159	-0.665
whr	Vis 1	0.995	0.984	1.006	1.010	1.000	1.021	-0.015	-0.031	0.000
	Vis 2	0.995	0.984	1.006	0.999	0.988	1.010	-0.004	-0.019	0.012
	Vis 3	0.996	0.985	1.007	1.005	0.993	1.016	-0.009	-0.024	0.007
	Vis 4	0.995	0.984	1.006	1.002	0.991	1.014	-0.008	-0.024	0.008
	Vis 5	1.003	0.992	1.014	1.003	0.991	1.014	0.000	-0.016	0.016
	Vis 6	0.997	0.986	1.008	1.005	0.993	1.016	-0.008	-0.024	0.009
	Vis 7	1.004	0.992	1.015	1.012	1.001	1.024	-0.009	-0.025	0.007
	V7-V1	0.008	0.000	0.016	0.002	-0.006	0.010	0.006	-0.005	0.018
gluc	Vis 1	10.513	10.100	10.926	10.081	9.669	10.493	0.432	-0.151	1.016
	Vis 2	8.511	8.078	8.944	8.952	8.508	9.396	-0.441	-1.061	0.178
	Vis 3	8.069	7.631	8.508	8.888	8.432	9.344	-0.819	-1.452	-0.186
	Vis 4	7.967	7.526	8.408	8.514	8.057	8.972	-0.547	-1.183	0.088
	Vis 5	8.073	7.630	8.515	8.771	8.311	9.231	-0.698	-1.336	-0.060
	Vis 6	8.239	7.788	8.689	8.377	7.902	8.852	-0.138	-0.793	0.516
	Vis 7	8.365	7.937	8.792	8.404	7.970	8.839	-0.040	-0.649	0.570
	V7-V1	-2.149	-2.652	-1.645	-1.677	-2.186	-1.167	-0.472	-1.188	0.244
ins(l)	Vis 1	60.962	53.422	69.567	71.436	62.636	81.472	0.853	0.708	1.028
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	40.857	35.585	46.909	44.923	39.068	51.655	0.909	0.747	1.107
	V7-V1	0.670	0.581	0.773	0.629	0.545	0.726	1.066	0.870	1.305
cpep(l)	Vis 1	645.505	572.334	728.030	718.305	637.068	809.901	0.899	0.758	1.065
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	471.955	417.412	533.626	496.210	438.595	561.394	0.951	0.799	1.132
	V7-V1	0.731	0.669	0.799	0.691	0.632	0.755	1.058	0.933	1.200
idos(l)	Vis 1	38.051	34.794	41.614	37.710	34.482	41.241	1.009	0.889	1.145
	Vis 2	68.297	62.381	74.775	88.058	80.381	96.468	0.776	0.682	0.882
	Vis 3	75.726	69.149	82.928	102.072	93.091	111.919	0.742	0.652	0.844
	Vis 4	78.702	71.850	86.206	107.778	98.271	118.206	0.730	0.641	0.831
	Vis 5	80.419	73.397	88.113	110.059	100.281	120.791	0.731	0.641	0.832
	Vis 6	81.898	74.708	89.781	111.060	101.120	121.977	0.737	0.647	0.841
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.152	2.019	2.294	2.945	2.756	3.147	0.731	0.667	0.801
ipkg(l)	Vis 1	0.396	0.365	0.430	0.393	0.362	0.426	1.009	0.898	1.132
	Vis 2	0.708	0.651	0.769	0.905	0.832	0.984	0.782	0.695	0.880
	Vis 3	0.782	0.720	0.850	1.036	0.952	1.128	0.755	0.670	0.850
	Vis 4	0.809	0.744	0.880	1.086	0.997	1.182	0.745	0.662	0.840
	Vis 5	0.829	0.763	0.902	1.098	1.008	1.196	0.755	0.670	0.852
	Vis 6	0.842	0.774	0.916	1.107	1.016	1.207	0.761	0.674	0.858
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.127	1.998	2.263	2.820	2.642	3.009	0.754	0.689	0.825

	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.788	0.769	0.806	0.785	0.766	0.804	0.002	-0.025	0.029
	V7-V1	-0.001	-0.011	0.010	-0.014	-0.024	-0.003	0.013	-0.002	0.028
fimtmax	Vis 1	0.953	0.931	0.974	0.959	0.938	0.980	-0.007	-0.036	0.023
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.950	0.929	0.972	0.945	0.923	0.967	0.005	-0.025	0.036
	V7-V1	-0.003	-0.015	0.010	-0.014	-0.027	-0.002	0.012	-0.006	0.029
iem	Vis 1	2380.505	2240.531	2520.480	2313.666	2174.403	2452.928	66.839	-130.612	264.291
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2332.882	2187.003	2478.762	2142.933	1995.801	2290.066	189.949	-17.244	397.142
	V7-V1	-47.623	-174.233	78.987	-170.732	-297.213	-44.251	123.110	-55.853	302.072
csc2	Vis 1	2.541	2.398	2.684	2.597	2.454	2.739	-0.055	-0.257	0.147
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.555	2.407	2.704	2.676	2.527	2.826	-0.121	-0.332	0.090
	V7-V1	0.014	-0.109	0.136	0.080	-0.042	0.202	-0.066	-0.239	0.107
imtareal	Vis 1	18.795	18.139	19.452	19.332	18.676	19.988	-0.536	-1.464	0.391
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	18.960	18.292	19.627	19.090	18.419	19.761	-0.130	-1.077	0.816
	V7-V1	0.164	-0.196	0.525	-0.242	-0.602	0.117	0.406	-0.103	0.915
n.pl(1)	Vis 1	2.433	2.164	2.735	2.844	2.512	3.221	0.855	0.721	1.015
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.937	2.611	3.303	3.165	2.792	3.589	0.928	0.781	1.102
	V7-V1	1.207	1.131	1.288	1.113	1.037	1.194	1.085	0.986	1.193
> round(ftable(Eff[, "IT", "Conf", , ,], col.vars=4:3), 3)										
		Met			Plc			Dif		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
var	par									
hba1c	Vis 1	8.901	8.588	9.214	8.790	8.469	9.111	0.111	-0.104	0.325
	Vis 2	8.316	8.001	8.631	9.030	8.707	9.354	-0.715	-0.934	-0.495
	Vis 3	8.015	7.700	8.330	8.538	8.213	8.863	-0.524	-0.745	-0.302
	Vis 4	8.025	7.709	8.340	8.523	8.198	8.849	-0.499	-0.722	-0.275
	Vis 5	8.060	7.744	8.376	8.522	8.195	8.848	-0.462	-0.686	-0.237
	Vis 6	8.043	7.726	8.360	8.420	8.092	8.748	-0.377	-0.605	-0.149
	Vis 7	8.120	7.805	8.436	8.435	8.110	8.759	-0.314	-0.535	-0.094
	V7-V1	-0.781	-0.919	-0.642	-0.355	-0.496	-0.214	-0.425	-0.623	-0.227
weight	Vis 1	89.743	84.978	94.507	89.485	84.598	94.372	0.258	-2.578	3.094
	Vis 2	90.113	85.347	94.879	90.798	85.907	95.688	-0.685	-3.527	2.158
	Vis 3	90.684	85.917	95.450	92.033	87.142	96.925	-1.350	-4.195	1.495
	Vis 4	91.186	86.419	95.953	92.842	87.950	97.734	-1.656	-4.503	1.191
	Vis 5	91.057	86.289	95.824	93.303	88.411	98.196	-2.247	-5.095	0.602
	Vis 6	91.299	86.531	96.067	93.698	88.804	98.592	-2.399	-5.251	0.452
	Vis 7	91.326	86.560	96.093	93.627	88.736	98.518	-2.301	-5.145	0.544
	V7-V1	1.584	1.060	2.108	4.142	3.614	4.671	-2.559	-3.303	-1.814

bmi	Vis 1	32.822	31.414	34.230	32.521	31.077	33.965	0.301	-0.539	1.141
	Vis 2	32.954	31.546	34.362	32.950	31.505	34.395	0.004	-0.838	0.847
	Vis 3	33.141	31.732	34.549	33.355	31.910	34.800	-0.214	-1.058	0.629
	Vis 4	33.300	31.891	34.708	33.628	32.182	35.073	-0.328	-1.172	0.516
	Vis 5	33.258	31.849	34.666	33.781	32.335	35.227	-0.523	-1.368	0.321
	Vis 6	33.328	31.919	34.737	33.918	32.472	35.365	-0.590	-1.436	0.256
	Vis 7	33.275	31.866	34.683	33.886	32.440	35.331	-0.611	-1.454	0.232
	V7-V1	0.453	0.279	0.626	1.365	1.189	1.540	-0.912	-1.159	-0.665
whr	Vis 1	0.943	0.923	0.963	0.958	0.937	0.978	-0.014	-0.028	-0.001
	Vis 2	0.944	0.924	0.964	0.946	0.926	0.967	-0.003	-0.016	0.011
	Vis 3	0.944	0.924	0.964	0.952	0.931	0.973	-0.008	-0.021	0.006
	Vis 4	0.943	0.923	0.963	0.950	0.929	0.971	-0.007	-0.021	0.007
	Vis 5	0.951	0.931	0.971	0.950	0.929	0.971	0.001	-0.013	0.015
	Vis 6	0.945	0.925	0.966	0.952	0.931	0.973	-0.007	-0.021	0.008
	Vis 7	0.952	0.932	0.972	0.960	0.939	0.980	-0.008	-0.022	0.006
	V7-V1	0.008	0.000	0.017	0.002	-0.006	0.010	0.007	-0.005	0.018
gluc	Vis 1	11.000	10.297	11.703	10.599	9.881	11.317	0.400	-0.177	0.977
	Vis 2	9.013	8.299	9.728	9.481	8.741	10.221	-0.468	-1.081	0.145
	Vis 3	8.578	7.859	9.297	9.417	8.671	10.164	-0.839	-1.466	-0.213
	Vis 4	8.469	7.748	9.191	9.038	8.292	9.784	-0.568	-1.197	0.060
	Vis 5	8.580	7.857	9.303	9.289	8.539	10.038	-0.709	-1.340	-0.078
	Vis 6	8.748	8.020	9.476	8.903	8.143	9.663	-0.155	-0.803	0.493
	Vis 7	8.867	8.154	9.580	8.930	8.195	9.666	-0.063	-0.666	0.540
	V7-V1	-2.132	-2.636	-1.629	-1.669	-2.179	-1.159	-0.463	-1.180	0.253
ins(l)	Vis 1	67.697	51.052	89.771	78.255	58.650	104.413	0.865	0.719	1.041
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	45.192	33.987	60.091	49.284	36.725	66.138	0.917	0.754	1.114
	V7-V1	0.668	0.579	0.770	0.630	0.546	0.727	1.060	0.866	1.297
cpep(l)	Vis 1	721.460	558.457	932.041	783.905	603.206	1018.735	0.920	0.785	1.079
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	527.758	408.006	682.657	542.762	416.649	707.047	0.972	0.826	1.145
	V7-V1	0.732	0.670	0.799	0.692	0.633	0.757	1.057	0.932	1.198
idos(l)	Vis 1	41.975	34.784	50.651	41.401	34.151	50.190	1.014	0.899	1.143
	Vis 2	75.364	62.421	90.991	96.701	79.692	117.340	0.779	0.690	0.881
	Vis 3	83.551	69.199	100.880	112.005	92.267	135.965	0.746	0.660	0.844
	Vis 4	86.813	71.893	104.829	118.297	97.434	143.627	0.734	0.649	0.830
	Vis 5	88.721	73.458	107.156	120.790	99.448	146.713	0.735	0.649	0.832
	Vis 6	90.341	74.777	109.145	121.879	100.305	148.094	0.741	0.654	0.840
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.152	2.019	2.294	2.944	2.755	3.146	0.731	0.667	0.802
ipkg(l)	Vis 1	0.471	0.398	0.558	0.466	0.391	0.554	1.012	0.906	1.129
	Vis 2	0.842	0.710	0.999	1.075	0.902	1.280	0.784	0.701	0.877
	Vis 3	0.931	0.785	1.104	1.229	1.031	1.465	0.757	0.676	0.848
	Vis 4	0.963	0.812	1.142	1.288	1.081	1.536	0.747	0.667	0.837
	Vis 5	0.987	0.832	1.171	1.302	1.092	1.553	0.758	0.676	0.849
	Vis 6	1.002	0.844	1.189	1.313	1.101	1.567	0.763	0.680	0.856
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.127	1.999	2.263	2.820	2.643	3.009	0.754	0.689	0.825
sys	Vis 1	136.062	132.004	140.120	133.787	129.631	137.943	2.275	-0.699	5.250
	Vis 2	130.369	126.287	134.451	132.480	128.271	136.688	-2.111	-5.170	0.948
	Vis 3	132.324	128.233	136.414	129.803	125.580	134.027	2.520	-0.566	5.607
	Vis 4	130.946	126.849	135.044	129.803	125.567	134.040	1.143	-1.977	4.264
	Vis 5	129.659	125.547	133.771	129.316	125.059	133.573	0.343	-2.807	3.493
	Vis 6	129.630	125.505	133.755	128.502	124.219	132.786	1.128	-2.075	4.331
	Vis 7	130.372	126.249	134.495	128.405	124.160	132.649	1.967	-1.195	5.129
	V7-V1	-5.691	-7.965	-3.416	-5.383	-7.705	-3.060	-0.308	-3.558	2.943
dia	Vis 1	85.497	83.168	87.826	85.352	82.966	87.737	0.145	-1.534	1.824
	Vis 2	83.090	80.748	85.431	84.953	82.539	87.366	-1.863	-3.588	-0.138

	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.866	0.818	0.913	0.861	0.812	0.910	0.005	-0.025	0.034	
	V7-V1	-0.003	-0.015	0.010	-0.014	-0.026	-0.002	0.011	-0.006	0.029	
iem	Vis 1	2020.026	1732.683	2307.368	1963.645	1670.320	2256.969	56.381	-128.536	241.298	
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1975.240	1685.088	2265.392	1793.291	1494.832	2091.749	181.950	-12.840	376.739	
	V7-V1	-44.786	-170.824	81.253	-170.354	-296.309	-44.399	125.568	-52.627	303.764	
csc2	Vis 1	2.946	2.653	3.239	2.990	2.690	3.289	-0.044	-0.231	0.143	
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.956	2.660	3.251	3.069	2.764	3.373	-0.113	-0.309	0.084	
	V7-V1	0.010	-0.112	0.132	0.079	-0.043	0.201	-0.069	-0.241	0.104	
imtareal	Vis 1	15.267	13.870	16.664	15.826	14.400	17.252	-0.559	-1.412	0.294	
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	15.438	14.036	16.840	15.575	14.140	17.011	-0.137	-1.011	0.736	
	V7-V1	0.171	-0.189	0.531	-0.251	-0.610	0.109	0.421	-0.087	0.930	
n.pl(1)	Vis 1	1.452	1.088	1.937	1.639	1.219	2.205	0.886	0.750	1.046	
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.755	1.315	2.340	1.828	1.358	2.460	0.960	0.812	1.135	
	V7-V1	1.209	1.133	1.289	1.115	1.040	1.196	1.084	0.985	1.192	

> round(ftable(Eff[, "IT", "Conf", , ,], col.vars=4:3), 3)

		Met			Plc			Dif		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
var	par									
hba1c	Vis 1	8.901	8.588	9.214	8.790	8.469	9.111	0.111	-0.104	0.325
	Vis 2	8.316	8.001	8.631	9.030	8.707	9.354	-0.715	-0.934	-0.495
	Vis 3	8.015	7.700	8.330	8.538	8.213	8.863	-0.524	-0.745	-0.302
	Vis 4	8.025	7.709	8.340	8.523	8.198	8.849	-0.499	-0.722	-0.275
	Vis 5	8.060	7.744	8.376	8.522	8.195	8.848	-0.462	-0.686	-0.237
	Vis 6	8.043	7.726	8.360	8.420	8.092	8.748	-0.377	-0.605	-0.149
	Vis 7	8.120	7.805	8.436	8.435	8.110	8.759	-0.314	-0.535	-0.094
	V7-V1	-0.781	-0.919	-0.642	-0.355	-0.496	-0.214	-0.425	-0.623	-0.227
weight	Vis 1	89.743	84.978	94.507	89.485	84.598	94.372	0.258	-2.578	3.094
	Vis 2	90.113	85.347	94.879	90.798	85.907	95.688	-0.685	-3.527	2.158
	Vis 3	90.684	85.917	95.450	92.033	87.142	96.925	-1.350	-4.195	1.495
	Vis 4	91.186	86.419	95.953	92.842	87.950	97.734	-1.656	-4.503	1.191
	Vis 5	91.057	86.289	95.824	93.303	88.411	98.196	-2.247	-5.095	0.602
	Vis 6	91.299	86.531	96.067	93.698	88.804	98.592	-2.399	-5.251	0.452
	Vis 7	91.326	86.560	96.093	93.627	88.736	98.518	-2.301	-5.145	0.544
	V7-V1	1.584	1.060	2.108	4.142	3.614	4.671	-2.559	-3.303	-1.814
bmi	Vis 1	32.822	31.414	34.230	32.521	31.077	33.965	0.301	-0.539	1.141
	Vis 2	32.954	31.546	34.362	32.950	31.505	34.395	0.004	-0.838	0.847
	Vis 3	33.141	31.732	34.549	33.355	31.910	34.800	-0.214	-1.058	0.629
	Vis 4	33.300	31.891	34.708	33.628	32.182	35.073	-0.328	-1.172	0.516
	Vis 5	33.258	31.849	34.666	33.781	32.335	35.227	-0.523	-1.368	0.321
	Vis 6	33.328	31.919	34.737	33.918	32.472	35.365	-0.590	-1.436	0.256
	Vis 7	33.275	31.866	34.683	33.886	32.440	35.331	-0.611	-1.454	0.232
	V7-V1	0.453	0.279	0.626	1.365	1.189	1.540	-0.912	-1.159	-0.665
whr	Vis 1	0.943	0.923	0.963	0.958	0.937	0.978	-0.014	-0.028	-0.001
	Vis 2	0.944	0.924	0.964	0.946	0.926	0.967	-0.003	-0.016	0.011

	Vis 3	0.944	0.924	0.964	0.952	0.931	0.973	-0.008	-0.021	0.006
	Vis 4	0.943	0.923	0.963	0.950	0.929	0.971	-0.007	-0.021	0.007
	Vis 5	0.951	0.931	0.971	0.950	0.929	0.971	0.001	-0.013	0.015
	Vis 6	0.945	0.925	0.966	0.952	0.931	0.973	-0.007	-0.021	0.008
	Vis 7	0.952	0.932	0.972	0.960	0.939	0.980	-0.008	-0.022	0.006
	V7-V1	0.008	0.000	0.017	0.002	-0.006	0.010	0.007	-0.005	0.018
gluc	Vis 1	11.000	10.297	11.703	10.599	9.881	11.317	0.400	-0.177	0.977
	Vis 2	9.013	8.299	9.728	9.481	8.741	10.221	-0.468	-1.081	0.145
	Vis 3	8.578	7.859	9.297	9.417	8.671	10.164	-0.839	-1.466	-0.213
	Vis 4	8.469	7.748	9.191	9.038	8.292	9.784	-0.568	-1.197	0.060
	Vis 5	8.580	7.857	9.303	9.289	8.539	10.038	-0.709	-1.340	-0.078
	Vis 6	8.748	8.020	9.476	8.903	8.143	9.663	-0.155	-0.803	0.493
	Vis 7	8.867	8.154	9.580	8.930	8.195	9.666	-0.063	-0.666	0.540
	V7-V1	-2.132	-2.636	-1.629	-1.669	-2.179	-1.159	-0.463	-1.180	0.253
ins(1)	Vis 1	67.697	51.052	89.771	78.255	58.650	104.413	0.865	0.719	1.041
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	45.192	33.987	60.091	49.284	36.725	66.138	0.917	0.754	1.114
	V7-V1	0.668	0.579	0.770	0.630	0.546	0.727	1.060	0.866	1.297
cpep(1)	Vis 1	721.460	558.457	932.041	783.905	603.206	1018.735	0.920	0.785	1.079
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	527.758	408.006	682.657	542.762	416.649	707.047	0.972	0.826	1.145
	V7-V1	0.732	0.670	0.799	0.692	0.633	0.757	1.057	0.932	1.198
idos(1)	Vis 1	41.975	34.784	50.651	41.401	34.151	50.190	1.014	0.899	1.143
	Vis 2	75.364	62.421	90.991	96.701	79.692	117.340	0.779	0.690	0.881
	Vis 3	83.551	69.199	100.880	112.005	92.267	135.965	0.746	0.660	0.844
	Vis 4	86.813	71.893	104.829	118.297	97.434	143.627	0.734	0.649	0.830
	Vis 5	88.721	73.458	107.156	120.790	99.448	146.713	0.735	0.649	0.832
	Vis 6	90.341	74.777	109.145	121.879	100.305	148.094	0.741	0.654	0.840
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.152	2.019	2.294	2.944	2.755	3.146	0.731	0.667	0.802
ipkg(1)	Vis 1	0.471	0.398	0.558	0.466	0.391	0.554	1.012	0.906	1.129
	Vis 2	0.842	0.710	0.999	1.075	0.902	1.280	0.784	0.701	0.877
	Vis 3	0.931	0.785	1.104	1.229	1.031	1.465	0.757	0.676	0.848
	Vis 4	0.963	0.812	1.142	1.288	1.081	1.536	0.747	0.667	0.837
	Vis 5	0.987	0.832	1.171	1.302	1.092	1.553	0.758	0.676	0.849
	Vis 6	1.002	0.844	1.189	1.313	1.101	1.567	0.763	0.680	0.856
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.127	1.999	2.263	2.820	2.643	3.009	0.754	0.689	0.825
sys	Vis 1	136.062	132.004	140.120	133.787	129.631	137.943	2.275	-0.699	5.250
	Vis 2	130.369	126.287	134.451	132.480	128.271	136.688	-2.111	-5.170	0.948
	Vis 3	132.324	128.233	136.414	129.803	125.580	134.027	2.520	-0.566	5.607
	Vis 4	130.946	126.849	135.044	129.803	125.567	134.040	1.143	-1.977	4.264
	Vis 5	129.659	125.547	133.771	129.316	125.059	133.573	0.343	-2.807	3.493
	Vis 6	129.630	125.505	133.755	128.502	124.219	132.786	1.128	-2.075	4.331
	Vis 7	130.372	126.249	134.495	128.405	124.160	132.649	1.967	-1.195	5.129
	V7-V1	-5.691	-7.965	-3.416	-5.383	-7.705	-3.060	-0.308	-3.558	2.943
dia	Vis 1	85.497	83.168	87.826	85.352	82.966	87.737	0.145	-1.534	1.824
	Vis 2	83.090	80.748	85.431	84.953	82.539	87.366	-1.863	-3.588	-0.138
	Vis 3	83.876	81.530	86.222	83.387	80.966	85.809	0.489	-1.250	2.228
	Vis 4	83.604	81.254	85.954	83.692	81.264	86.121	-0.088	-1.846	1.669
	Vis 5	82.475	80.118	84.832	83.223	80.785	85.662	-0.749	-2.522	1.025
	Vis 6	82.784	80.420	85.148	83.266	80.813	85.719	-0.482	-2.283	1.320
	Vis 7	81.973	79.610	84.336	82.343	79.910	84.776	-0.370	-2.150	1.409
	V7-V1	-3.524	-4.769	-2.279	-3.009	-4.281	-1.737	-0.515	-2.295	1.265
pulse	Vis 1	80.976	77.575	84.378	81.874	78.386	85.362	-0.898	-3.178	1.382
	Vis 2	80.562	77.146	83.977	79.943	76.428	83.458	0.618	-1.711	2.948
	Vis 3	79.863	76.445	83.281	79.318	75.792	82.843	0.545	-1.803	2.894
	Vis 4	80.485	77.064	83.907	79.512	75.983	83.041	0.974	-1.386	3.333

	Vis 7	1975.240	1685.088	2265.392	1793.291	1494.832	2091.749	181.950	-12.840	376.739
	V7-V1	-44.786	-170.824	81.253	-170.354	-296.309	-44.399	125.568	-52.627	303.764
csc2	Vis 1	2.946	2.653	3.239	2.990	2.690	3.289	-0.044	-0.231	0.143
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.956	2.660	3.251	3.069	2.764	3.373	-0.113	-0.309	0.084
	V7-V1	0.010	-0.112	0.132	0.079	-0.043	0.201	-0.069	-0.241	0.104
imtareal	Vis 1	15.267	13.870	16.664	15.826	14.400	17.252	-0.559	-1.412	0.294
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	15.438	14.036	16.840	15.575	14.140	17.011	-0.137	-1.011	0.736
	V7-V1	0.171	-0.189	0.531	-0.251	-0.610	0.109	0.421	-0.087	0.930
n.pl(1)	Vis 1	1.452	1.088	1.937	1.639	1.219	2.205	0.886	0.750	1.046
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.755	1.315	2.340	1.828	1.358	2.460	0.960	0.812	1.135
	V7-V1	1.209	1.133	1.289	1.115	1.040	1.196	1.084	0.985	1.192

```

> #for( vv in 1:(dim(Eff)[1]) )
> # {
> #   cat( "-----\n", dimnames(Eff)[[1]][vv], "\n" )
> #   dec <- 3 - ( max(Eff[vv,,,,1:3])>100 ) -
> #             ( max(Eff[vv,,,,1:3])>1000 )
> #   print( round( ftable( Eff[vv,,,,], col.vars=5:4 ), dec ) )
> # }

```

and then tests in those table:

```

> for( vv in dimnames(Tst)[[1]] )
+ {
+   cat( "-----\n", vv, "\n" )
+   print( round( ftable( Tst[vv,,,,,"Pval"], col.vars=3 ), 4 ) )
+ }

```

```

-----
hba1c

```

	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.0000	0.0063	0.0000	0.0000	0.0000
	Rest	0.0000	0.0065	0.0000	0.0000	0.0000
	Conf	0.0000	0.0052	0.0000	0.0000	0.0000
PP	Prim	0.0000	0.0173	0.0000	0.0000	0.0000
	Rest	0.0000	0.0164	0.0000	0.0000	0.0000
	Conf	0.0000	0.0142	0.0000	0.0000	0.0000

```

-----
weight

```

	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.0000	0.1111	0.0000	0.0000	0.0000
	Rest	0.0000	0.1046	0.0000	0.0000	0.0000
	Conf	0.0000	0.1129	0.0000	0.0000	0.0000
PP	Prim	0.0000	0.1148	0.0000	0.0000	0.0000
	Rest	0.0000	0.0933	0.0000	0.0000	0.0000
	Conf	0.0000	0.1216	0.0000	0.0000	0.0000

```

-----
bmi

```

	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						

IT	Prim	0.0000	0.1123	0.0000	0.0000	0.0000
	Rest	0.0000	0.1056	0.0000	0.0000	0.0000
	Conf	0.0000	0.1555	0.0000	0.0000	0.0000
PP	Prim	0.0000	0.2444	0.0000	0.0000	0.0000
	Rest	0.0000	0.2046	0.0000	0.0000	0.0000
	Conf	0.0000	0.2942	0.0000	0.0000	0.0000

whr		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0.2582	0.2752	0.2834	0.0433	0.6177
	Rest		0.2568	0.2664	0.2839	0.0439	0.6205
	Conf		0.2353	0.2601	0.2607	0.0383	0.6340
PP	Prim		0.3915	0.3034	0.3879	0.0526	0.4824
	Rest		0.3876	0.2885	0.3881	0.0527	0.4824
	Conf		0.3690	0.2631	0.3827	0.0514	0.4845

gluc		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0.0121	0.9281	0.2008	0.0000	0.0000
	Rest		0.0109	0.8981	0.1964	0.0000	0.0000
	Conf		0.0103	0.8376	0.2049	0.0000	0.0000
PP	Prim		0.0145	0.8879	0.1574	0.0000	0.0000
	Rest		0.0131	0.8557	0.1583	0.0000	0.0000
	Conf		0.0120	0.7882	0.1599	0.0000	0.0000

ins(1)		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0.2561	0.3676	0.5312	0.0000	0.0000
	Rest		0.2422	0.3438	0.5376	0.0000	0.0000
	Conf		0.3003	0.3837	0.5723	0.0000	0.0000
PP	Prim		0.2881	0.3547	0.5678	0.0000	0.0000
	Rest		0.2620	0.3302	0.5602	0.0000	0.0000
	Conf		0.2862	0.3452	0.5771	0.0000	0.0000

cpep(1)		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0.4014	0.6174	0.3477	0.0000	0.0000
	Rest		0.4134	0.5727	0.3768	0.0000	0.0000
	Conf		0.5158	0.7361	0.3912	0.0000	0.0000
PP	Prim		0.6073	0.9250	0.3800	0.0000	0.0000
	Rest		0.5917	0.8437	0.3913	0.0000	0.0000
	Conf		0.6373	0.9879	0.3881	0.0000	0.0000

idos(1)		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0	0	0	0	0
	Rest		0	0	0	0	0
	Conf		0	0	0	0	0
PP	Prim		0	0	0	0	0
	Rest		0	0	0	0	0
	Conf		0	0	0	0	0

ipkg(1)		test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod							
IT	Prim		0	0	0	0	0
	Rest		0	0	0	0	0
	Conf		0	0	0	0	0
PP	Prim		0	0	0	0	0
	Rest		0	0	0	0	0
	Conf		0	0	0	0	0

sys						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.0946	0.2301	0.8434	0.0000	0.0000
	Rest	0.0930	0.2170	0.8536	0.0000	0.0000
	Conf	0.0949	0.2227	0.8527	0.0000	0.0000
PP	Prim	0.0768	0.2429	0.8004	0.0000	0.0000
	Rest	0.0725	0.2202	0.7928	0.0000	0.0000
	Conf	0.0734	0.2201	0.7984	0.0000	0.0000

dia						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.2594	0.8207	0.5383	0.0000	0.0000
	Rest	0.2528	0.7257	0.5200	0.0000	0.0000
	Conf	0.2482	0.6835	0.5706	0.0000	0.0000
PP	Prim	0.2160	0.6296	0.6458	0.0000	0.0000
	Rest	0.1935	0.4953	0.6417	0.0000	0.0000
	Conf	0.1984	0.5473	0.6500	0.0000	0.0000

pulse						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1033	0.0987	0.0100	0.6752	0.0001
	Rest	0.1148	0.1161	0.0107	0.6539	0.0001
	Conf	0.1139	0.1433	0.0096	0.6774	0.0001
PP	Prim	0.0822	0.0887	0.0084	0.7057	0.0001
	Rest	0.0916	0.1110	0.0086	0.6985	0.0001
	Conf	0.0908	0.1163	0.0082	0.7111	0.0000

chol						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.3108	0.6632	0.1089	0.2239	0.0005
	Rest	0.3013	0.6410	0.1085	0.2260	0.0005
	Conf	0.2722	0.3784	0.1047	0.2061	0.0004
PP	Prim	0.1965	0.8877	0.0665	0.2185	0.0002
	Rest	0.1985	0.8493	0.0679	0.2145	0.0002
	Conf	0.2111	0.6081	0.0683	0.2125	0.0002

ldl						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.0190	0.0408	0.0101	0.4538	0.0000
	Rest	0.0174	0.0368	0.0100	0.4558	0.0000
	Conf	0.0095	0.0137	0.0103	0.4217	0.0000
PP	Prim	0.0158	0.0953	0.0054	0.5226	0.0000
	Rest	0.0148	0.0838	0.0055	0.5198	0.0000
	Conf	0.0108	0.0448	0.0055	0.5055	0.0000

hdl						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1490	0.7419	0.4577	0.4640	0.7486
	Rest	0.1455	0.6951	0.4505	0.4634	0.7367
	Conf	0.1495	0.8654	0.4541	0.4591	0.7483
PP	Prim	0.1416	0.9719	0.4325	0.5373	0.6213
	Rest	0.1444	0.9091	0.4370	0.5442	0.6216
	Conf	0.1372	0.9157	0.4285	0.5347	0.6173

vldl(1)						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.0884	0.0219	0.3042	0.5577	0.3853
	Rest	0.1143	0.0308	0.3152	0.5609	0.4010

PP	Conf	0.0792	0.0193	0.3295	0.5637	0.4222
PP	Prim	0.0651	0.0152	0.4463	0.5871	0.5934
	Rest	0.0946	0.0243	0.4459	0.5801	0.5998
	Conf	0.0668	0.0161	0.4467	0.5905	0.5905

trig(1)						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1499	0.0159	0.4735	0.6733	0.5544
	Rest	0.1717	0.0208	0.4837	0.6740	0.5693
	Conf	0.1230	0.0129	0.5156	0.6609	0.6309
PP	Prim	0.0431	0.0040	0.7074	0.6641	0.9209
	Rest	0.0628	0.0065	0.7001	0.6532	0.9218
	Conf	0.0495	0.0047	0.7037	0.6533	0.9271

fimtavg						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.2092	0.9559	0.0898	0.8785	0.0115
	Rest	0.2133	0.8697	0.0857	0.8889	0.0109
	Conf	0.2157	0.9058	0.0897	0.8779	0.0114
PP	Prim	0.2067	0.8997	0.0833	0.9919	0.0150
	Rest	0.2264	0.7383	0.0859	0.9731	0.0149
	Conf	0.2125	0.8548	0.0838	0.9883	0.0150

fimtmax						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.4223	0.8168	0.1943	0.6755	0.0257
	Rest	0.4170	0.7399	0.1868	0.6842	0.0244
	Conf	0.4265	0.7565	0.1935	0.6754	0.0255
PP	Prim	0.3859	0.6900	0.1676	0.8018	0.0295
	Rest	0.3846	0.5542	0.1717	0.7834	0.0292
	Conf	0.3867	0.6386	0.1685	0.7980	0.0295

iem						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1998	0.0884	0.1749	0.4648	0.0080
	Rest	0.1715	0.0724	0.1776	0.4610	0.0082
	Conf	0.1637	0.0671	0.1672	0.4862	0.0080
PP	Prim	0.1859	0.0674	0.3236	0.5116	0.0406
	Rest	0.1322	0.0443	0.3548	0.4736	0.0433
	Conf	0.1608	0.0567	0.3022	0.5564	0.0411

csc2						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.5853	0.3228	0.4534	0.8318	0.2029
	Rest	0.5129	0.2601	0.4539	0.8242	0.1998
	Conf	0.5124	0.2602	0.4334	0.8739	0.2050
PP	Prim	0.4555	0.2099	0.5808	0.9636	0.4629
	Rest	0.3286	0.1376	0.6149	0.9828	0.4642
	Conf	0.4274	0.1923	0.5424	0.8945	0.4667

imtareal						
	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1802	0.6683	0.1160	0.3756	0.1811
	Rest	0.2162	0.7876	0.1177	0.3721	0.1867
	Conf	0.1794	0.7576	0.1044	0.3528	0.1714
PP	Prim	0.2472	0.8815	0.1215	0.3161	0.2352
	Rest	0.3021	0.9219	0.1312	0.3282	0.2474
	Conf	0.2399	0.9642	0.1107	0.2895	0.2314

n.pl(1)						

	test	All equal	Visit 7 equal	Change equal	Met chg = 0	Plc chg = 0
ana mod						
IT	Prim	0.1059	0.4361	0.0979	0.0000	0.0028
	Rest	0.0936	0.3929	0.0955	0.0000	0.0028
	Conf	0.1515	0.6313	0.0982	0.0000	0.0024
PP	Prim	0.1252	0.6174	0.0783	0.0000	0.0031
	Rest	0.1282	0.6122	0.0801	0.0000	0.0029
	Conf	0.1726	0.9049	0.0782	0.0000	0.0027

7.3 Graphs of trajectories

Finally we want to plot the estimates, so we put the plotting of a single variable into a function. But first we need a convenience function to place text on the graph:

```
> source( "cnr.R" )
> cnr
function (xf, yf)
{
  cn <- par()$usr
  xf <- ifelse(xf > 1, xf/100, xf)
  yf <- ifelse(yf > 1, yf/100, yf)
  xx <- (1 - xf) * cn[1] + xf * cn[2]
  yy <- (1 - yf) * cn[3] + yf * cn[4]
  if (par()$xlog)
    xx <- 10^xx
  if (par()$ylog)
    yy <- 10^yy
  list(x = xx, y = yy)
}

> pleff <-
+ function( var,
+         ytxt = var,
+         yl = NULL, # yaxis limits
+         yt = NULL, # yaxis major ticks
+         ym = NULL, # yaxis minor ticks
+         hl = ym )
+ #      ltyp = if ltrf[match(var,vnam)] "pch" else "ach",
+ #      # Type of labelling of curves:
+ #      # "pch" - percent change
+ #      # "ach" - absolute change
+ #      # Any other text will be printed
+ #      lval = NULL ) # Values plotted at end of curves )
+ {
+ # Get the estimates, but only for the times where they are, otherwise
+ # the the points will not be connected (a feature)
+ var <- dimnames(Eff)$var[grep(var,vnam <- dimnames(Eff)$var)]
+ eff <- Eff[var,"IT","Prim",,,]
+ pef <- cbind( eff[-8,,"Met"],
+              eff[-8,,"Plc"] )
+ pef <- pef[complete.cases(pef),]
+ tim <- (as.numeric( gsub("Vis ", "",rownames(pef) ) )-1)*3
+
+ if( is.null(yl) ) yl <- range(pef)*c(0.9,1.2)
+ matplot( tim, pef, type="n",
+          xlab="Months since trial entry", xaxt="n", xlim=c(0,19.5),
+          ylab=ytxt, ylim=yl, yaxs="i", yaxt="n", bty="n" )
+ if( !is.null(hl) ) abline( h=hl, col=gray(0.8) )
+ axis( side=1, at=0:6*3, col=clr[4] )
+ axis( side=2, if(!is.null(yt)) at=yt, col=clr[4] )
+ axis( side=2, if(!is.null(ym)) at=ym, labels=rep("",length(ym)), col=clr[4] )
+ text( cnr(c(98,98),c(92,98)), gN, col=clr[2:1],
+       font=2, adj=c(1,1), cex=1.2 )
}
```

```

+ if( FALSE )
+ {
+ text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+       substitute( "Equal over 0-18 mth: P = "*pval,
+                   list( pval = formatC( Tst[var,"IT","Prim"," All equal","Pval"],
+                                       format="f", digits=4 ) ) ),
+       col=clr[4], adj=1 )
+ text( cnr(98,78)[[1]], cnr(98,78)[[2]],
+       substitute( "Equal at end: P = "*pval,
+                   list( pval = formatC( Tst[var,"IT","Prim","Visit 7 equal","Pval"],
+                                       format="f", digits=4 ) ) ),
+       col=clr[4], adj=1 )
+ }
+ text( cnr(98,82)[[1]], cnr(98,82)[[2]],
+       substitute( "Equal change: P = "*pval,
+                   list( pval = formatC( Tst[var,"IT","Prim"," Change equal","Pval"],
+                                       format="f", digits=4 ) ) ),
+       col=clr[4], adj=1 )
+ if( ltrf[match(var,vnam)] ) { text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+                                   "% change\nfrom baseline", col=clr[4], adj=c(1,0.5) )
+ } else {
+   text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+         "Change\nfrom baseline", col=clr[4], adj=c(1,0.5) ) }
+ #####Experimental
+ #if( ltyp=="pch" ) text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+ #                       "% change\nfrom baseline", col=clr[4], adj=c(1,0.5) )
+ #else
+ #if( ltyp=="ach" ) text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+ #                       "Change\nfrom baseline", col=clr[4], adj=c(1,0.5) )
+ #else text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+ #          ltyp, col=clr[4], adj=c(1,0.5) )
+ EF <- eff[8,"Est",c("Met","Plc")]
+ # It might not be visit 7 that is the last non-missing, so find that
+ ends <- eff[1:7,"Est",c("Met","Plc")]
+ ends <- ends[max(which(!is.na(ends[,1]))),]
+ dv <- ends-mean(ends) ; dv <- dv/abs(dv)
+ if( abs(diff(ends)) < diff(y1)/20 ) ends <- mean(ends)+dv*diff(y1)/30
+ if( ltrf[match(var,vnam)] ) EF <- (EF-1)*100
+ print( c(EF, ends) )
+ text( c(20,20), ends,
+       paste( formatC( EF, format="f", digits=1 ), sep="" ),
+       col=clr[1:2], adj=1, font=2 )
+ matlines( tim, pef, type="l", lwd=c(5,1,1), lty=1, col=rep(clr[1:2],each=3) )
+ }

```

So we can draw two example graphs, groomed to look nice:

```

> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
> pleff( "hba1c", expression("Hb"*A[1][c]*" (%) [Mean (95% CI)]"),
+       y1 = c(7,10),
+       yt = 7:10,
+       ym = seq(7,10,0.5) )
      Met      Plc      Met      Plc
-0.7809503 -0.3561552  7.9689621  8.2745338

> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
> pleff("trig","Triglycerides (mmol/l) [Mean (95% CI)]",
+       y1 = c(1,2.5), # yaxis limits
+       yt = 0:4, # yaxis major ticks
+       ym = seq(1,3,0.25) ) # yaxis minor ticks
      Met      Plc      Met      Plc
 1.272308 -1.775583  1.759488  1.549417

```

With this function in place it is now simple to produce plots for all the variables, as a first guide to how they should be individually adjusted to look sensible:

```

> tmpl <-
+ function()
+ {
+ par( mfrow=c(2,2), mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
+ # HbA1c:
+ pleff( "hba1c",
+       expression("Hb"*A[1][c]*" (%) [Mean (95% CI)]"),
+       yl = c(7,10),
+       yt = 7:10,
+       ym = seq(7,10,0.5) )
+ text( cnr(2,98), "a", adj=c(0,1), font=2, cex=1.5 )
+ # Gluc
+ pleff("gluc","Fasting p-glucose (mmol/L) [Mean (95% CI)]",
+       yl = c(7,12), # yaxis limits
+       yt = seq(7,13,2), # yaxis major ticks
+       ym = seq(7,13,1) ) # yaxis minor ticks
+ text( cnr(2,98), "b", adj=c(0,1), font=2, cex=1.5 )
+ # Insulin dose
+ pleff("ipkg","Insulin dose (IU/day/kg) [Mean (95% CI)]",
+       yl = c(0.0,2.4), # yaxis limits
+       yt = seq(0.0,2.0,1.0), # yaxis major ticks
+       ym = seq(0.0,2.4,0.2) ) # yaxis minor ticks
+ text( cnr(2,98), "c", adj=c(0,1), font=2, cex=1.5 )
+ # Weight:
+ pleff("weight","Weight (kg) [Mean (95% CI)]",
+       yl = c(90,120), # yaxis limits
+       yt = seq(90,120,10), # yaxis major ticks
+       ym = seq(90,120,5) ) # yaxis minor ticks
+ text( cnr(2,98), "d", adj=c(0,1), font=2, cex=1.5 )
+ }
> tmpl()

```

Met	Plc	Met	Plc
-0.7809503	-0.3561552	7.9689621	8.2745338
Met	Plc	Met	Plc
-2.139541	-1.672106	8.220279	8.553612
Met	Plc	Met	Plc
112.689476	181.777199	1.038848	1.360663
Met	Plc	Met	Plc
1.584021	4.148280	100.041043	102.456710

```

> win.metafile( "./results/first4-met.emf", height=9, width=8 )
> tmpl()

```

Met	Plc	Met	Plc
-0.7809503	-0.3561552	7.9689621	8.2745338
Met	Plc	Met	Plc
-2.139541	-1.672106	8.220279	8.553612
Met	Plc	Met	Plc
112.689476	181.777199	1.038848	1.360663
Met	Plc	Met	Plc
1.584021	4.148280	100.041043	102.456710

```

> dev.off()
null device
1

```

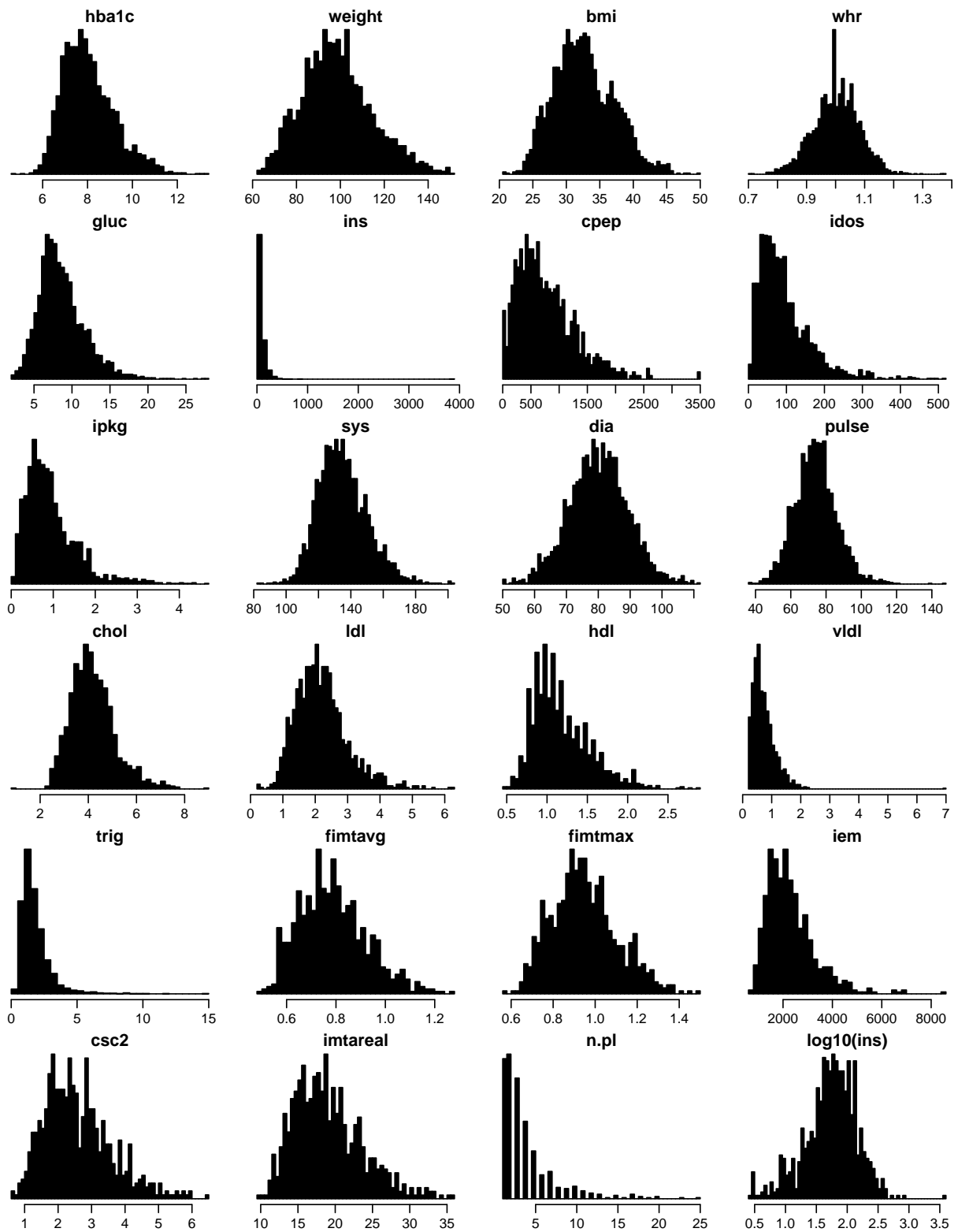


Figure 7.2: *Histograms of the marginal distribution of all chosen variables.*

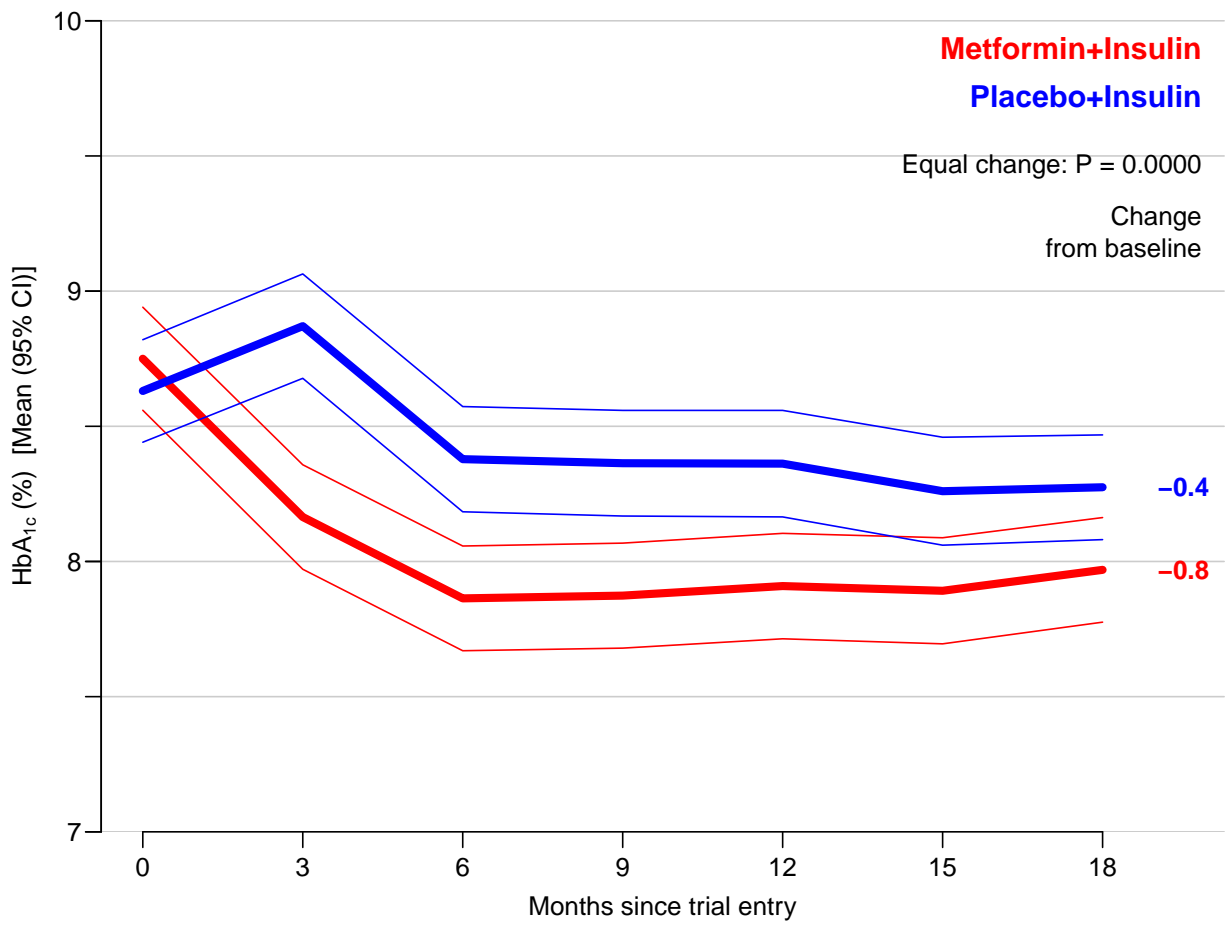


Figure 7.3: Trajectories for HbA_{1c}, illustrating how parameters translate into the graph.

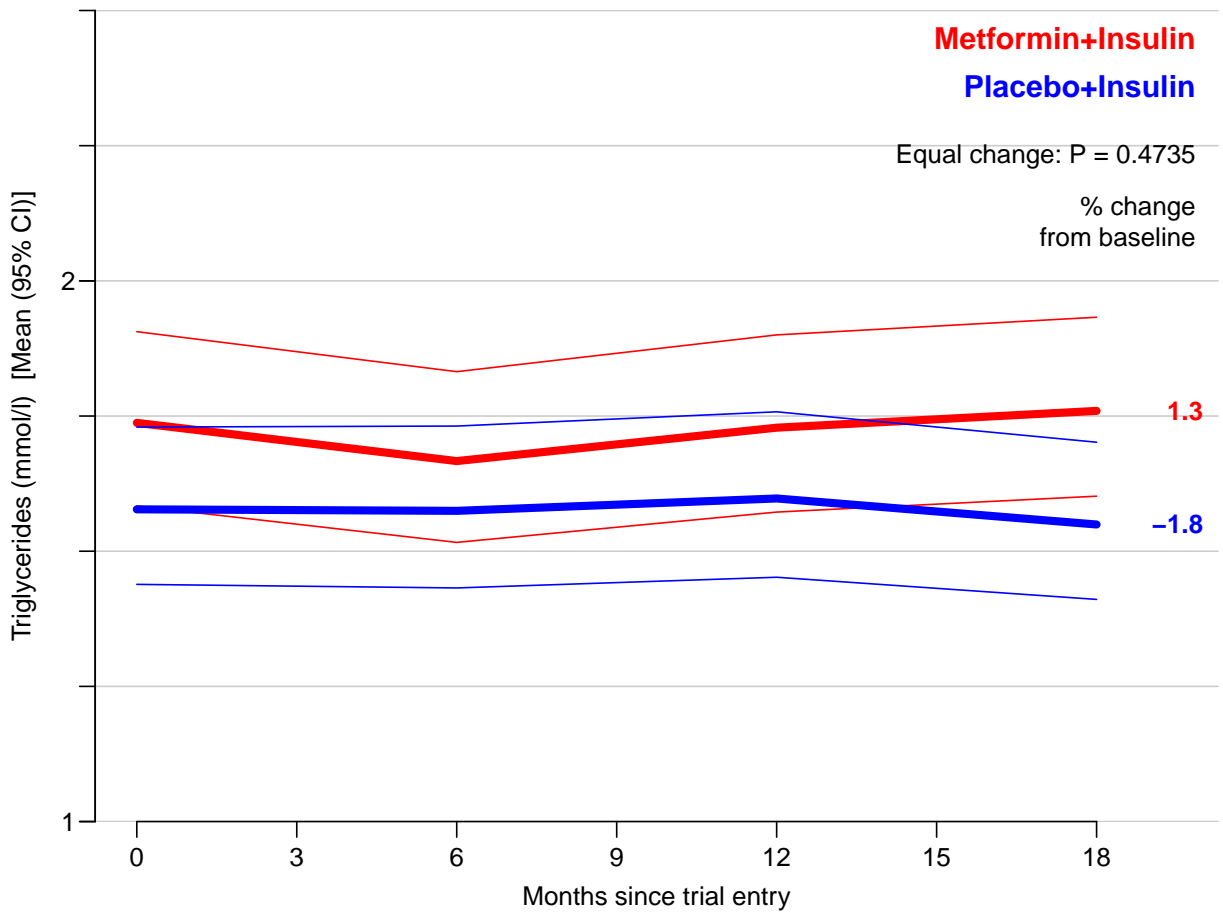


Figure 7.4: Trajectories for Triglycerides, illustrating how parameters translate into the graph.

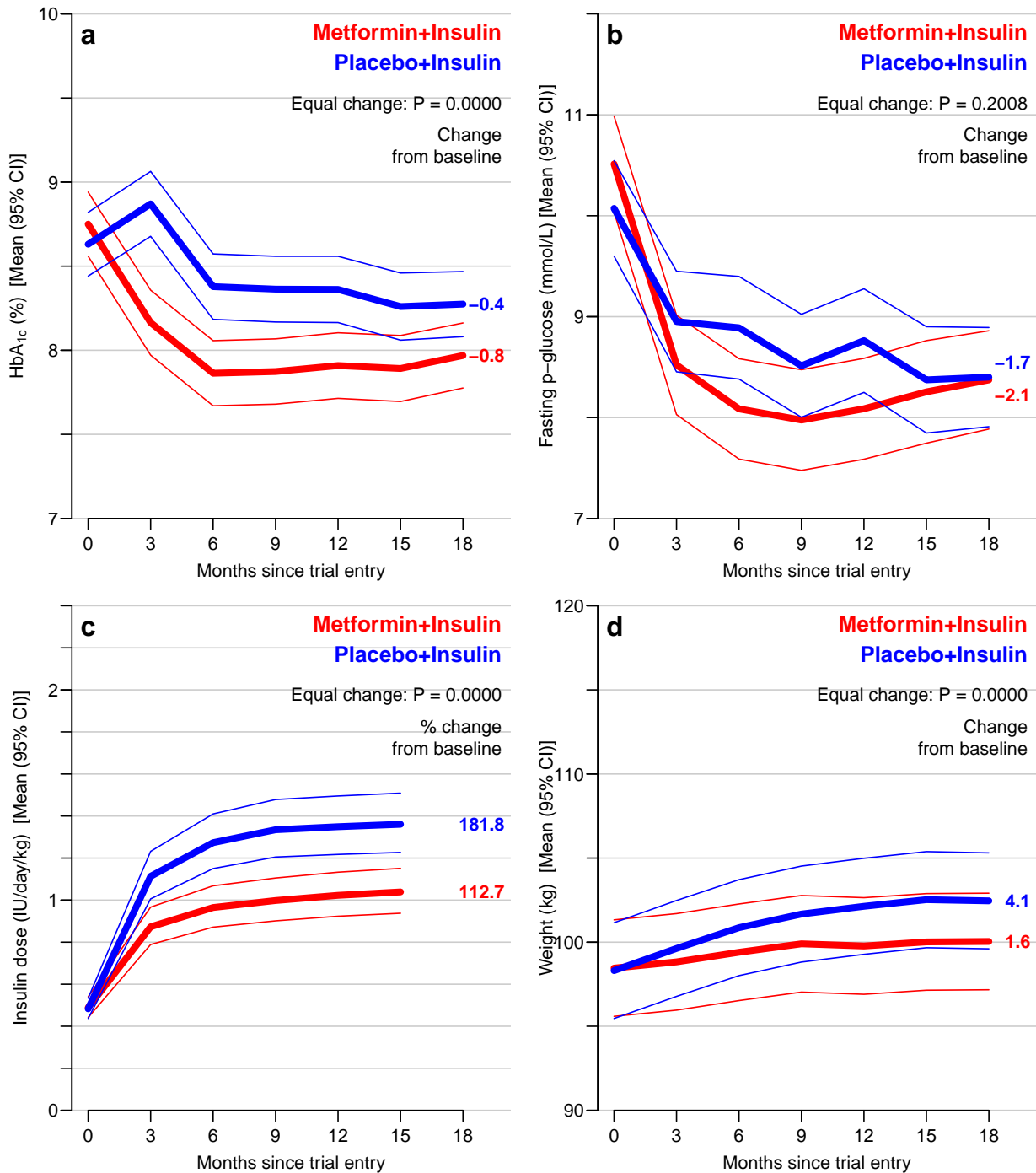


Figure 7.5: Trajectory plots for the first 4 variables.

Chapter 8

Secondary outcomes: insulin regimen

Initially we load the collected analysis dataset, and tabulate records and persons by randomization status and per protocol status:

```
> library( Epi )
> library( lme4 )
> library( abind )
> load( file="./data/AD.Rda" )
> with( AD, ftable( addmargins( table(grp,igr,PP=pp),
+                               2:3 ) ) )
```

	PP	FALSE	TRUE	Sum
grp igr				
Plc Biph		7	425	432
AspD		7	448	455
Detm		17	355	372
Sum		31	1228	1259
Met Biph		4	465	469
AspD		8	403	411
Detm		10	438	448
Sum		22	1306	1328

```
> with( AD, ftable( addmargins( tapply( subjid,
+                                       list(grp,igr,PP=pp),
+                                       function(x) length(unique(x)) ),
+                               2:3 ) ) )
```

	PP	FALSE	TRUE	Sum
Plc Biph		5	62	67
AspD		5	68	73
Detm		12	54	66
Sum		22	184	206
Met Biph		3	67	70
AspD		5	60	65
Detm		7	64	71
Sum		15	191	206

8.1 HbA_{1c}

8.1.1 HbA_{1c} at end of study

Initially we make a simple tabulation of the patients that achieve a HbA_{1c} ≤ 7.0%:

```
> load( file="./data/base.Rda" )
> tt <- addmargins( with( base, table( igr, hba1c.b7>7.0 ) ) )
> cbind( tt, round( 100*tt/tt[,3], 1 ) )[, -6]
```

	FALSE	TRUE	Sum	FALSE	TRUE
Biph	38	88	126	30.2	69.8
AspD	31	96	127	24.4	75.6
Detm	12	108	120	10.0	90.0
Sum	81	292	373	21.7	78.3

A more formal analysis is achieved by using a binomial model, in this case with a log-link, so that we directly get the proportions:

```
> m1 <- glm( hba1c.b7<=7.0 ~ igr -1, family=binomial(link="log"), data=base )
> round( 100*ci.exp( m1 ), 1 )
      exp(Est.) 2.5% 97.5%
igrBiph      30.2 23.1 39.3
igrAspD      24.4 18.0 33.1
igrDetm      10.0  5.8 17.1
> anova( m1, update( m1, . ~ 1 ), test="Chisq" )
Analysis of Deviance Table

Model 1: hba1c.b7 <= 7 ~ igr - 1
Model 2: hba1c.b7 <= 7 ~ 1
  Resid. Df Resid. Dev Df Deviance Pr(>Chi)
1         370      373.46
2         372      390.37 -2  -16.916 0.0002122
```

Thus the p-value for equal fraction of patients achieving a HbA_{1c} less than or equal to 7.0 is 0.0002.

We can also compute the RRs and the corresponding p-values for the three differences between

```
> CM = rbind( c(-1,1,0), c(-1,0,1), c(0,-1,1) )
> rownames( CM ) <- paste( levels(base$igr)[c(2,3,3)], "vs.",
+                          levels(base$igr)[c(1,1,2)] )
> CM
      [,1] [,2] [,3]
AspD vs. Biph  -1    1    0
Detm vs. Biph  -1    0    1
Detm vs. AspD   0   -1    1
> round( ci.exp( m1 ), 2 )
      exp(Est.) 2.5% 97.5%
igrBiph      0.30 0.23 0.39
igrAspD      0.24 0.18 0.33
igrDetm      0.10 0.06 0.17
> cbind(
+ round( ci.exp( m1, ctr.mat= CM ), 2 ),
+ round( ci.exp( m1, ctr.mat=-CM ), 2 ),
+ round( ci.lin( m1, ctr.mat= CM )[,4,drop=F], 3 ) )
      exp(Est.) 2.5% 97.5% exp(Est.) 2.5% 97.5%      P
AspD vs. Biph  0.81 0.54 1.21      1.24 0.82 1.85 0.306
Detm vs. Biph  0.33 0.18 0.60      3.02 1.66 5.49 0.000
Detm vs. AspD  0.41 0.22 0.76      2.44 1.32 4.53 0.005
```

8.1.2 HbA_{1c} trajectories

We shall use the analysis of HbA_{1c} to set up the model for analyzing the other glucose related outcomes by insulin group.

We set up a random effects model using `lmer`, first fitted to the entire dataset (intention to treat) and then to the restricted (per protocol) — analysis I. We use a model (ITa)

allowing for baseline imbalance between the groups, but it might be argued that a model with identical baseline among the randomized groups would be better. Unlikely to produce dramatically different results, though.

```
> MM <- model.matrix( ~ igr:factor(visit), data=AD )[,-(1:4)]
> colnames( MM )
  [1] "igrBiph:factor(visit)v2" "igrAspD:factor(visit)v2" "igrDetm:factor(visit)v2"
  [4] "igrBiph:factor(visit)v3" "igrAspD:factor(visit)v3" "igrDetm:factor(visit)v3"
  [7] "igrBiph:factor(visit)v4" "igrAspD:factor(visit)v4" "igrDetm:factor(visit)v4"
 [10] "igrBiph:factor(visit)v5" "igrAspD:factor(visit)v5" "igrDetm:factor(visit)v5"
 [13] "igrBiph:factor(visit)v6" "igrAspD:factor(visit)v6" "igrDetm:factor(visit)v6"
 [16] "igrBiph:factor(visit)v7" "igrAspD:factor(visit)v7" "igrDetm:factor(visit)v7"

> ITO <- lmer( hba1c ~ MM +
+             sdc + over.65 + pre.ins +
+             (1|subjid),
+             data = AD )
> round( ci.lin( ITO ), 3 )
```

	Estimate	StdErr	z	P	2.5%	97.5%
(Intercept)	8.698	0.079	109.427	0.000	8.543	8.854
MMigrBiph:factor(visit)v2	-0.415	0.080	-5.214	0.000	-0.571	-0.259
MMigrAspD:factor(visit)v2	-0.485	0.080	-6.038	0.000	-0.642	-0.327
MMigrDetm:factor(visit)v2	0.397	0.082	4.813	0.000	0.235	0.558
MMigrBiph:factor(visit)v3	-0.913	0.081	-11.290	0.000	-1.072	-0.755
MMigrAspD:factor(visit)v3	-0.727	0.081	-8.973	0.000	-0.885	-0.568
MMigrDetm:factor(visit)v3	-0.057	0.083	-0.677	0.499	-0.220	0.107
MMigrBiph:factor(visit)v4	-0.880	0.081	-10.899	0.000	-1.038	-0.721
MMigrAspD:factor(visit)v4	-0.697	0.082	-8.454	0.000	-0.859	-0.535
MMigrDetm:factor(visit)v4	-0.128	0.084	-1.518	0.129	-0.293	0.037
MMigrBiph:factor(visit)v5	-0.823	0.080	-10.225	0.000	-0.981	-0.665
MMigrAspD:factor(visit)v5	-0.642	0.083	-7.692	0.000	-0.805	-0.478
MMigrDetm:factor(visit)v5	-0.190	0.086	-2.200	0.028	-0.360	-0.021
MMigrBiph:factor(visit)v6	-0.885	0.081	-10.875	0.000	-1.044	-0.725
MMigrAspD:factor(visit)v6	-0.614	0.086	-7.178	0.000	-0.782	-0.447
MMigrDetm:factor(visit)v6	-0.335	0.089	-3.787	0.000	-0.509	-0.162
MMigrBiph:factor(visit)v7	-0.964	0.081	-11.957	0.000	-1.122	-0.806
MMigrAspD:factor(visit)v7	-0.467	0.080	-5.803	0.000	-0.624	-0.309
MMigrDetm:factor(visit)v7	-0.267	0.083	-3.235	0.001	-0.429	-0.105
sdcnnotSDC	0.102	0.090	1.134	0.257	-0.075	0.280
over.65>65	-0.340	0.098	-3.463	0.001	-0.533	-0.148
pre.insnoIns	-0.337	0.098	-3.432	0.001	-0.529	-0.144

```
> ITa <- lmer( hba1c ~ igr + igr:factor(visit) - 1 +
+             sdc + over.65 + pre.ins +
+             (1|subjid),
+             data = AD )
> round( ci.lin( ITa ), 3 )
```

	Estimate	StdErr	z	P	2.5%	97.5%
igrBiph	8.776	0.110	79.486	0.000	8.559	8.992
igrAspD	8.644	0.110	78.744	0.000	8.429	8.859
igrDetm	8.677	0.110	78.820	0.000	8.461	8.893
sdcnnotSDC	0.103	0.090	1.138	0.255	-0.074	0.280
over.65>65	-0.341	0.098	-3.470	0.001	-0.534	-0.148
pre.insnoIns	-0.338	0.098	-3.439	0.001	-0.530	-0.145
igrBiph:factor(visit)v2	-0.446	0.085	-5.226	0.000	-0.613	-0.279
igrAspD:factor(visit)v2	-0.463	0.086	-5.386	0.000	-0.631	-0.294
igrDetm:factor(visit)v2	0.405	0.088	4.609	0.000	0.233	0.578
igrBiph:factor(visit)v3	-0.944	0.087	-10.912	0.000	-1.114	-0.775
igrAspD:factor(visit)v3	-0.705	0.087	-8.138	0.000	-0.874	-0.535
igrDetm:factor(visit)v3	-0.048	0.089	-0.536	0.592	-0.222	0.127
igrBiph:factor(visit)v4	-0.911	0.086	-10.544	0.000	-1.080	-0.741
igrAspD:factor(visit)v4	-0.675	0.088	-7.675	0.000	-0.847	-0.503
igrDetm:factor(visit)v4	-0.119	0.090	-1.327	0.184	-0.295	0.057
igrBiph:factor(visit)v5	-0.854	0.086	-9.911	0.000	-1.023	-0.685
igrAspD:factor(visit)v5	-0.620	0.089	-6.974	0.000	-0.794	-0.446

```

igrDetm:factor(visit)v5 -0.181 0.092 -1.977 0.048 -0.361 -0.002
igrBiph:factor(visit)v6 -0.916 0.087 -10.529 0.000 -1.086 -0.745
igrAspD:factor(visit)v6 -0.592 0.091 -6.516 0.000 -0.770 -0.414
igrDetm:factor(visit)v6 -0.327 0.094 -3.483 0.000 -0.510 -0.143
igrBiph:factor(visit)v7 -0.995 0.086 -11.531 0.000 -1.164 -0.826
igrAspD:factor(visit)v7 -0.445 0.086 -5.167 0.000 -0.613 -0.276
igrDetm:factor(visit)v7 -0.258 0.088 -2.932 0.003 -0.431 -0.086

> # Per protocol analysis
> PPa <- update( ITa, data = subset( AD, pp ) )

```

We then do the parallel analyses not adjusted for the stratification variables (II)

```

> ITr <- update( ITa, . ~ igr + igr:factor(visit) - 1 + (1/subject) )
> PPr <- update( ITr, data = subset( AD, pp ) )

```

Finally we expand the first analysis by including further potential confounders (III):

```

> ITc <- update( ITa, . ~ . + sex + statin + gad.pos + cvd )
> PPc <- update( ITc, data = subset( AD, pp ) )

```

So now we have 6 different models for the same outcome, which either will show approximately the same, or in the case they show slightly different results, enables us to pick the results that suits or prejudices best.

8.1.3 Extraction of estimated effects

From this model we want to extract first the average level of HbA_{1c} at each visit, and additionally the estimated change from visit 1 to visit 7, so we set up the corresponding contrast matrix, which will extract these from the models

```

> eM <- rbind( cbind(1, rbind(0, diag(6))), rep(0:1, c(6, 1)) )
> rownames( eM ) <- c( paste( "Vis", 1:7, sep="" ), "v7-v1" )
> eM

```

	[,1]	[,2]	[,3]	[,4]	[,5]	[,6]	[,7]
Vis1	1	0	0	0	0	0	0
Vis2	1	1	0	0	0	0	0
Vis3	1	0	1	0	0	0	0
Vis4	1	0	0	1	0	0	0
Vis5	1	0	0	0	1	0	0
Vis6	1	0	0	0	0	1	0
Vis7	1	0	0	0	0	0	1
v7-v1	0	0	0	0	0	0	1

With a first look at the entire parameter vector for the model we can see what subset to extract to get the desired estimates:

```

> round( ci.exp( ITa, Exp=F ), 3 )

```

	Estimate	2.5%	97.5%
igrBiph	8.776	8.559	8.992
igrAspD	8.644	8.429	8.859
igrDetm	8.677	8.461	8.893
sdcnnotSDC	0.103	-0.074	0.280
over.65>65	-0.341	-0.534	-0.148
pre.insnoIns	-0.338	-0.530	-0.145
igrBiph:factor(visit)v2	-0.446	-0.613	-0.279
igrAspD:factor(visit)v2	-0.463	-0.631	-0.294
igrDetm:factor(visit)v2	0.405	0.233	0.578
igrBiph:factor(visit)v3	-0.944	-1.114	-0.775
igrAspD:factor(visit)v3	-0.705	-0.874	-0.535
igrDetm:factor(visit)v3	-0.048	-0.222	0.127

```

igrBiph:factor(visit)v4 -0.911 -1.080 -0.741
igrAspD:factor(visit)v4 -0.675 -0.847 -0.503
igrDetm:factor(visit)v4 -0.119 -0.295 0.057
igrBiph:factor(visit)v5 -0.854 -1.023 -0.685
igrAspD:factor(visit)v5 -0.620 -0.794 -0.446
igrDetm:factor(visit)v5 -0.181 -0.361 -0.002
igrBiph:factor(visit)v6 -0.916 -1.086 -0.745
igrAspD:factor(visit)v6 -0.592 -0.770 -0.414
igrDetm:factor(visit)v6 -0.327 -0.510 -0.143
igrBiph:factor(visit)v7 -0.995 -1.164 -0.826
igrAspD:factor(visit)v7 -0.445 -0.613 -0.276
igrDetm:factor(visit)v7 -0.258 -0.431 -0.086

> round( ci.exp( ITa, subset="Biph", Exp=F ), 3 )

              Estimate  2.5% 97.5%
igrBiph              8.776 8.559 8.992
igrBiph:factor(visit)v2 -0.446 -0.613 -0.279
igrBiph:factor(visit)v3 -0.944 -1.114 -0.775
igrBiph:factor(visit)v4 -0.911 -1.080 -0.741
igrBiph:factor(visit)v5 -0.854 -1.023 -0.685
igrBiph:factor(visit)v6 -0.916 -1.086 -0.745
igrBiph:factor(visit)v7 -0.995 -1.164 -0.826

> round( ci.exp( ITa, subset="AspD", Exp=F ), 3 )

              Estimate  2.5% 97.5%
igrAspD              8.644 8.429 8.859
igrAspD:factor(visit)v2 -0.463 -0.631 -0.294
igrAspD:factor(visit)v3 -0.705 -0.874 -0.535
igrAspD:factor(visit)v4 -0.675 -0.847 -0.503
igrAspD:factor(visit)v5 -0.620 -0.794 -0.446
igrAspD:factor(visit)v6 -0.592 -0.770 -0.414
igrAspD:factor(visit)v7 -0.445 -0.613 -0.276

> round( ci.exp( ITa, subset="Detm", Exp=F ), 3 )

              Estimate  2.5% 97.5%
igrDetm              8.677 8.461 8.893
igrDetm:factor(visit)v2 0.405 0.233 0.578
igrDetm:factor(visit)v3 -0.048 -0.222 0.127
igrDetm:factor(visit)v4 -0.119 -0.295 0.057
igrDetm:factor(visit)v5 -0.181 -0.361 -0.002
igrDetm:factor(visit)v6 -0.327 -0.510 -0.143
igrDetm:factor(visit)v7 -0.258 -0.431 -0.086

> round( ci.exp( ITa, subint=c("Detm","v7"), Exp=F ), 3 )

              Estimate  2.5% 97.5%
igrDetm:factor(visit)v7 -0.258 -0.431 -0.086

> ( ilev <- levels( AD$igr ) )
[1] "Biph" "AspD" "Detm"

> c.1 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[1], Exp=F )
> c.2 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[2], Exp=F )
> c.3 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[3], Exp=F )
> c.21 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(2,1)], Exp=F )
> c.31 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,1)], Exp=F )
> c.32 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,2)], Exp=F )
> eff <- cbind( c.1, c.2, c.3 )
> colnames(eff)[1+0:2*3] <- ilev
> dff <- cbind( c.21, c.31, c.32 )
> colnames(dff)[1+0:2*3] <- paste( ilev[c(2,3,3)], "-",
+                               ilev[c(1,1,2)], sep="" )
> round( eff, 3 )

```

```

      Biph  2.5% 97.5%  AspD  2.5% 97.5%  Detm  2.5% 97.5%
Vis1  8.776 8.559 8.992 8.644 8.429 8.859 8.677 8.461 8.893
Vis2  8.330 8.112 8.548 8.181 7.963 8.400 9.082 8.860 9.304
Vis3  7.831 7.611 8.051 7.939 7.720 8.159 8.629 8.406 8.853
Vis4  7.865 7.645 8.085 7.969 7.747 8.191 8.558 8.333 8.783
Vis5  7.922 7.702 8.141 8.024 7.801 8.248 8.495 8.267 8.724
Vis6  7.860 7.639 8.080 8.052 7.825 8.278 8.350 8.119 8.582
Vis7  7.780 7.561 8.000 8.199 7.981 8.418 8.419 8.196 8.641
v7-v1 -0.995 -1.164 -0.826 -0.445 -0.613 -0.276 -0.258 -0.431 -0.086

> round( dff, 3 )
      AspD-Biph  2.5% 97.5% Detm-Biph  2.5% 97.5% Detm-AspD  2.5% 97.5%
Vis1  -0.132 -0.390 0.127  -0.099 -0.357 0.160  0.033 -0.225 0.291
Vis2  -0.149 -0.412 0.115  0.752 0.487 1.018  0.901 0.634 1.167
Vis3  0.108 -0.157 0.374  0.798 0.529 1.067  0.690 0.421 0.958
Vis4  0.104 -0.163 0.371  0.693 0.423 0.962  0.589 0.318 0.860
Vis5  0.103 -0.165 0.370  0.574 0.302 0.846  0.471 0.196 0.746
Vis6  0.192 -0.079 0.464  0.491 0.215 0.766  0.299 0.018 0.579
Vis7  0.419 0.155 0.684  0.638 0.371 0.906  0.219 -0.048 0.486
v7-v1 0.551 0.312 0.790  0.737 0.495 0.979  0.186 -0.055 0.428

```

We also want to test whether the trajectories of the outcome (HbA_{1c}) is the same in the three randomization groups, whether the values at the last visit is the same, and whether the change from first to last visit is the same. These three tests are accomplished by using the same contrast matrix that we just set up:

```

> test <- rbind( Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[-8,] ),
+               Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[-8,] ),
+               Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[-8,] ),
+               Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+               Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+               Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+               Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+               Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+               Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+               Wald( ITa, subint=c(ilev[1],"v7" ) ),
+               Wald( ITa, subint=c(ilev[2],"v7" ) ),
+               Wald( ITa, subint=c(ilev[3],"v7" ) ) )
> tnames <-
+ rownames( test ) <- c( paste( rep(c(" All equal",
+                               "Visit 7 equal",
+                               " Change equal"),each=3),
+                           rep( paste( ilev[c(2,3,3)], "vs. ",
+                                       ilev[c(1,1,2)] ), 3 ) ),
+                           paste( " ", ilev, "change=0" ) )
> round( test, 4 )
      Chisq d.f.      P
All equal AspD vs. Biph 30.3248 7 0.0001
All equal Detm vs. Biph 96.3668 7 0.0000
All equal Detm vs. AspD 84.1411 7 0.0000
Visit 7 equal AspD vs. Biph 9.6418 1 0.0019
Visit 7 equal Detm vs. Biph 21.9093 1 0.0000
Visit 7 equal Detm vs. AspD 2.5916 1 0.1074
Change equal AspD vs. Biph 20.4151 1 0.0000
Change equal Detm vs. Biph 35.6933 1 0.0000
Change equal Detm vs. AspD 2.2875 1 0.1304
Biph change=0 132.9665 1 0.0000
AspD change=0 26.6997 1 0.0000
Detm change=0 8.5939 1 0.0034

> round( test[c(1,4,7,2,5,8,3,6,9),], 4 )
      Chisq d.f.      P
All equal AspD vs. Biph 30.3248 7 0.0001
Visit 7 equal AspD vs. Biph 9.6418 1 0.0019

```



```

Change equal AspD vs. Biph 20.4151    1 0.0000
  All equal Detm vs. Biph 96.3668    7 0.0000
Visit 7 equal Detm vs. Biph 21.9093    1 0.0000
Change equal Detm vs. Biph 35.6933    1 0.0000
  All equal Detm vs. AspD 84.1411    7 0.0000
Visit 7 equal Detm vs. AspD 2.5916    1 0.1074
Change equal Detm vs. AspD 2.2875    1 0.1304

```

For convenience we pack these extractors and tests in a function, that takes a particular model as argument:

```

> ilev <- levels( AD$igr )
> resfun <-
+ function( ITa )
+ {
+ c.1 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[1], Exp=F )
+ c.2 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[2], Exp=F )
+ c.3 <- ci.exp( ITa, ctr.mat=eM, subset=ilev[3], Exp=F )
+ c.21 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(2,1)], Exp=F )
+ c.31 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,1)], Exp=F )
+ c.32 <- ci.exp( ITa, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,2)], Exp=F )
+ eff <- cbind( c.1, c.2, c.3 )
+ colnames(eff)[1+0:2*3] <- ilev
+ dff <- cbind( c.21, c.31, c.32 )
+ colnames(dff)[1+0:2*3] <- paste( ilev[c(2,3,3)], "-",
+                               ilev[c(1,1,2)], sep="" )
+ test <- rbind( Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[-8,] ),
+              Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[-8,] ),
+              Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[-8,] ),
+              Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+              Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+              Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[7,,drop=F] ),
+              Wald( ITa, subset=ilev[c(2,1)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+              Wald( ITa, subset=ilev[c(3,1)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+              Wald( ITa, subset=ilev[c(3,2)], ctr.mat=cbind(-eM,eM)[8,,drop=F] ),
+              Wald( ITa, subint=c(ilev[1],"v7" ) ),
+              Wald( ITa, subint=c(ilev[2],"v7" ) ),
+              Wald( ITa, subint=c(ilev[3],"v7" ) ) )
+ rownames( test ) <- tnames
+ print( round( eff, 3 ) )
+ print( round( dff, 3 ) )
+ print( round( test, 4 ) )
+ invisible( list( eff=eff, dff=dff, test=test ) )
+ }

```

This can now be applied to all fitted models, but we only store the results from the primary model:

```

> hbr <- resfun( ITa )

```

	Biph	2.5%	97.5%	AspD	2.5%	97.5%	Detm	2.5%	97.5%
Vis1	8.776	8.559	8.992	8.644	8.429	8.859	8.677	8.461	8.893
Vis2	8.330	8.112	8.548	8.181	7.963	8.400	9.082	8.860	9.304
Vis3	7.831	7.611	8.051	7.939	7.720	8.159	8.629	8.406	8.853
Vis4	7.865	7.645	8.085	7.969	7.747	8.191	8.558	8.333	8.783
Vis5	7.922	7.702	8.141	8.024	7.801	8.248	8.495	8.267	8.724
Vis6	7.860	7.639	8.080	8.052	7.825	8.278	8.350	8.119	8.582
Vis7	7.780	7.561	8.000	8.199	7.981	8.418	8.419	8.196	8.641
v7-v1	-0.995	-1.164	-0.826	-0.445	-0.613	-0.276	-0.258	-0.431	-0.086
	AspD-Biph	2.5%	97.5%	Detm-Biph	2.5%	97.5%	Detm-AspD	2.5%	97.5%
Vis1	-0.132	-0.390	0.127	-0.099	-0.357	0.160	0.033	-0.225	0.291
Vis2	-0.149	-0.412	0.115	0.752	0.487	1.018	0.901	0.634	1.167
Vis3	0.108	-0.157	0.374	0.798	0.529	1.067	0.690	0.421	0.958
Vis4	0.104	-0.163	0.371	0.693	0.423	0.962	0.589	0.318	0.860
Vis5	0.103	-0.165	0.370	0.574	0.302	0.846	0.471	0.196	0.746
Vis6	0.192	-0.079	0.464	0.491	0.215	0.766	0.299	0.018	0.579


```

Vis7      0.419  0.155  0.684      0.638  0.371  0.906      0.219 -0.048  0.486
v7-v1    0.551  0.312  0.790      0.737  0.495  0.979      0.186 -0.055  0.428

```

```

                Chisq d.f.      P
All equal AspD vs. Biph 30.3248      7 0.0001
All equal Detm vs. Biph 96.3668      7 0.0000
All equal Detm vs. AspD 84.1411      7 0.0000
Visit 7 equal AspD vs. Biph 9.6418      1 0.0019
Visit 7 equal Detm vs. Biph 21.9093      1 0.0000
Visit 7 equal Detm vs. AspD 2.5916      1 0.1074
Change equal AspD vs. Biph 20.4151      1 0.0000
Change equal Detm vs. Biph 35.6933      1 0.0000
Change equal Detm vs. AspD 2.2875      1 0.1304
  Biph change=0      132.9665      1 0.0000
  AspD change=0      26.6997      1 0.0000
  Detm change=0      8.5939      1 0.0034

```

> resfun(ITr)

```

                Biph  2.5% 97.5%  AspD  2.5% 97.5%  Detm  2.5% 97.5%
Vis1  8.622  8.436  8.808  8.497  8.312  8.682  8.531  8.345  8.717
Vis2  8.175  7.986  8.363  8.034  7.845  8.224  8.934  8.741  9.127
Vis3  7.677  7.486  7.867  7.792  7.601  7.983  8.483  8.288  8.678
Vis4  7.711  7.520  7.901  7.822  7.629  8.015  8.412  8.215  8.608
Vis5  7.768  7.578  7.958  7.876  7.682  8.071  8.349  8.149  8.549
Vis6  7.706  7.515  7.898  7.905  7.707  8.103  8.203  7.999  8.406
Vis7  7.626  7.436  7.816  8.052  7.862  8.241  8.272  8.079  8.466
v7-v1 -0.996 -1.165 -0.827 -0.445 -0.614 -0.277 -0.259 -0.432 -0.087
  AspD-Biph  2.5% 97.5% Detm-Biph  2.5% 97.5% Detm-AspD  2.5% 97.5%
Vis1  -0.125 -0.387  0.138  -0.091 -0.353  0.172  0.034 -0.228  0.297
Vis2  -0.140 -0.407  0.127  0.760  0.490  1.030  0.900  0.629  1.170
Vis3  0.115 -0.154  0.385  0.806  0.533  1.079  0.691  0.418  0.963
Vis4  0.111 -0.160  0.382  0.701  0.427  0.974  0.590  0.315  0.865
Vis5  0.109 -0.163  0.381  0.581  0.305  0.857  0.472  0.193  0.751
Vis6  0.199 -0.077  0.474  0.497  0.217  0.776  0.298  0.014  0.582
Vis7  0.426  0.157  0.695  0.646  0.375  0.918  0.220 -0.051  0.491
v7-v1  0.551  0.312  0.790      0.737  0.495  0.978      0.186 -0.055  0.427

```

```

                Chisq d.f.      P
All equal AspD vs. Biph 30.2862      7 0.0001
All equal Detm vs. Biph 95.8334      7 0.0000
All equal Detm vs. AspD 83.1796      7 0.0000
Visit 7 equal AspD vs. Biph 9.6498      1 0.0019
Visit 7 equal Detm vs. Biph 21.7785      1 0.0000
Visit 7 equal Detm vs. AspD 2.5396      1 0.1110
Change equal AspD vs. Biph 20.4156      1 0.0000
Change equal Detm vs. Biph 35.6658      1 0.0000
Change equal Detm vs. AspD 2.2812      1 0.1310
  Biph change=0      133.1757      1 0.0000
  AspD change=0      26.7887      1 0.0000
  Detm change=0      8.6569      1 0.0033

```

> resfun(ITc)

```

                Biph  2.5% 97.5%  AspD  2.5% 97.5%  Detm  2.5% 97.5%
Vis1  8.917  8.588  9.246  8.785  8.456  9.114  8.823  8.488  9.158
Vis2  8.472  8.141  8.802  8.322  7.991  8.653  9.229  8.889  9.569
Vis3  7.973  7.641  8.305  8.080  7.748  8.412  8.776  8.435  9.116
Vis4  8.007  7.675  8.339  8.110  7.777  8.443  8.705  8.363  9.046
Vis5  8.064  7.732  8.395  8.165  7.830  8.500  8.642  8.298  8.986
Vis6  8.002  7.669  8.334  8.193  7.856  8.529  8.497  8.151  8.843
Vis7  7.922  7.590  8.254  8.340  8.009  8.672  8.565  8.225  8.905
v7-v1 -0.995 -1.164 -0.825 -0.445 -0.613 -0.276 -0.258 -0.431 -0.085
  AspD-Biph  2.5% 97.5% Detm-Biph  2.5% 97.5% Detm-AspD  2.5% 97.5%
Vis1  -0.132 -0.391  0.127  -0.094 -0.353  0.166  0.038 -0.221  0.298
Vis2  -0.150 -0.414  0.114  0.757  0.491  1.024  0.907  0.640  1.174
Vis3  0.107 -0.159  0.374  0.803  0.533  1.072  0.696  0.426  0.965
Vis4  0.103 -0.165  0.371  0.698  0.428  0.968  0.595  0.323  0.867
Vis5  0.101 -0.167  0.370  0.579  0.306  0.851  0.477  0.201  0.753
Vis6  0.191 -0.081  0.464  0.496  0.220  0.772  0.304  0.023  0.585

```

```

Vis7      0.418  0.153  0.683      0.643  0.375  0.911      0.225 -0.043  0.493
v7-v1    0.550  0.311  0.789      0.737  0.495  0.978      0.187 -0.055  0.428
          Chisq d.f.      P
All equal AspD vs. Biph 30.2721      7 0.0001
All equal Detm vs. Biph 96.5161      7 0.0000
All equal Detm vs. AspD 84.4559      7 0.0000
Visit 7 equal AspD vs. Biph 9.5300      1 0.0020
Visit 7 equal Detm vs. Biph 22.1220      1 0.0000
Visit 7 equal Detm vs. AspD 2.7131      1 0.0995
Change equal AspD vs. Biph 20.3656      1 0.0000
Change equal Detm vs. Biph 35.6577      1 0.0000
Change equal Detm vs. AspD 2.2955      1 0.1297
  Biph change=0      132.7498      1 0.0000
  AspD change=0      26.6907      1 0.0000
  Detm change=0      8.5642      1 0.0034

```

```
> resfun( PPa )
```

```

          Biph  2.5% 97.5%  AspD  2.5% 97.5%  Detm  2.5% 97.5%
Vis1  8.808  8.586  9.030  8.693  8.470  8.916  8.710  8.480  8.939
Vis2  8.323  8.101  8.545  8.201  7.978  8.424  9.048  8.818  9.277
Vis3  7.844  7.622  8.067  7.966  7.742  8.190  8.621  8.391  8.851
Vis4  7.878  7.656  8.101  7.995  7.770  8.221  8.550  8.319  8.781
Vis5  7.935  7.713  8.157  8.051  7.823  8.278  8.488  8.253  8.722
Vis6  7.873  7.649  8.097  8.079  7.848  8.309  8.343  8.105  8.580
Vis7  7.792  7.569  8.015  8.216  7.992  8.440  8.379  8.149  8.609
v7-v1 -1.015 -1.185 -0.846 -0.477 -0.648 -0.307 -0.331 -0.508 -0.154
      AspD-Biph  2.5% 97.5% Detm-Biph  2.5% 97.5% Detm-AspD  2.5% 97.5%
Vis1  -0.115 -0.382  0.153  -0.098 -0.371  0.175  0.017 -0.257  0.290
Vis2  -0.122 -0.390  0.146  0.725  0.451  0.998  0.847  0.573  1.120
Vis3  0.121 -0.148  0.391  0.777  0.502  1.051  0.655  0.381  0.930
Vis4  0.117 -0.153  0.388  0.672  0.397  0.947  0.554  0.277  0.832
Vis5  0.116 -0.156  0.387  0.553  0.275  0.830  0.437  0.156  0.718
Vis6  0.206 -0.070  0.481  0.470  0.189  0.751  0.264 -0.022  0.550
Vis7  0.423  0.154  0.693  0.586  0.312  0.861  0.163 -0.112  0.438
v7-v1 0.538  0.297  0.779  0.685  0.439  0.930  0.146 -0.099  0.392
          Chisq d.f.      P
All equal AspD vs. Biph 28.7065      7 0.0002
All equal Detm vs. Biph 88.5191      7 0.0000
All equal Detm vs. AspD 78.2415      7 0.0000
Visit 7 equal AspD vs. Biph 9.4877      1 0.0021
Visit 7 equal Detm vs. Biph 17.5220      1 0.0000
Visit 7 equal Detm vs. AspD 1.3493      1 0.2454
Change equal AspD vs. Biph 19.1991      1 0.0000
Change equal Detm vs. Biph 29.9446      1 0.0000
Change equal Detm vs. AspD 1.3631      1 0.2430
  Biph change=0      137.2700      1 0.0000
  AspD change=0      30.0547      1 0.0000
  Detm change=0      13.4474      1 0.0002

```

```
> resfun( PPr )
```

```

          Biph  2.5% 97.5%  AspD  2.5% 97.5%  Detm  2.5% 97.5%
Vis1  8.635  8.443  8.827  8.529  8.336  8.722  8.543  8.342  8.744
Vis2  8.150  7.958  8.343  8.037  7.844  8.230  8.881  8.680  9.082
Vis3  7.672  7.478  7.865  7.801  7.607  7.995  8.455  8.254  8.657
Vis4  7.706  7.513  7.899  7.831  7.635  8.027  8.385  8.182  8.587
Vis5  7.763  7.570  7.956  7.886  7.688  8.084  8.321  8.115  8.527
Vis6  7.702  7.507  7.896  7.915  7.713  8.116  8.176  7.966  8.385
Vis7  7.620  7.426  7.813  8.051  7.857  8.246  8.213  8.011  8.414
v7-v1 -1.015 -1.185 -0.845 -0.478 -0.648 -0.307 -0.331 -0.507 -0.154
      AspD-Biph  2.5% 97.5% Detm-Biph  2.5% 97.5% Detm-AspD  2.5% 97.5%
Vis1  -0.106 -0.378  0.166  -0.092 -0.370  0.186  0.014 -0.264  0.293
Vis2  -0.114 -0.386  0.159  0.731  0.453  1.009  0.845  0.566  1.123
Vis3  0.129 -0.145  0.403  0.783  0.504  1.063  0.654  0.374  0.933
Vis4  0.125 -0.150  0.400  0.678  0.399  0.958  0.553  0.271  0.836
Vis5  0.123 -0.153  0.400  0.559  0.276  0.841  0.436  0.150  0.721
Vis6  0.213 -0.067  0.493  0.474  0.189  0.760  0.261 -0.029  0.552

```

```

Vis7      0.431  0.157  0.706      0.593  0.313  0.872      0.161 -0.119  0.441
v7-v1     0.537  0.297  0.778      0.684  0.439  0.930      0.147 -0.099  0.393
          Chisq d.f.      P
All equal AspD vs. Biph 28.7025  7 0.0002
All equal Detm vs. Biph 87.9288  7 0.0000
All equal Detm vs. AspD 77.5136  7 0.0000
Visit 7 equal AspD vs. Biph 9.5056  1 0.0020
Visit 7 equal Detm vs. Biph 17.2775  1 0.0000
Visit 7 equal Detm vs. AspD 1.2743  1 0.2590
Change equal AspD vs. Biph 19.1436  1 0.0000
Change equal Detm vs. Biph 29.9325  1 0.0000
Change equal Detm vs. AspD 1.3750  1 0.2410
  Biph change=0      137.1791  1 0.0000
  AspD change=0      30.1099  1 0.0000
  Detm change=0      13.4316  1 0.0002
> resfun( PPC )
          Biph  2.5%  97.5%  AspD  2.5%  97.5%  Detm  2.5%  97.5%
Vis1  8.922  8.578  9.266  8.802  8.458  9.145  8.826  8.471  9.180
Vis2  8.438  8.094  8.782  8.310  7.966  8.653  9.164  8.810  9.519
Vis3  7.959  7.614  8.303  8.074  7.730  8.418  8.738  8.383  9.092
Vis4  7.993  7.648  8.337  8.104  7.759  8.449  8.666  8.311  9.022
Vis5  8.049  7.705  8.394  8.159  7.813  8.506  8.604  8.246  8.962
Vis6  7.987  7.642  8.332  8.187  7.839  8.536  8.459  8.099  8.819
Vis7  7.907  7.562  8.251  8.324  7.980  8.668  8.495  8.140  8.850
v7-v1 -1.015 -1.185 -0.846 -0.477 -0.648 -0.307 -0.331 -0.508 -0.154
      AspD-Biph  2.5%  97.5%  Detm-Biph  2.5%  97.5%  Detm-AspD  2.5%  97.5%
Vis1  -0.121 -0.389  0.148  -0.096 -0.370  0.178  0.024 -0.250  0.299
Vis2  -0.128 -0.397  0.141  0.726  0.453  1.000  0.854  0.580  1.129
Vis3  0.115 -0.155  0.386  0.779  0.503  1.054  0.663  0.388  0.939
Vis4  0.111 -0.161  0.383  0.674  0.398  0.949  0.563  0.284  0.841
Vis5  0.110 -0.163  0.382  0.555  0.277  0.833  0.445  0.163  0.727
Vis6  0.200 -0.076  0.476  0.472  0.190  0.753  0.272 -0.015  0.559
Vis7  0.418  0.147  0.688  0.588  0.313  0.864  0.171 -0.105  0.447
v7-v1  0.538  0.297  0.779  0.685  0.439  0.930  0.147 -0.099  0.392
          Chisq d.f.      P
All equal AspD vs. Biph 28.6045  7 0.0002
All equal Detm vs. Biph 88.5015  7 0.0000
All equal Detm vs. AspD 78.6358  7 0.0000
Visit 7 equal AspD vs. Biph 9.1546  1 0.0025
Visit 7 equal Detm vs. Biph 17.5428  1 0.0000
Visit 7 equal Detm vs. AspD 1.4731  1 0.2249
Change equal AspD vs. Biph 19.1875  1 0.0000
Change equal Detm vs. Biph 29.9532  1 0.0000
Change equal Detm vs. AspD 1.3679  1 0.2422
  Biph change=0      137.2637  1 0.0000
  AspD change=0      30.0723  1 0.0000
  Detm change=0      13.4377  1 0.0002

```

We now have the results from all 6 analyses analysis, but we only plot the estimated trajectories of the HbA_{1c} over the seven visits:

```

> plt <-
+ function()
+ {
+ matplot( 0:6*3, hbr$eff[1:7,],
+          xlab="Months since trial entry", xaxt="n", xlim=c(0,19.5),
+          ylim=c(7,9.5), yaxs="i", yaxt="n",
+          ylab=expression( "Hb"*A[1][c]*" (%) [Mean (95% CI)]" ),
+          type="n", lwd=c(4,1,1), lty=1, col=rep(iclr[1:3],each=3) )
+ abline( h=seq(7,9.5,0.2), col=gray(0.8) )
+ matlines( 0:6*3, hbr$eff[1:7,],
+          type="l", lwd=c(5,1,1), lty=1, col=rep(iclr[1:3],each=3) )
+ axis( side=1, at=0:6*3, col=clr[4] )
+ axis( side=2, at=7:9, col=clr[4] )
+ text( c(20,20,20), c(9.3,9.1,8.9), iN, col=iclr[1:3],

```

```

+ font=2, adj=1, cex=1 )
+ #text( 20, 8.9, substitute( "Equal change in Hb*A[1][c]*" 0-18 mth: P ="*pval,
+ # list(pval = formatC( hbr$test[3,3], format="f", digits=4 )) ),
+ # col=clr[4], adj=1 )
+ #text( 19.9, 8.7, "HbA1c change\n from baseline", col=clr[4], adj=c(1,0.5) )
+ #text( c(20,20), hbr$eff[7,c(1,4)],
+ # paste( formatC( hbr$eff[8,c(1,4)],
+ # format="f", digits=1 ), "%", sep="" ),
+ # col=clr[1:2], adj=1 )
+ }
> oldpar <- par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1, bty="n" )
> plt()

```

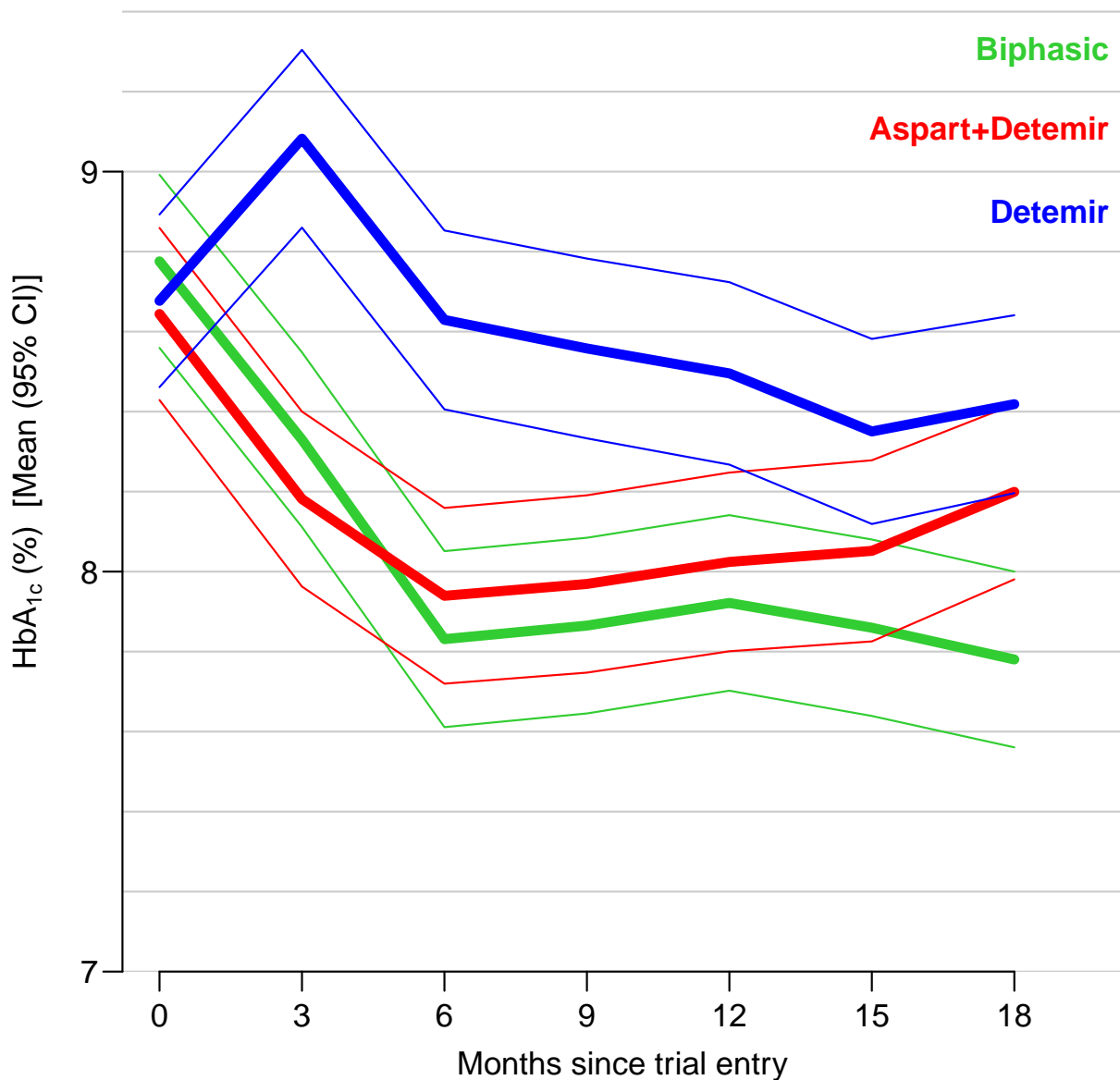


Figure 8.1: Fitted mean HbA_{1c} from a mixed model with 95% c.i.

8.2 A general lay-out of the analysis

The above analysis of HbA_{1c} can be groomed into a single function that does all analyses, shows the tables and ultimately give a result that can be used as input for a graph.

Some computer programs produce means corresponding to population means for a population with the same stratum composition as the study population. If we were to produce estimates (essentially just adding some fixed quantity, namely a suitably weighted sum of the stratum effects) corresponding to some population composition we would have to argue *a priori* exactly which population composition would be of interest. This would of course be totally arbitrary, so we have chosen the largest group of patients as reference group, that is we report the estimated means in a population of patients from Steno Diabetes Center, under 65 with previous insulin use — a particular, yet still totally arbitrary choice.

First the analysis function, that basically only takes the name of the variable as input. It should return a list of 3 arrays, one with mean estimates, one with standard deviation estimates and one with tests:

```
> var <- "hba1c"
> mod <- ITa
```

Then a function to generate a contrast matrix to *either* get the effects or the test statistics. This is called from `eFUN` and `tFUN`:

```
> CM <-
+ function( mod, eff )
+ {
+ # Contrast matrix to fish out the estimates, resp tests
+ cM <- cbind(1,rbind(0,diag(6)))
+ rownames( cM ) <- paste( "Vis", 1:7 )
+ # Find missing visits for the variable, make two versions of the matrix
+ tp <- sapply( strsplit(rownames(ci.exp(mod,subset=ilev[1])), "" ),
+             function(x) x[length(x)] )
+ tp[1] <- 1
+ tp <- as.numeric( tp )
+ # The contrast row should be between the last existing measurement and
+ # the first:
+ cM <- rbind( cM, cM[tp[length(tp)],]-cM[1,] )
+ # Are there any missing timepoints in this analysis?
+ mv <- setdiff(1:7,tp)
+ if( length(mv) > 0 )
+ {
+ # If used to extract effects keep rows for all timepoints, but
+ # return NAs for timepoints with no measurements:
+ cM[mv,] <- NA
+ cM <- if(eff) cM[,-mv] else cM[-mv,-mv]
+ }
+ cM
+ }
```

Then we need a function to get the mean value estimates from a model

```
> eFUN <-
+ function( mod )
+ {
+ eM <- CM( mod, eff=TRUE )
+ # Insert some NA-rows to get results in right dimension
+ c.1 <- ci.exp( mod, ctr.mat=eM, subset=ilev[1], Exp=F )
+ c.2 <- ci.exp( mod, ctr.mat=eM, subset=ilev[2], Exp=F )
+ c.3 <- ci.exp( mod, ctr.mat=eM, subset=ilev[3], Exp=F )
+ c.21 <- ci.exp( mod, ctr.mat=cbind(eM,-eM), subset=ilev[c(2,1)], Exp=F )
```

```
+ c.31 <- ci.exp( mod, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,1)], Exp=F )
+ c.32 <- ci.exp( mod, ctr.mat=cbind(eM,-eM), subset=ilev[c(3,2)], Exp=F )
+ aa <- abind( list( c.1, c.2, c.3, c.21, c.31, c.32 ), rev.along=0 )
+ dimnames( aa )[[3]] <- c( ilev, paste( ilev[c(2,3,3)], "-",
+                                     ilev[c(1,1,2)], sep="" ) )
+ aa
+ }
```

A function to get the between person and the residual sd from a model:

```
> sFUN <-
+ function( mod )
+ {
+   res <- c( attr( VarCorr( mod )$subjid, "stddev" ),
+            attr( VarCorr( mod ), "sc" ) )
+   names( res ) <- c("Btw","Res")
+   res
+ }
```

A function to compute the relevant tests from a fitted model

```
> tFUN <-
+ function( mod )
+ {
+   eX <- CM( mod, eff=FALSE )
+   np <- nrow( eX )
+   # Find the position of the last parameter
+   last1 <- grep( ilev[1], rownames(ci.exp(mod)) ) ; last1 <- last1[length(last1)]
+   last2 <- grep( ilev[2], rownames(ci.exp(mod)) ) ; last2 <- last2[length(last2)]
+   last3 <- grep( ilev[3], rownames(ci.exp(mod)) ) ; last3 <- last3[length(last3)]
+   test <- rbind( Wald( mod, subset=ilev[c(2,1)], ctr.mat=cbind(-eX,eX)[-np,] ),
+                 Wald( mod, subset=ilev[c(3,1)], ctr.mat=cbind(-eX,eX)[-np,] ),
+                 Wald( mod, subset=ilev[c(3,2)], ctr.mat=cbind(-eX,eX)[-np,] ),
+                 Wald( mod, subset=ilev[c(2,1)], ctr.mat=cbind(-eX,eX)[np-1,,drop=F] ),
+                 Wald( mod, subset=ilev[c(3,1)], ctr.mat=cbind(-eX,eX)[np-1,,drop=F] ),
+                 Wald( mod, subset=ilev[c(3,2)], ctr.mat=cbind(-eX,eX)[np-1,,drop=F] ),
+                 Wald( mod, subset=ilev[c(2,1)], ctr.mat=cbind(-eX,eX)[np,,drop=F] ),
+                 Wald( mod, subset=ilev[c(3,1)], ctr.mat=cbind(-eX,eX)[np,,drop=F] ),
+                 Wald( mod, subset=ilev[c(3,2)], ctr.mat=cbind(-eX,eX)[np,,drop=F] ),
+                 Wald( mod, subset=last1 ),
+                 Wald( mod, subset=last2 ),
+                 Wald( mod, subset=last3 ) )
+   rownames( test ) <- tnames
+   test
+ }
```

Then we can define the function to use, including a few useful arrays that will be filled out:

```
> # Names of variable to be used in repeated measures analyses
> vnam <- c("hba1c","weight","bmi","whr","gluc","ins","cpep",
+          "idos","ipkg","sys","dia","pulse",
+          "chol","ldl","hdl","vldl","trig",
+          "fimtavg","fimtmax","iem","csc2","imtareal","n.pl")
> match( vnam, names(AD) )
      [1] 11  8  9 10 12 13 16 14 15 22 23 24 17 18 19 20 21 143 145 158 157
     [22] 150 187
```

In the previous chapter we saw that the insulin variables and vldl, trig and the no. of plaques need a log transform:

```
> ltrf <- rep( FALSE, length(vnam) )
> ltrf[c(6:9,16,17,23)] <- TRUE
> vnam[ltrf]
```

```
[1] "ins" "cpep" "idos" "ipkg" "vldl" "trig" "n.pl"
```

Now we can set up arrays to hold the results from the analyses — for each variable we do 6 analyses in order to 1) make the confusion complete 2) be able to choose the results that fits our prejudices better 3) and make the p-values smaller.

First, we set up a couple of arrays to hold the results from the analyses:

```
> # Arrays to hold results over variables
> # Variance components
> Std <- NArray( list( var = paste( vnam, ifelse(ltrf,"(1)",""), sep="" ),
+                       ana = c("IT","PP"),
+                       mod = c("Prim","Rest","Conf"),
+                       std = c("Btw","Res") ) )
> # Estimates
> Eff <- NArray( c( dimnames(Std)[-4],
+                  list( par = c(paste("Vis",1:7),"V7-V1"),
+                            c("Est","lo","hi"),
+                            c( levels(AD$igr),
+                              paste( levels(AD$igr)[c(2,3,3)], "vs.",
+                                    levels(AD$igr)[c(1,1,2)] ) ) ) ) )
> # Tests
> Tst <- NArray( c( dimnames(Std)[-4],
+                  list( test = tnames,
+                        what = c("Chisq","df","Pval") ) ) )
> # Smaller versions of the arrys to be used inside the function that
> # does the calculations for each response variable
> std <- NArray( dimnames(Std)[-1] )
> eff <- NArray( dimnames(Eff)[-1] )
> tst <- NArray( dimnames(Tst)[-1] )
```

With these structures in place we can set up a function that fits the relevant models and extracts the results. The only argument is the name of the response variable, and an indicator of whether it should be log-transformed before analysis. We first define a log-function that returns NA instead of $-\text{Inf}$, since the variables we want to log-transform logically cannot have a 0 value.

```
> # Function to do PPplots for residuals
> PPplot <-
+ function( x, xl )
+ {
+   n <- length(x)
+   plot( pnorm( sort(x/sd(x)) ), (1:n-0.5)/n,
+         pch=16, cex=0.4,
+         xlim=0:1, ylim=0:1,
+         xlab="", ylab="",
+         xaxt="n", yaxt="n" )
+   text( 0, 1, xl, adj=c(0,1) )
+   abline( 0, 1 )
+ }
> # A function that returns NA instead of -Inf for 0 argument
> logI <- function(x) ifelse(x>0,log(x),NA)
> # Function that makes all analyses for one response variable
> ana.fun <-
+ function( var, log.tr=FALSE, respI=FALSE )
+ {
+   # We need a single name of the response variable
+   AD$Y <- if(log.tr) logI(AD[,var]) else AD[,var]
+   # Fit models to total and PP part of dataset:
+   # r: Reduced model
+   # a: Primary model
+   # c: Confounder-expanded model
+   ITr <- lmer( Y ~ igr + igr:factor(visit) - 1 + (1/subject), data = AD )
+   ITa <- lmer( Y ~ igr + igr:factor(visit) - 1 + sdc + over.65 + pre.ins
```



```

+                                     + (1|subjid), data = AD )
+ ITc <- lmer( Y ~ igr + igr:factor(visit) - 1 + sdc + over.65 + pre.ins
+                                     + sex + statin + gad.pos + cvd
+                                     + (1|subjid), data = AD )
+ PPa <- update( ITa, data = subset( AD, pp ) )
+ PPr <- update( ITr, data = subset( AD, pp ) )
+ PPc <- update( ITc, data = subset( AD, pp ) )
+
+ # Plots if specified - but only for ITa analysis - note the S4 way of
+ # extracting slots from the objects, does not work for medMod objects
+ if( respl )
+ {
+ PPplot( ranef(ITa), paste(var,if(log.tr)"(log-tr)","\\nptt") )
+ PPplot( resid(ITa), paste(var,if(log.tr)"(log-tr)","\\nres") )
+ }
+
+ # Fixed effects
+ eff["IT","Prim",,,] <- eFUN( ITa )
+ eff["IT","Rest",,,] <- eFUN( ITr )
+ eff["IT","Conf",,,] <- eFUN( ITc )
+ eff["PP","Prim",,,] <- eFUN( PPa )
+ eff["PP","Rest",,,] <- eFUN( PPr )
+ eff["PP","Conf",,,] <- eFUN( PPc )
+ if( log.tr ) eff <- exp( eff )
+ # Variance components
+ std["IT","Prim",,] <- sFUN( ITa )
+ std["IT","Rest",,] <- sFUN( ITr )
+ std["IT","Conf",,] <- sFUN( ITc )
+ std["PP","Prim",,] <- sFUN( PPa )
+ std["PP","Rest",,] <- sFUN( PPr )
+ std["PP","Conf",,] <- sFUN( PPc )
+ # Tests
+ tst["IT","Prim",,] <- tFUN( ITa )
+ tst["IT","Rest",,] <- tFUN( ITr )
+ tst["IT","Conf",,] <- tFUN( ITc )
+ tst["PP","Prim",,] <- tFUN( PPa )
+ tst["PP","Rest",,] <- tFUN( PPr )
+ tst["PP","Conf",,] <- tFUN( PPc )
+ # Return all in a list
+ invisible( list( eff=eff, std=std, tst=tst ) )
+ }

```

With this specification of models we can now fill in the arrays:

```

> # par( mfrow=c(8,6), mar=c(0,0,0,0), omi=c(3,3,1,1)/4 )
> for( i in 1:length(vnam) )
+ {
+   res <- ana.fun( vnam[i], ltrf[i], respl=FALSE )
+   cat( vnam[i], " done\n" )
+   flush.console()
+   Eff[i,,,,] <- res$eff
+   Std[i,,,] <- res$std
+   Tst[i,,,] <- res$tst
+   # mtext( expression(Phi-1*[sort(std. res.)]),
+   #       side=1, line=2, outer=TRUE )
+   # mtext( "Uniform[0,1]", side=2, line=2, outer=TRUE )
+ }

hba1c done
weight done
bmi done
whr done
gluc done
ins done
cpep done
idos done
ipkg done

```



```

sys done
dia done
pulse done
chol done
ldl done
hdl done
vldl done
trig done
fimtavg done
fimtmax done
iem done
csc2 done
imtareal done
n.pl done

```

Once this has been accomplished we can list the estimated parameters, the values for visit 1–7 are estimated means in a certain group:

Prim for the primary analysis it is the estimated means for the reference group which is patients from Steno, under 65 and with previous insulin use.

Rest restricted analysis, it is the estimated overall mean in each treatment group, assuming no differences between strata.

Conf conforunter controlled, here we have the estimated mean in the reference stratum, among GAD-negative females not on statins and with no heartfailure.

For the differences between the treatment groups, these are for all three models estimated under the assumption that the differences only depend on time (at visit).

The results for the intention to treat analysis is for all variables laid out in this table:

```

> dimnames( Eff )[[6]][4:6] <- c("Asp-Det", "Asp-Bip", "Det-Bip")
> round( ftable( Eff[, "IT", "Prim", , , 1:3 ], col.vars=4:3 ), 3 )

```

var	par	Biph			AspD			Detm		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
hba1c	Vis 1	8.776	8.559	8.992	8.644	8.429	8.859	8.677	8.461	8.893
	Vis 2	8.330	8.112	8.548	8.181	7.963	8.400	9.082	8.860	9.304
	Vis 3	7.831	7.611	8.051	7.939	7.720	8.159	8.629	8.406	8.853
	Vis 4	7.865	7.645	8.085	7.969	7.747	8.191	8.558	8.333	8.783
	Vis 5	7.922	7.702	8.141	8.024	7.801	8.248	8.495	8.267	8.724
	Vis 6	7.860	7.639	8.080	8.052	7.825	8.278	8.350	8.119	8.582
	Vis 7	7.780	7.561	8.000	8.199	7.981	8.418	8.419	8.196	8.641
	V7-V1	-0.995	-1.164	-0.826	-0.445	-0.613	-0.276	-0.258	-0.431	-0.086
weight	Vis 1	96.863	93.631	100.095	98.668	95.456	101.879	99.629	96.410	102.849
	Vis 2	98.323	95.088	101.557	100.233	97.019	103.448	99.031	95.804	102.259
	Vis 3	99.101	95.866	102.336	101.253	98.037	104.469	99.907	96.677	103.136
	Vis 4	99.506	96.272	102.741	101.933	98.714	105.153	100.814	97.584	104.045
	Vis 5	99.748	96.513	102.983	101.806	98.586	105.026	101.137	97.903	104.371
	Vis 6	99.978	96.742	103.214	101.964	98.741	105.186	101.715	98.479	104.951
	Vis 7	100.207	96.972	103.443	101.900	98.684	105.116	101.552	98.324	104.780
	V7-V1	3.344	2.699	3.990	3.233	2.587	3.878	1.923	1.260	2.586
bmi	Vis 1	32.045	31.125	32.965	32.416	31.502	33.330	32.568	31.651	33.484
	Vis 2	32.527	31.606	33.448	32.937	32.021	33.853	32.371	31.452	33.291
	Vis 3	32.776	31.854	33.697	33.280	32.364	34.196	32.655	31.735	33.576
	Vis 4	32.916	31.994	33.837	33.498	32.581	34.415	32.953	32.032	33.874
	Vis 5	32.990	32.068	33.911	33.466	32.549	34.384	33.058	32.136	33.980
	Vis 6	33.073	32.151	33.995	33.512	32.593	34.431	33.241	32.318	34.163
	Vis 7	33.122	32.201	34.044	33.434	32.518	34.351	33.164	32.244	34.084
	V7-V1	1.077	0.863	1.292	1.019	0.804	1.233	0.596	0.376	0.817
whr	Vis 1	1.001	0.985	1.017	1.006	0.989	1.022	1.009	0.993	1.025
	Vis 2	0.994	0.977	1.010	1.004	0.988	1.021	1.001	0.984	1.017

	Vis 3	0.996	0.979	1.012	1.009	0.993	1.026	1.003	0.987	1.020	
	Vis 4	0.996	0.979	1.012	1.007	0.991	1.023	1.000	0.983	1.016	
	Vis 5	0.999	0.983	1.015	1.011	0.995	1.028	1.005	0.988	1.022	
	Vis 6	0.996	0.979	1.012	1.009	0.992	1.026	1.005	0.988	1.022	
	Vis 7	0.997	0.981	1.014	1.014	0.998	1.030	1.020	1.003	1.037	
gluc	V7-V1	-0.003	-0.013	0.006	0.008	-0.001	0.018	0.011	0.001	0.021	
	Vis 1	10.664	10.111	11.217	9.857	9.305	10.408	10.366	9.814	10.918	
	Vis 2	9.133	8.560	9.706	8.574	7.996	9.151	8.475	7.886	9.063	
	Vis 3	8.720	8.137	9.302	8.557	7.967	9.147	8.123	7.527	8.720	
	Vis 4	8.149	7.573	8.726	8.645	8.048	9.242	7.926	7.324	8.528	
	Vis 5	8.988	8.414	9.562	8.615	8.016	9.213	7.545	6.933	8.156	
	Vis 6	8.758	8.177	9.338	8.323	7.709	8.937	7.791	7.158	8.424	
	Vis 7	8.657	8.089	9.226	8.560	7.993	9.127	7.926	7.346	8.506	
	V7-V1	-2.007	-2.624	-1.389	-1.297	-1.913	-0.680	-2.440	-3.068	-1.812	
	ins(l)	Vis 1	58.542	48.321	70.926	72.676	60.091	87.897	64.213	53.042	77.737
Vis 2		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Vis 3		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Vis 4		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Vis 5		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Vis 6		NA	NA	NA	NA	NA	NA	NA	NA	NA	
Vis 7		53.798	44.136	65.575	41.203	33.861	50.138	33.585	27.500	41.016	
V7-V1		0.919	0.775	1.090	0.567	0.480	0.670	0.523	0.440	0.621	
cpep(l)		Vis 1	529.985	445.819	630.040	634.449	534.261	753.426	615.653	517.997	731.719
		Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Vis 7	450.203	377.847	536.415	443.919	372.776	528.640	370.043	310.301	441.286	
	V7-V1	0.849	0.764	0.944	0.700	0.630	0.778	0.601	0.540	0.669	
	idos(l)	Vis 1	47.090	41.523	53.402	49.362	43.564	55.932	46.198	40.746	52.379
		Vis 2	80.883	71.269	91.794	101.684	89.632	115.358	112.734	99.197	128.119
Vis 3		89.433	78.788	101.516	110.767	97.568	125.751	136.333	119.878	155.046	
Vis 4		92.321	81.333	104.794	115.123	101.365	130.750	146.673	128.915	166.878	
Vis 5		93.342	82.224	105.963	116.933	102.901	132.878	153.170	134.486	174.449	
Vis 6		95.175	83.795	108.101	115.674	101.694	131.575	157.960	138.625	179.992	
Vis 7		NA	NA	NA	NA	NA	NA	NA	NA	NA	
V7-V1		2.021	1.874	2.180	2.343	2.166	2.535	3.419	3.153	3.708	
ipkg(l)		Vis 1	0.492	0.439	0.551	0.506	0.452	0.566	0.468	0.418	0.524
		Vis 2	0.832	0.743	0.933	1.025	0.915	1.149	1.151	1.025	1.292
	Vis 3	0.912	0.814	1.023	1.108	0.988	1.242	1.382	1.230	1.552	
	Vis 4	0.938	0.837	1.052	1.144	1.020	1.284	1.474	1.312	1.657	
	Vis 5	0.947	0.845	1.062	1.159	1.032	1.301	1.534	1.363	1.726	
	Vis 6	0.964	0.859	1.081	1.148	1.022	1.290	1.577	1.401	1.775	
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	V7-V1	1.959	1.820	2.108	2.269	2.103	2.449	3.368	3.113	3.645	
	sys	Vis 1	136.086	133.109	139.062	137.256	134.296	140.216	137.366	134.400	140.331
		Vis 2	132.814	129.805	135.823	133.870	130.858	136.883	133.459	130.384	136.534
Vis 3		133.307	130.284	136.329	132.829	129.801	135.857	133.109	130.008	136.209	
Vis 4		132.122	129.096	135.148	132.376	129.299	135.454	132.619	129.497	135.741	
Vis 5		132.627	129.605	135.649	130.565	127.464	133.666	130.996	127.813	134.178	
Vis 6		132.517	129.473	135.561	130.066	126.916	133.216	130.295	127.061	133.529	
Vis 7		129.420	126.382	132.457	131.287	128.186	134.388	133.822	130.637	137.006	
V7-V1		-6.666	-9.407	-3.926	-5.970	-8.783	-3.156	-3.544	-6.441	-0.647	
dia		Vis 1	83.220	81.515	84.926	83.492	81.797	85.188	82.815	81.116	84.514
		Vis 2	82.144	80.421	83.867	82.174	80.450	83.898	80.975	79.217	82.734
	Vis 3	81.413	79.683	83.143	81.377	79.645	83.110	81.491	79.719	83.263	
	Vis 4	81.549	79.817	83.281	81.607	79.848	83.365	81.126	79.343	82.909	
	Vis 5	80.913	79.183	82.643	80.765	78.994	82.536	80.124	78.308	81.939	
	Vis 6	81.884	80.143	83.625	80.558	78.761	82.355	79.747	77.904	81.589	
	Vis 7	79.889	78.151	81.627	80.586	78.815	82.357	79.315	77.499	81.131	
	V7-V1	-3.331	-4.834	-1.827	-2.907	-4.451	-1.363	-3.500	-5.091	-1.910	
	pulse	Vis 1	77.025	74.647	79.402	76.234	73.866	78.601	76.811	74.440	79.182
		Vis 2	76.328	73.928	78.727	75.891	73.497	78.285	74.361	71.930	76.792
Vis 3		75.499	73.092	77.906	75.202	72.791	77.613	73.908	71.465	76.352	
Vis 4		76.140	73.736	78.543	74.912	72.488	77.336	74.815	72.358	77.273	

	Vis 7	1992.023	1788.994	2195.052	1935.767	1732.873	2138.662	1902.175	1699.921	2104.429
	V7-V1	-68.835	-222.595	84.926	-101.565	-256.927	53.797	-154.692	-310.045	0.662
csc2	Vis 1	2.837	2.637	3.037	2.902	2.703	3.100	2.869	2.667	3.071
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.878	2.670	3.085	2.927	2.720	3.134	2.942	2.736	3.149
	V7-V1	0.040	-0.109	0.189	0.025	-0.126	0.175	0.073	-0.077	0.223
imtareal	Vis 1	17.441	16.482	18.400	18.156	17.204	19.108	18.362	17.399	19.325
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	17.582	16.609	18.556	18.147	17.177	19.116	18.094	17.121	19.066
	V7-V1	0.142	-0.297	0.580	-0.010	-0.454	0.435	-0.268	-0.713	0.176
n.pl(1)	Vis 1	2.262	1.893	2.702	2.041	1.691	2.464	2.422	2.010	2.918
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.709	2.266	3.238	2.380	1.969	2.876	2.713	2.249	3.273
	V7-V1	1.197	1.106	1.297	1.166	1.071	1.269	1.120	1.029	1.220
<p>> round(ftable(Eff[, "IT", "Prim", ,, 1:3+3], col.vars=4:3), 3)</p>										
		Asp-Det			Asp-Bip			Det-Bip		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
var	par									
hba1c	Vis 1	-0.132	-0.390	0.127	-0.099	-0.357	0.160	0.033	-0.225	0.291
	Vis 2	-0.149	-0.412	0.115	0.752	0.487	1.018	0.901	0.634	1.167
	Vis 3	0.108	-0.157	0.374	0.798	0.529	1.067	0.690	0.421	0.958
	Vis 4	0.104	-0.163	0.371	0.693	0.423	0.962	0.589	0.318	0.860
	Vis 5	0.103	-0.165	0.370	0.574	0.302	0.846	0.471	0.196	0.746
	Vis 6	0.192	-0.079	0.464	0.491	0.215	0.766	0.299	0.018	0.579
	Vis 7	0.419	0.155	0.684	0.638	0.371	0.906	0.219	-0.048	0.486
	V7-V1	0.551	0.312	0.790	0.737	0.495	0.979	0.186	-0.055	0.428
weight	Vis 1	1.805	-1.825	5.434	2.766	-0.870	6.403	0.962	-2.668	4.591
	Vis 2	1.911	-1.725	5.546	0.709	-2.937	4.354	-1.202	-4.841	2.437
	Vis 3	2.152	-1.485	5.789	0.806	-2.842	4.454	-1.346	-4.988	2.296
	Vis 4	2.427	-1.213	6.067	1.308	-2.341	4.957	-1.119	-4.765	2.527
	Vis 5	2.058	-1.583	5.699	1.389	-2.263	5.042	-0.669	-4.319	2.981
	Vis 6	1.985	-1.659	5.629	1.737	-1.918	5.392	-0.249	-3.902	3.405
	Vis 7	1.693	-1.945	5.331	1.345	-2.303	4.993	-0.348	-3.989	3.293
	V7-V1	-0.112	-1.024	0.801	-1.421	-2.347	-0.496	-1.310	-2.235	-0.384
bmi	Vis 1	0.371	-0.664	1.406	0.523	-0.514	1.560	0.152	-0.883	1.187
	Vis 2	0.410	-0.627	1.447	-0.155	-1.196	0.885	-0.566	-1.604	0.473
	Vis 3	0.504	-0.534	1.542	-0.120	-1.162	0.921	-0.625	-1.665	0.415
	Vis 4	0.582	-0.457	1.621	0.037	-1.004	1.079	-0.545	-1.586	0.496
	Vis 5	0.477	-0.563	1.516	0.068	-0.975	1.111	-0.408	-1.451	0.634
	Vis 6	0.439	-0.602	1.479	0.167	-0.877	1.212	-0.271	-1.316	0.773
	Vis 7	0.312	-0.726	1.350	0.042	-0.999	1.083	-0.270	-1.310	0.769
	V7-V1	-0.059	-0.362	0.244	-0.481	-0.788	-0.174	-0.422	-0.729	-0.115
whr	Vis 1	0.005	-0.014	0.023	0.008	-0.011	0.027	0.004	-0.015	0.023
	Vis 2	0.011	-0.008	0.030	0.007	-0.012	0.026	-0.004	-0.023	0.015
	Vis 3	0.014	-0.005	0.033	0.008	-0.012	0.027	-0.006	-0.025	0.013
	Vis 4	0.011	-0.008	0.031	0.004	-0.015	0.023	-0.007	-0.027	0.012
	Vis 5	0.012	-0.007	0.032	0.006	-0.013	0.026	-0.006	-0.026	0.014
	Vis 6	0.013	-0.006	0.033	0.010	-0.010	0.029	-0.004	-0.024	0.016
	Vis 7	0.016	-0.003	0.036	0.023	0.003	0.042	0.006	-0.013	0.025
	V7-V1	0.012	-0.002	0.026	0.014	0.000	0.028	0.002	-0.012	0.016
gluc	Vis 1	-0.807	-1.510	-0.104	-0.298	-1.001	0.406	0.509	-0.194	1.212
	Vis 2	-0.560	-1.301	0.182	-0.658	-1.408	0.091	-0.099	-0.852	0.654
	Vis 3	-0.163	-0.922	0.596	-0.597	-1.360	0.167	-0.434	-1.202	0.335
	Vis 4	0.495	-0.264	1.255	-0.223	-0.987	0.541	-0.718	-1.496	0.059

	Vis 7	-0.004	-0.231	0.223	0.011	-0.218	0.241	0.016	-0.213	0.244
	V7-V1	-0.120	-0.316	0.077	0.022	-0.177	0.221	0.142	-0.056	0.340
ldl	Vis 1	0.141	-0.050	0.333	0.039	-0.153	0.231	-0.102	-0.294	0.090
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.167	-0.032	0.366	0.089	-0.112	0.290	-0.078	-0.280	0.123
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	0.057	-0.143	0.258	0.079	-0.124	0.281	0.021	-0.182	0.225
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.047	-0.149	0.243	0.050	-0.149	0.248	0.003	-0.195	0.201
	V7-V1	-0.094	-0.259	0.071	0.011	-0.157	0.178	0.105	-0.062	0.272
hdl	Vis 1	-0.079	-0.160	0.003	-0.087	-0.168	-0.005	-0.008	-0.089	0.073
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	-0.099	-0.182	-0.016	-0.105	-0.189	-0.021	-0.006	-0.090	0.078
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	-0.105	-0.188	-0.021	-0.096	-0.180	-0.012	0.008	-0.076	0.093
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-0.120	-0.203	-0.038	-0.132	-0.216	-0.049	-0.012	-0.095	0.071
	V7-V1	-0.042	-0.093	0.010	-0.046	-0.098	0.006	-0.004	-0.056	0.047
vldl(l)	Vis 1	1.014	0.905	1.135	1.026	0.917	1.150	1.013	0.904	1.134
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.116	0.987	1.262	1.142	1.010	1.291	1.023	0.903	1.159
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.135	1.002	1.286	1.130	0.997	1.280	0.995	0.876	1.130
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.071	0.953	1.203	1.082	0.962	1.216	1.010	0.899	1.135
	V7-V1	1.057	0.956	1.168	1.054	0.952	1.166	0.997	0.901	1.103
trig(l)	Vis 1	1.053	0.930	1.191	1.040	0.919	1.177	0.988	0.873	1.118
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.137	1.000	1.294	1.086	0.954	1.236	0.955	0.839	1.087
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.089	0.957	1.238	1.076	0.945	1.225	0.988	0.867	1.127
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.083	0.955	1.229	1.092	0.961	1.241	1.008	0.888	1.145
	V7-V1	1.029	0.930	1.139	1.050	0.947	1.164	1.020	0.921	1.131
fimtavg	Vis 1	0.011	-0.020	0.042	0.014	-0.017	0.045	0.003	-0.028	0.034
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.020	-0.011	0.051	0.010	-0.021	0.042	-0.010	-0.041	0.022
	V7-V1	0.009	-0.009	0.027	-0.004	-0.022	0.014	-0.012	-0.031	0.006
fimtmax	Vis 1	0.006	-0.029	0.041	0.017	-0.018	0.053	0.011	-0.024	0.047
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.017	-0.019	0.053	0.011	-0.025	0.047	-0.006	-0.042	0.030
	V7-V1	0.011	-0.010	0.032	-0.006	-0.027	0.015	-0.017	-0.039	0.004
iem	Vis 1	-23.526	-249.448	202.397	-3.991	-231.981	223.998	19.534	-208.531	247.600
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-56.256	-296.642	184.131	-89.848	-329.124	149.427	-33.592	-272.968	205.783
	V7-V1	-32.730	-251.312	185.852	-85.857	-304.454	132.740	-53.127	-272.842	166.589
csc2	Vis 1	0.064	-0.166	0.295	0.032	-0.201	0.264	-0.033	-0.265	0.200
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.049	-0.195	0.293	0.065	-0.179	0.308	0.016	-0.228	0.259
	V7-V1	-0.015	-0.227	0.196	0.033	-0.179	0.244	0.048	-0.164	0.261

	Vis 7	54.688	46.186	64.756	41.804	35.405	49.360	34.268	28.888	40.651
	V7-V1	0.920	0.776	1.092	0.566	0.479	0.669	0.524	0.441	0.623
cpep(1)	Vis 1	610.995	527.532	707.663	728.729	629.519	843.575	709.238	612.025	821.892
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	518.490	446.232	602.449	509.869	439.063	592.095	427.012	366.984	496.859
	V7-V1	0.849	0.763	0.944	0.700	0.630	0.778	0.602	0.541	0.671
idos(1)	Vis 1	37.426	33.549	41.752	39.400	35.346	43.919	36.840	33.023	41.098
	Vis 2	64.290	57.571	71.792	81.186	72.724	90.632	89.841	80.320	100.490
	Vis 3	71.108	63.659	79.429	88.480	79.187	98.863	108.687	97.088	121.671
	Vis 4	73.405	65.715	81.994	91.929	82.239	102.761	116.960	104.429	130.995
	Vis 5	74.230	66.446	82.926	93.343	83.456	104.401	122.134	108.924	136.946
	Vis 6	75.696	67.716	84.616	92.351	82.482	103.401	125.947	112.267	141.294
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.023	1.875	2.182	2.344	2.166	2.536	3.419	3.153	3.707
ipkg(1)	Vis 1	0.396	0.359	0.438	0.409	0.370	0.451	0.378	0.342	0.418
	Vis 2	0.671	0.607	0.742	0.829	0.750	0.917	0.928	0.838	1.028
	Vis 3	0.736	0.665	0.814	0.897	0.810	0.992	1.115	1.005	1.236
	Vis 4	0.757	0.684	0.837	0.926	0.836	1.025	1.190	1.072	1.319
	Vis 5	0.764	0.691	0.845	0.937	0.846	1.038	1.238	1.114	1.375
	Vis 6	0.777	0.702	0.861	0.928	0.837	1.029	1.272	1.144	1.414
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.961	1.822	2.110	2.270	2.104	2.451	3.365	3.110	3.642
sys	Vis 1	138.528	135.937	141.120	139.687	137.105	142.269	139.806	137.221	142.392
	Vis 2	135.237	132.606	137.869	136.301	133.657	138.944	135.899	133.190	138.608
	Vis 3	135.713	133.059	138.366	135.261	132.602	137.921	135.543	132.801	138.284
	Vis 4	134.523	131.863	137.182	134.799	132.081	137.517	135.055	132.290	137.820
	Vis 5	135.035	132.382	137.688	132.999	130.258	135.740	133.436	130.605	136.267
	Vis 6	134.920	132.241	137.600	132.500	129.703	135.296	132.744	129.858	135.629
	Vis 7	131.817	129.144	134.490	133.697	130.949	136.445	136.241	133.403	139.080
	V7-V1	-6.711	-9.452	-3.970	-5.990	-8.804	-3.176	-3.565	-6.463	-0.667
dia	Vis 1	82.160	80.612	83.709	82.459	80.916	84.002	81.815	80.269	83.360
	Vis 2	81.046	79.477	82.616	81.116	79.541	82.691	79.975	78.364	81.586
	Vis 3	80.294	78.713	81.875	80.321	78.737	81.905	80.512	78.884	82.140
	Vis 4	80.430	78.846	82.014	80.548	78.934	82.161	80.152	78.512	81.792
	Vis 5	79.799	78.218	81.381	79.701	78.075	81.326	79.149	77.475	80.823
	Vis 6	80.783	79.189	82.378	79.486	77.832	81.140	78.776	77.074	80.478
	Vis 7	78.783	77.192	80.374	79.519	77.890	81.148	78.331	76.653	80.008
	V7-V1	-3.378	-4.883	-1.873	-2.940	-4.486	-1.394	-3.484	-5.078	-1.890
pulse	Vis 1	76.598	74.590	78.606	75.834	73.827	77.840	76.433	74.425	78.441
	Vis 2	75.885	73.848	77.921	75.484	73.446	77.522	73.985	71.907	76.062
	Vis 3	75.047	72.998	77.095	74.791	72.734	76.848	73.546	71.451	75.641
	Vis 4	75.683	73.638	77.728	74.498	72.424	76.571	74.454	72.343	76.565
	Vis 5	74.394	72.349	76.439	73.775	71.690	75.860	74.212	72.066	76.358
	Vis 6	73.930	71.875	75.985	73.224	71.102	75.346	74.651	72.487	76.816
	Vis 7	75.230	73.168	77.291	75.287	73.186	77.387	73.413	71.264	75.563
	V7-V1	-1.368	-3.074	0.337	-0.547	-2.310	1.216	-3.019	-4.831	-1.207
chol	Vis 1	4.126	3.968	4.284	4.246	4.088	4.403	4.121	3.963	4.279
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	4.216	4.052	4.380	4.388	4.223	4.553	4.266	4.098	4.433
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	4.284	4.121	4.447	4.261	4.094	4.427	4.287	4.117	4.457
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	4.294	4.132	4.457	4.294	4.133	4.455	4.314	4.149	4.479
	V7-V1	0.168	0.029	0.308	0.048	-0.090	0.186	0.193	0.051	0.335
ldl	Vis 1	2.104	1.967	2.241	2.246	2.110	2.383	2.148	2.011	2.285
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	2.196	2.054	2.337	2.365	2.223	2.507	2.291	2.146	2.435
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	2.189	2.047	2.331	2.247	2.104	2.391	2.273	2.126	2.419
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.258	2.118	2.398	2.306	2.167	2.446	2.314	2.171	2.456
	V7-V1	0.154	0.037	0.271	0.060	-0.056	0.177	0.166	0.046	0.285

		Vis 3	Vis 4	Vis 5	Vis 6	Vis 7	V7-V1													
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
		3.152	2.728	3.642	2.795	2.402	3.252	3.181	2.736	3.700										
		1.198	1.107	1.298	1.167	1.072	1.270	1.120	1.028	1.219										
<pre>> round(ftable(Eff[, "IT", "Rest", ,, 1:3+3], col.vars=4:3), 3)</pre>																				
		Asp-Det			Asp-Bip			Det-Bip												
	par	Est	lo	hi	Est	lo	hi	Est	lo	hi										
var	hba1c	Vis 1	-0.125	-0.387	0.138	-0.091	-0.353	0.172	0.034	-0.228	0.297									
		Vis 2	-0.140	-0.407	0.127	0.760	0.490	1.030	0.900	0.629	1.170									
		Vis 3	0.115	-0.154	0.385	0.806	0.533	1.079	0.691	0.418	0.963									
		Vis 4	0.111	-0.160	0.382	0.701	0.427	0.974	0.590	0.315	0.865									
		Vis 5	0.109	-0.163	0.381	0.581	0.305	0.857	0.472	0.193	0.751									
		Vis 6	0.199	-0.077	0.474	0.497	0.217	0.776	0.298	0.014	0.582									
		Vis 7	0.426	0.157	0.695	0.646	0.375	0.918	0.220	-0.051	0.491									
		V7-V1	0.551	0.312	0.790	0.737	0.495	0.978	0.186	-0.055	0.427									
	weight	Vis 1	1.882	-1.854	5.618	2.896	-0.847	6.638	1.014	-2.722	4.750									
		Vis 2	1.989	-1.752	5.731	0.841	-2.911	4.592	-1.149	-4.894	2.597									
		Vis 3	2.231	-1.512	5.974	0.941	-2.813	4.695	-1.290	-5.038	2.458									
		Vis 4	2.506	-1.240	6.251	1.443	-2.312	5.198	-1.062	-4.814	2.690									
		Vis 5	2.137	-1.610	5.884	1.524	-2.234	5.283	-0.612	-4.368	3.143									
		Vis 6	2.063	-1.687	5.813	1.871	-1.890	5.632	-0.192	-3.951	3.567									
		Vis 7	1.771	-1.973	5.515	1.480	-2.274	5.233	-0.291	-4.038	3.456									
		V7-V1	-0.111	-1.024	0.801	-1.416	-2.341	-0.491	-1.305	-2.230	-0.379									
	bmi	Vis 1	0.389	-0.667	1.445	0.554	-0.504	1.612	0.165	-0.891	1.221									
		Vis 2	0.428	-0.630	1.487	-0.124	-1.185	0.938	-0.552	-1.612	0.508									
		Vis 3	0.523	-0.536	1.582	-0.088	-1.150	0.975	-0.610	-1.671	0.450									
		Vis 4	0.601	-0.459	1.661	0.070	-0.992	1.133	-0.530	-1.593	0.532									
		Vis 5	0.495	-0.565	1.555	0.101	-0.963	1.165	-0.394	-1.458	0.670									
		Vis 6	0.457	-0.605	1.518	0.200	-0.865	1.265	-0.257	-1.322	0.808									
		Vis 7	0.330	-0.729	1.390	0.075	-0.988	1.137	-0.256	-1.316	0.805									
		V7-V1	-0.059	-0.362	0.244	-0.479	-0.786	-0.172	-0.420	-0.728	-0.113									
	whr	Vis 1	0.005	-0.014	0.024	0.009	-0.010	0.028	0.004	-0.015	0.023									
		Vis 2	0.011	-0.008	0.030	0.007	-0.012	0.027	-0.004	-0.023	0.016									
		Vis 3	0.014	-0.005	0.033	0.008	-0.011	0.028	-0.006	-0.025	0.014									
		Vis 4	0.012	-0.008	0.031	0.004	-0.015	0.024	-0.007	-0.027	0.012									
		Vis 5	0.013	-0.007	0.032	0.007	-0.013	0.026	-0.006	-0.026	0.014									
		Vis 6	0.014	-0.006	0.033	0.010	-0.010	0.030	-0.004	-0.024	0.016									
		Vis 7	0.017	-0.003	0.036	0.023	0.004	0.042	0.006	-0.013	0.026									
		V7-V1	0.012	-0.002	0.026	0.014	0.000	0.028	0.002	-0.012	0.016									
	gluc	Vis 1	-0.793	-1.506	-0.081	-0.278	-0.991	0.435	0.515	-0.197	1.228									
		Vis 2	-0.527	-1.278	0.224	-0.625	-1.383	0.134	-0.098	-0.860	0.665									
		Vis 3	-0.145	-0.913	0.623	-0.561	-1.333	0.211	-0.416	-1.194	0.362									
		Vis 4	0.523	-0.246	1.291	-0.184	-0.957	0.590	-0.706	-1.493	0.081									
		Vis 5	-0.357	-1.125	0.411	-1.414	-2.191	-0.636	-1.057	-1.852	-0.262									
		Vis 6	-0.415	-1.199	0.369	-0.938	-1.736	-0.139	-0.523	-1.344	0.299									
		Vis 7	-0.082	-0.820	0.656	-0.700	-1.448	0.048	-0.618	-1.365	0.129									
		V7-V1	0.711	-0.161	1.584	-0.422	-1.303	0.459	-1.133	-2.013	-0.253									
	ins(1)	Vis 1	1.243	0.991	1.559	1.100	0.876	1.380	0.885	0.706	1.110									
		Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 7	0.764	0.603	0.969	0.627	0.493	0.797	0.820	0.646	1.040									
		V7-V1	0.615	0.484	0.781	0.570	0.447	0.726	0.926	0.729	1.178									
	cpep(1)	Vis 1	1.193	0.969	1.467	1.161	0.943	1.429	0.973	0.791	1.198									
		Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA									
		Vis 7	0.983	0.796	1.215	0.824	0.665	1.019	0.837	0.677	1.036									
		V7-V1	0.824	0.710	0.958	0.709	0.610	0.825	0.861	0.740	1.001									

	Vis 3	1.118	0.987	1.266	1.148	1.014	1.300	1.027	0.905	1.165
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.137	1.002	1.289	1.135	1.000	1.288	0.999	0.878	1.136
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.071	0.952	1.205	1.086	0.964	1.223	1.014	0.901	1.141
	V7-V1	1.056	0.956	1.168	1.055	0.953	1.167	0.998	0.902	1.105
trig(l)	Vis 1	1.054	0.930	1.195	1.043	0.920	1.182	0.989	0.873	1.121
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.140	1.001	1.298	1.092	0.958	1.245	0.958	0.840	1.093
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.090	0.957	1.242	1.080	0.947	1.232	0.991	0.868	1.132
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.084	0.954	1.232	1.097	0.964	1.248	1.011	0.889	1.150
	V7-V1	1.029	0.929	1.139	1.052	0.949	1.166	1.022	0.923	1.133
fimtavg	Vis 1	0.010	-0.022	0.043	0.012	-0.020	0.045	0.002	-0.030	0.034
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.019	-0.013	0.052	0.009	-0.024	0.042	-0.010	-0.043	0.022
	V7-V1	0.009	-0.009	0.027	-0.004	-0.022	0.015	-0.013	-0.031	0.006
fimtmax	Vis 1	0.005	-0.032	0.042	0.016	-0.021	0.053	0.011	-0.026	0.048
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.017	-0.021	0.054	0.010	-0.027	0.047	-0.007	-0.044	0.031
	V7-V1	0.011	-0.010	0.033	-0.006	-0.027	0.015	-0.018	-0.039	0.004
iem	Vis 1	-44.854	-286.148	196.439	-17.641	-261.046	225.764	27.214	-216.268	270.695
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-71.550	-326.848	183.747	-112.875	-367.098	141.348	-41.325	-295.753	213.104
	V7-V1	-26.696	-246.059	192.668	-95.234	-314.578	124.110	-68.538	-289.079	152.002
csc2	Vis 1	0.085	-0.161	0.332	0.046	-0.203	0.294	-0.040	-0.288	0.209
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.067	-0.193	0.326	0.088	-0.171	0.347	0.021	-0.238	0.280
	V7-V1	-0.018	-0.230	0.193	0.042	-0.170	0.254	0.061	-0.152	0.274
imtareal	Vis 1	0.636	-0.496	1.768	0.860	-0.279	1.998	0.224	-0.914	1.361
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.493	-0.666	1.652	0.444	-0.715	1.603	-0.049	-1.208	1.109
	V7-V1	-0.143	-0.767	0.481	-0.416	-1.040	0.208	-0.273	-0.901	0.356
n.pl(l)	Vis 1	0.911	0.739	1.122	1.080	0.878	1.329	1.186	0.960	1.466
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.887	0.719	1.093	1.009	0.819	1.244	1.138	0.919	1.410
	V7-V1	0.974	0.867	1.093	0.934	0.832	1.049	0.959	0.851	1.081

> round(ftable(Eff[, "IT", "Conf", , , 1:3], col.vars=4:3), 3)

var	par	Biph Est	lo	hi	AspD Est	lo	hi	Detm Est	lo	hi
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hba1c	Vis 1	8.917	8.588	9.246	8.785	8.456	9.114	8.823	8.488	9.158
	Vis 2	8.472	8.141	8.802	8.322	7.991	8.653	9.229	8.889	9.569
	Vis 3	7.973	7.641	8.305	8.080	7.748	8.412	8.776	8.435	9.116
	Vis 4	8.007	7.675	8.339	8.110	7.777	8.443	8.705	8.363	9.046
	Vis 5	8.064	7.732	8.395	8.165	7.830	8.500	8.642	8.298	8.986
	Vis 6	8.002	7.669	8.334	8.193	7.856	8.529	8.497	8.151	8.843
	Vis 7	7.922	7.590	8.254	8.340	8.009	8.672	8.565	8.225	8.905
	V7-V1	-0.995	-1.164	-0.825	-0.445	-0.613	-0.276	-0.258	-0.431	-0.085
weight	Vis 1	88.238	83.246	93.231	89.607	84.611	94.603	90.594	85.498	95.689
	Vis 2	89.695	84.700	94.690	91.173	86.176	96.171	89.991	84.890	95.092
	Vis 3	90.473	85.477	95.468	92.190	87.192	97.189	90.866	85.764	95.969
	Vis 4	90.878	85.883	95.874	92.872	87.872	97.873	91.773	86.669	96.876
	Vis 5	91.119	86.124	96.115	92.744	87.743	97.746	92.097	86.991	97.202
	Vis 6	91.350	86.353	96.346	92.901	87.898	97.904	92.674	87.567	97.781
	Vis 7	91.579	86.583	96.575	92.839	87.840	97.838	92.512	87.410	97.614
	V7-V1	3.340	2.695	3.986	3.232	2.586	3.877	1.918	1.255	2.581
bmi	Vis 1	32.293	30.821	33.766	32.743	31.269	34.216	32.853	31.350	34.356
	Vis 2	32.776	31.302	34.249	33.264	31.789	34.738	32.656	31.151	34.161
	Vis 3	33.025	31.551	34.499	33.607	32.132	35.082	32.940	31.435	34.446
	Vis 4	33.165	31.691	34.638	33.825	32.350	35.300	33.238	31.732	34.744
	Vis 5	33.239	31.765	34.713	33.793	32.318	35.269	33.342	31.835	34.849
	Vis 6	33.322	31.848	34.796	33.839	32.363	35.315	33.525	32.018	35.032
	Vis 7	33.371	31.897	34.845	33.761	32.286	35.236	33.449	31.943	34.954
	V7-V1	1.078	0.864	1.292	1.019	0.804	1.233	0.596	0.376	0.816
whr	Vis 1	0.948	0.927	0.969	0.950	0.928	0.971	0.953	0.932	0.975
	Vis 2	0.940	0.919	0.962	0.949	0.927	0.970	0.945	0.923	0.967
	Vis 3	0.942	0.921	0.964	0.953	0.932	0.975	0.947	0.926	0.969
	Vis 4	0.942	0.921	0.964	0.951	0.930	0.973	0.944	0.922	0.966
	Vis 5	0.946	0.924	0.967	0.955	0.934	0.977	0.949	0.927	0.972
	Vis 6	0.942	0.921	0.964	0.953	0.931	0.975	0.950	0.927	0.972
	Vis 7	0.944	0.923	0.966	0.958	0.937	0.979	0.964	0.942	0.986
	V7-V1	-0.004	-0.013	0.006	0.008	-0.001	0.018	0.011	0.001	0.021
gluc	Vis 1	11.087	10.330	11.845	10.287	9.529	11.044	10.805	10.036	11.574
	Vis 2	9.560	8.783	10.336	9.004	8.227	9.781	8.918	8.120	9.716
	Vis 3	9.143	8.361	9.926	8.986	8.200	9.772	8.568	7.763	9.373
	Vis 4	8.576	7.796	9.355	9.071	8.281	9.862	8.370	7.561	9.179
	Vis 5	9.416	8.638	10.194	9.041	8.249	9.834	7.986	7.168	8.804
	Vis 6	9.185	8.404	9.967	8.756	7.950	9.562	8.233	7.399	9.066
	Vis 7	9.084	8.310	9.858	8.992	8.221	9.762	8.372	7.579	9.165
	V7-V1	-2.003	-2.621	-1.386	-1.295	-1.912	-0.679	-2.433	-3.061	-1.805
ins(l)	Vis 1	64.286	47.785	86.487	80.062	59.513	107.706	70.705	52.197	95.774
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	59.039	43.634	79.882	45.437	33.644	61.364	36.914	27.071	50.334
	V7-V1	0.918	0.774	1.089	0.568	0.480	0.671	0.522	0.440	0.620
cpep(l)	Vis 1	667.027	510.175	872.105	800.894	612.434	1047.347	780.662	593.168	1027.421
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	568.525	433.829	745.042	560.649	427.932	734.526	469.679	355.892	619.847
	V7-V1	0.852	0.767	0.948	0.700	0.630	0.778	0.602	0.540	0.670
idos(l)	Vis 1	41.179	33.814	50.150	43.018	35.337	52.370	40.074	32.767	49.010
	Vis 2	70.713	58.020	86.183	88.653	72.761	108.017	97.822	79.874	119.803
	Vis 3	78.176	64.133	95.292	96.573	79.233	117.709	118.303	96.551	144.954
	Vis 4	80.700	66.205	98.370	100.367	82.326	122.362	127.272	103.836	155.997
	Vis 5	81.591	66.931	99.462	101.930	83.569	124.326	132.927	108.376	163.039
	Vis 6	83.199	68.224	101.461	100.830	82.615	123.062	137.057	111.705	168.164
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.020	1.873	2.180	2.344	2.166	2.536	3.420	3.154	3.709
ipkg(l)	Vis 1	0.470	0.394	0.562	0.484	0.405	0.578	0.446	0.372	0.535
	Vis 2	0.796	0.666	0.951	0.981	0.821	1.172	1.098	0.914	1.318

	Vis 5	1.746	1.482	2.057	1.911	1.620	2.254	1.884	1.591	2.231
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.730	1.468	2.038	1.882	1.599	2.217	1.893	1.601	2.238
	V7-V1	0.976	0.908	1.049	1.002	0.933	1.076	1.023	0.951	1.102
fimtavg	Vis 1	0.716	0.672	0.760	0.727	0.683	0.771	0.728	0.683	0.773
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.707	0.663	0.751	0.727	0.683	0.771	0.716	0.671	0.761
	V7-V1	-0.009	-0.022	0.004	0.000	-0.013	0.013	-0.013	-0.026	0.000
fimtmax	Vis 1	0.865	0.815	0.915	0.871	0.821	0.921	0.880	0.829	0.931
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.855	0.805	0.905	0.872	0.822	0.922	0.864	0.813	0.915
	V7-V1	-0.010	-0.025	0.005	0.001	-0.014	0.016	-0.016	-0.031	-0.001
iem	Vis 1	2014.330	1710.327	2318.334	1982.322	1680.162	2284.481	2007.021	1695.961	2318.081
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1945.748	1635.151	2256.345	1884.895	1577.985	2191.806	1851.932	1536.390	2167.474
	V7-V1	-68.583	-222.237	85.072	-97.426	-252.684	57.831	-155.089	-310.361	0.184
csc2	Vis 1	2.925	2.615	3.234	2.999	2.691	3.306	2.962	2.645	3.278
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.965	2.649	3.280	3.018	2.706	3.330	3.034	2.714	3.355
	V7-V1	0.040	-0.109	0.188	0.020	-0.131	0.170	0.072	-0.078	0.222
imtareal	Vis 1	15.037	13.572	16.503	15.723	14.268	17.179	15.871	14.376	17.366
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	15.177	13.699	16.655	15.725	14.260	17.190	15.597	14.093	17.101
	V7-V1	0.140	-0.298	0.578	0.001	-0.443	0.446	-0.274	-0.718	0.170
n.pl(1)	Vis 1	1.537	1.142	2.069	1.364	0.997	1.864	1.619	1.198	2.189
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.845	1.371	2.483	1.595	1.166	2.181	1.815	1.341	2.455
	V7-V1	1.200	1.109	1.300	1.170	1.075	1.273	1.121	1.030	1.220

> round(ftable(Eff[, "IT", "Conf", , , 1:3+3], col.vars=4:3), 3)

		Asp-Det			Asp-Bip			Det-Bip		
	par	Est	lo	hi	Est	lo	hi	Est	lo	hi
var										
hba1c	Vis 1	-0.132	-0.391	0.127	-0.094	-0.353	0.166	0.038	-0.221	0.298
	Vis 2	-0.150	-0.414	0.114	0.757	0.491	1.024	0.907	0.640	1.174
	Vis 3	0.107	-0.159	0.374	0.803	0.533	1.072	0.696	0.426	0.965
	Vis 4	0.103	-0.165	0.371	0.698	0.428	0.968	0.595	0.323	0.867
	Vis 5	0.101	-0.167	0.370	0.579	0.306	0.851	0.477	0.201	0.753
	Vis 6	0.191	-0.081	0.464	0.496	0.220	0.772	0.304	0.023	0.585
	Vis 7	0.418	0.153	0.683	0.643	0.375	0.911	0.225	-0.043	0.493
	V7-V1	0.550	0.311	0.789	0.737	0.495	0.978	0.187	-0.055	0.428
weight	Vis 1	1.369	-2.089	4.826	2.355	-1.106	5.817	0.987	-2.472	4.446
	Vis 2	1.478	-1.986	4.942	0.296	-3.175	3.767	-1.182	-4.652	2.287

	Vis 3	1.718	-1.748	5.184	0.394	-3.080	3.867	-1.324	-4.796	2.148
	Vis 4	1.994	-1.475	5.463	0.895	-2.580	4.369	-1.099	-4.576	2.377
	Vis 5	1.625	-1.845	5.094	0.977	-2.501	4.455	-0.647	-4.127	2.833
	Vis 6	1.551	-1.922	5.024	1.324	-2.157	4.805	-0.227	-3.710	3.257
	Vis 7	1.260	-2.207	4.726	0.933	-2.540	4.406	-0.326	-3.797	3.145
	V7-V1	-0.109	-1.021	0.804	-1.422	-2.347	-0.497	-1.313	-2.238	-0.388
bmi	Vis 1	0.449	-0.573	1.472	0.559	-0.464	1.583	0.110	-0.913	1.133
	Vis 2	0.488	-0.537	1.513	-0.120	-1.147	0.908	-0.607	-1.634	0.419
	Vis 3	0.582	-0.443	1.608	-0.085	-1.113	0.943	-0.667	-1.695	0.361
	Vis 4	0.660	-0.366	1.687	0.073	-0.955	1.102	-0.587	-1.616	0.442
	Vis 5	0.555	-0.472	1.582	0.104	-0.926	1.133	-0.451	-1.482	0.580
	Vis 6	0.517	-0.511	1.545	0.203	-0.828	1.234	-0.314	-1.346	0.718
	Vis 7	0.390	-0.636	1.416	0.078	-0.950	1.106	-0.313	-1.340	0.715
	V7-V1	-0.059	-0.362	0.244	-0.482	-0.789	-0.175	-0.423	-0.730	-0.115
whr	Vis 1	0.002	-0.015	0.018	0.005	-0.011	0.022	0.004	-0.013	0.020
	Vis 2	0.008	-0.008	0.025	0.004	-0.012	0.021	-0.004	-0.021	0.013
	Vis 3	0.011	-0.006	0.028	0.005	-0.012	0.022	-0.006	-0.023	0.011
	Vis 4	0.009	-0.008	0.025	0.001	-0.015	0.018	-0.007	-0.024	0.010
	Vis 5	0.010	-0.007	0.026	0.004	-0.013	0.021	-0.006	-0.023	0.011
	Vis 6	0.011	-0.006	0.028	0.007	-0.010	0.024	-0.003	-0.021	0.014
	Vis 7	0.014	-0.003	0.030	0.020	0.003	0.037	0.006	-0.011	0.023
	V7-V1	0.012	-0.002	0.026	0.014	0.000	0.029	0.003	-0.011	0.016
gluc	Vis 1	-0.801	-1.504	-0.098	-0.282	-0.985	0.421	0.518	-0.185	1.221
	Vis 2	-0.556	-1.297	0.186	-0.641	-1.390	0.108	-0.086	-0.839	0.667
	Vis 3	-0.157	-0.916	0.602	-0.575	-1.338	0.188	-0.418	-1.187	0.351
	Vis 4	0.495	-0.264	1.255	-0.206	-0.970	0.557	-0.701	-1.479	0.077
	Vis 5	-0.375	-1.133	0.384	-1.430	-2.197	-0.662	-1.055	-1.841	-0.269
	Vis 6	-0.429	-1.204	0.346	-0.953	-1.742	-0.164	-0.524	-1.336	0.289
	Vis 7	-0.092	-0.821	0.636	-0.712	-1.450	0.026	-0.620	-1.357	0.118
	V7-V1	0.708	-0.164	1.581	-0.429	-1.310	0.451	-1.138	-2.018	-0.258
ins(1)	Vis 1	1.245	0.996	1.558	1.100	0.879	1.377	0.883	0.706	1.105
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.770	0.609	0.973	0.625	0.493	0.793	0.812	0.642	1.029
	V7-V1	0.618	0.487	0.785	0.568	0.446	0.724	0.920	0.724	1.169
cpep(1)	Vis 1	1.201	0.990	1.456	1.170	0.965	1.420	0.975	0.804	1.182
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.986	0.810	1.201	0.826	0.677	1.008	0.838	0.687	1.022
	V7-V1	0.821	0.707	0.954	0.706	0.607	0.821	0.859	0.739	0.999
idos(1)	Vis 1	1.045	0.903	1.208	0.973	0.841	1.126	0.932	0.805	1.078
	Vis 2	1.254	1.082	1.453	1.383	1.192	1.605	1.103	0.951	1.280
	Vis 3	1.235	1.065	1.433	1.513	1.303	1.757	1.225	1.054	1.423
	Vis 4	1.244	1.072	1.443	1.577	1.358	1.832	1.268	1.091	1.474
	Vis 5	1.249	1.076	1.450	1.629	1.401	1.894	1.304	1.120	1.518
	Vis 6	1.212	1.043	1.409	1.647	1.416	1.917	1.359	1.166	1.584
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.160	1.040	1.294	1.693	1.515	1.891	1.459	1.303	1.634
ipkg(1)	Vis 1	1.029	0.901	1.175	0.949	0.831	1.084	0.922	0.808	1.053
	Vis 2	1.233	1.078	1.411	1.380	1.204	1.580	1.119	0.977	1.281
	Vis 3	1.216	1.062	1.392	1.511	1.318	1.732	1.243	1.084	1.425
	Vis 4	1.221	1.066	1.399	1.567	1.367	1.798	1.284	1.118	1.474
	Vis 5	1.225	1.069	1.404	1.616	1.408	1.855	1.319	1.148	1.516
	Vis 6	1.193	1.040	1.368	1.632	1.421	1.876	1.369	1.189	1.575
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.159	1.043	1.288	1.721	1.545	1.916	1.485	1.330	1.657
sys	Vis 1	1.057	-2.583	4.698	1.189	-2.452	4.830	0.132	-3.505	3.769
	Vis 2	0.961	-2.753	4.674	0.546	-3.211	4.303	-0.415	-4.183	3.353
	Vis 3	-0.583	-4.323	3.157	-0.289	-4.085	3.507	0.294	-3.509	4.096
	Vis 4	0.156	-3.630	3.942	0.403	-3.414	4.221	0.247	-3.614	4.108

	Vis 7	0.020	-0.012	0.051	0.008	-0.023	0.040	-0.011	-0.043	0.020
	V7-V1	0.009	-0.009	0.027	-0.004	-0.022	0.014	-0.013	-0.031	0.006
fimtmax	Vis 1	0.006	-0.029	0.041	0.015	-0.020	0.051	0.009	-0.026	0.045
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.017	-0.018	0.053	0.009	-0.027	0.045	-0.008	-0.044	0.028
	V7-V1	0.011	-0.010	0.032	-0.006	-0.027	0.015	-0.017	-0.039	0.004
iem	Vis 1	-32.009	-256.844	192.827	-7.309	-233.874	219.255	24.699	-202.334	251.733
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-60.852	-300.084	178.380	-93.815	-331.691	144.061	-32.963	-271.333	205.407
	V7-V1	-28.844	-247.290	189.603	-86.506	-304.937	131.925	-57.662	-277.271	161.946
csc2	Vis 1	0.074	-0.153	0.301	0.037	-0.192	0.266	-0.037	-0.266	0.192
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.054	-0.187	0.295	0.070	-0.170	0.309	0.016	-0.224	0.256
	V7-V1	-0.020	-0.232	0.191	0.032	-0.179	0.244	0.053	-0.160	0.265
imtareal	Vis 1	0.686	-0.349	1.721	0.834	-0.206	1.873	0.148	-0.893	1.188
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.548	-0.516	1.612	0.420	-0.643	1.482	-0.128	-1.191	0.935
	V7-V1	-0.138	-0.762	0.486	-0.414	-1.038	0.210	-0.275	-0.903	0.353
n.pl(1)	Vis 1	0.887	0.725	1.086	1.053	0.862	1.287	1.187	0.968	1.457
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.865	0.706	1.059	0.984	0.804	1.204	1.138	0.925	1.399
	V7-V1	0.974	0.868	1.094	0.934	0.831	1.049	0.958	0.850	1.080

> round(ftable(Eff[, "PP", "Prim", , , 1:3], col.vars=4:3), 3)

		Biph			AspD			Detm		
		Est	lo	hi	Est	lo	hi	Est	lo	hi
var	par									
hba1c	Vis 1	8.808	8.586	9.030	8.693	8.470	8.916	8.710	8.480	8.939
	Vis 2	8.323	8.101	8.545	8.201	7.978	8.424	9.048	8.818	9.277
	Vis 3	7.844	7.622	8.067	7.966	7.742	8.190	8.621	8.391	8.851
	Vis 4	7.878	7.656	8.101	7.995	7.770	8.221	8.550	8.319	8.781
	Vis 5	7.935	7.713	8.157	8.051	7.823	8.278	8.488	8.253	8.722
	Vis 6	7.873	7.649	8.097	8.079	7.848	8.309	8.343	8.105	8.580
	Vis 7	7.792	7.569	8.015	8.216	7.992	8.440	8.379	8.149	8.609
	V7-V1	-1.015	-1.185	-0.846	-0.477	-0.648	-0.307	-0.331	-0.508	-0.154
weight	Vis 1	97.357	94.015	100.699	98.477	95.122	101.832	99.012	95.566	102.458
	Vis 2	98.868	95.526	102.210	100.093	96.738	103.449	98.491	95.045	101.937
	Vis 3	99.627	96.285	102.968	101.104	97.749	104.460	99.366	95.920	102.813
	Vis 4	100.032	96.690	103.374	101.785	98.427	105.144	100.274	96.826	103.722
	Vis 5	100.274	96.931	103.616	101.658	98.299	105.018	100.597	97.146	104.049
	Vis 6	100.504	97.161	103.847	101.815	98.454	105.177	101.175	97.722	104.628
	Vis 7	100.761	97.418	104.104	101.781	98.425	105.138	101.074	97.627	104.520
	V7-V1	3.404	2.756	4.053	3.304	2.653	3.956	2.061	1.388	2.735
bmi	Vis 1	32.204	31.251	33.158	32.434	31.477	33.391	32.452	31.469	33.435
	Vis 2	32.706	31.752	33.659	32.971	32.014	33.928	32.280	31.297	33.263
	Vis 3	32.948	31.995	33.901	33.312	32.354	34.269	32.565	31.581	33.548
	Vis 4	33.088	32.135	34.041	33.530	32.571	34.488	32.862	31.879	33.846

	Vis 5	33.162	32.208	34.115	33.498	32.539	34.457	32.967	31.982	33.952
	Vis 6	33.245	32.292	34.199	33.544	32.584	34.503	33.150	32.164	34.136
	Vis 7	33.305	32.351	34.259	33.476	32.518	34.433	33.094	32.110	34.077
whr	V7-V1	1.101	0.885	1.316	1.041	0.825	1.257	0.642	0.418	0.865
	Vis 1	1.001	0.984	1.018	1.004	0.988	1.021	1.013	0.995	1.030
	Vis 2	0.994	0.978	1.011	1.003	0.987	1.020	1.004	0.987	1.022
	Vis 3	0.996	0.979	1.012	1.008	0.992	1.025	1.007	0.989	1.024
	Vis 4	0.996	0.979	1.013	1.006	0.989	1.023	1.003	0.986	1.020
	Vis 5	0.999	0.983	1.016	1.010	0.993	1.027	1.009	0.991	1.026
	Vis 6	0.996	0.979	1.013	1.008	0.991	1.025	1.009	0.991	1.026
gluc	Vis 7	0.998	0.981	1.014	1.013	0.996	1.030	1.024	1.007	1.041
	V7-V1	-0.003	-0.013	0.007	0.009	-0.001	0.019	0.011	0.001	0.022
	Vis 1	10.760	10.199	11.320	9.933	9.369	10.497	10.607	10.025	11.190
	Vis 2	9.193	8.622	9.764	8.565	7.989	9.142	8.300	7.708	8.891
	Vis 3	8.774	8.195	9.352	8.573	7.985	9.160	8.124	7.530	8.718
	Vis 4	8.203	7.630	8.776	8.660	8.066	9.254	7.928	7.328	8.528
	Vis 5	9.042	8.472	9.612	8.631	8.035	9.226	7.547	6.938	8.157
ins(l)	Vis 6	8.811	8.235	9.388	8.340	7.730	8.950	7.795	7.164	8.425
	Vis 7	8.728	8.162	9.294	8.493	7.924	9.063	7.773	7.187	8.358
	V7-V1	-2.032	-2.649	-1.414	-1.440	-2.061	-0.819	-2.835	-3.478	-2.191
	Vis 1	57.923	47.548	70.563	73.917	60.669	90.058	63.247	51.612	77.506
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
cpep(l)	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	53.609	43.839	65.555	40.951	33.483	50.085	32.623	26.538	40.102
	V7-V1	0.926	0.779	1.100	0.554	0.467	0.657	0.516	0.432	0.616
	Vis 1	538.294	452.416	640.474	639.840	537.391	761.820	641.062	535.774	767.040
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
idos(l)	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	458.522	384.930	546.183	444.524	372.740	530.134	381.163	318.431	456.254
	V7-V1	0.852	0.766	0.948	0.695	0.624	0.773	0.595	0.533	0.664
	Vis 1	46.678	41.002	53.139	49.309	43.291	56.163	44.467	38.893	50.840
	Vis 2	80.586	70.787	91.741	101.131	88.788	115.189	109.185	95.474	124.866
ipkg(l)	Vis 3	88.834	78.025	101.140	110.318	96.798	125.725	132.084	115.480	151.076
	Vis 4	91.703	80.545	104.406	114.652	100.561	130.717	142.107	124.191	162.607
	Vis 5	92.718	81.429	105.572	116.450	102.084	132.839	148.401	129.562	169.979
	Vis 6	94.538	82.985	107.700	115.202	100.894	131.540	153.044	133.554	175.378
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	2.025	1.877	2.186	2.336	2.158	2.529	3.442	3.171	3.735
	Vis 1	0.485	0.432	0.545	0.506	0.450	0.569	0.455	0.403	0.513
sys	Vis 2	0.826	0.735	0.928	1.020	0.908	1.147	1.122	0.995	1.266
	Vis 3	0.903	0.803	1.014	1.104	0.982	1.242	1.348	1.195	1.521
	Vis 4	0.928	0.826	1.043	1.141	1.013	1.284	1.438	1.274	1.624
	Vis 5	0.937	0.834	1.053	1.155	1.026	1.300	1.497	1.324	1.692
	Vis 6	0.953	0.848	1.072	1.144	1.015	1.289	1.538	1.360	1.740
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.965	1.825	2.115	2.260	2.093	2.440	3.385	3.125	3.666
dia	Vis 1	136.532	133.514	139.551	137.349	134.319	140.380	137.022	133.898	140.146
	Vis 2	133.131	130.115	136.146	133.739	130.708	136.771	132.836	129.718	135.953
	Vis 3	133.635	130.615	136.654	132.905	129.870	135.940	132.890	129.765	136.016
	Vis 4	132.448	129.425	135.471	132.453	129.370	135.537	132.400	129.254	135.546
	Vis 5	132.954	129.936	135.973	130.645	127.537	133.752	130.779	127.572	133.985
	Vis 6	132.844	129.804	135.884	130.145	126.989	133.301	130.079	126.822	133.336
	Vis 7	129.748	126.714	132.782	131.363	128.256	134.470	133.601	130.393	136.809
dia	V7-V1	-6.784	-9.542	-4.026	-5.986	-8.822	-3.151	-3.422	-6.367	-0.476
	Vis 1	83.409	81.658	85.161	83.561	81.803	85.320	83.170	81.358	84.983
	Vis 2	82.133	80.383	83.883	82.103	80.344	83.862	81.223	79.414	83.032
	Vis 3	81.497	79.745	83.249	81.403	79.642	83.164	81.723	79.910	83.536
	Vis 4	81.633	79.879	83.387	81.633	79.846	83.419	81.358	79.534	83.182
	Vis 5	80.997	79.246	82.749	80.791	78.992	82.590	80.356	78.500	82.211
	Vis 6	81.969	80.206	83.732	80.584	78.760	82.408	79.979	78.098	81.861

	Vis 7	79.974	78.214	81.733	80.611	78.812	82.409	79.546	77.690	81.402
	V7-V1	-3.436	-4.952	-1.920	-2.950	-4.509	-1.391	-3.625	-5.244	-2.005
pulse	Vis 1	77.260	74.824	79.696	75.762	73.311	78.213	76.806	74.285	79.327
	Vis 2	76.401	73.961	78.841	75.435	72.986	77.884	74.333	71.816	76.850
	Vis 3	75.616	73.174	78.059	74.828	72.368	77.287	73.890	71.369	76.411
	Vis 4	76.256	73.817	78.696	74.538	72.066	77.010	74.797	72.263	77.331
	Vis 5	74.964	72.524	77.403	73.816	71.332	76.300	74.559	71.994	77.125
	Vis 6	74.494	72.047	76.941	73.263	70.749	75.776	74.997	72.415	77.579
	Vis 7	75.797	73.346	78.249	75.326	72.834	77.819	73.766	71.200	76.333
	V7-V1	-1.463	-3.179	0.253	-0.436	-2.211	1.339	-3.040	-4.875	-1.204
chol	Vis 1	4.138	3.951	4.325	4.251	4.063	4.439	4.133	3.939	4.326
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	4.241	4.052	4.431	4.405	4.213	4.597	4.285	4.089	4.480
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	4.308	4.119	4.497	4.277	4.084	4.471	4.306	4.108	4.504
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	4.323	4.134	4.512	4.311	4.121	4.500	4.332	4.138	4.527
	V7-V1	0.185	0.045	0.326	0.060	-0.080	0.200	0.200	0.055	0.345
ldl	Vis 1	2.140	1.974	2.306	2.309	2.143	2.476	2.198	2.027	2.369
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	2.240	2.072	2.409	2.424	2.255	2.593	2.339	2.166	2.512
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	2.233	2.064	2.402	2.307	2.136	2.477	2.322	2.147	2.497
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.307	2.139	2.475	2.368	2.200	2.535	2.363	2.190	2.535
	V7-V1	0.167	0.049	0.285	0.058	-0.060	0.177	0.164	0.042	0.287
hdl	Vis 1	1.169	1.096	1.242	1.094	1.021	1.168	1.083	1.008	1.159
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.223	1.149	1.296	1.127	1.053	1.201	1.119	1.043	1.195
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.220	1.146	1.293	1.119	1.044	1.193	1.125	1.049	1.201
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.199	1.126	1.272	1.082	1.009	1.156	1.068	0.992	1.143
	V7-V1	0.030	-0.007	0.067	-0.012	-0.049	0.024	-0.016	-0.053	0.022
vldl(l)	Vis 1	0.718	0.651	0.792	0.715	0.648	0.790	0.719	0.650	0.796
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.666	0.602	0.737	0.733	0.661	0.813	0.747	0.673	0.828
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	0.681	0.615	0.755	0.763	0.687	0.847	0.756	0.680	0.841
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.693	0.628	0.766	0.729	0.660	0.804	0.733	0.662	0.812
	V7-V1	0.966	0.899	1.037	1.019	0.948	1.095	1.020	0.947	1.098
trig(l)	Vis 1	1.614	1.451	1.794	1.654	1.487	1.840	1.628	1.459	1.817
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.521	1.366	1.694	1.695	1.520	1.890	1.616	1.447	1.805
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.590	1.428	1.769	1.695	1.519	1.891	1.671	1.495	1.869
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.578	1.418	1.756	1.667	1.498	1.856	1.680	1.505	1.876
	V7-V1	0.978	0.909	1.052	1.008	0.937	1.084	1.032	0.957	1.112
fimtavg	Vis 1	0.751	0.723	0.779	0.757	0.729	0.786	0.755	0.727	0.784
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.742	0.714	0.770	0.758	0.730	0.786	0.744	0.715	0.773
	V7-V1	-0.009	-0.022	0.004	0.000	-0.012	0.013	-0.011	-0.025	0.002
fimtmax	Vis 1	0.912	0.880	0.944	0.912	0.880	0.944	0.918	0.886	0.951
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.901	0.870	0.933	0.913	0.881	0.946	0.904	0.871	0.937
	V7-V1	-0.010	-0.025	0.005	0.001	-0.014	0.017	-0.014	-0.030	0.001

iem	Vis 1	2046.014	1845.255	2246.773	1988.263	1787.383	2189.143	2002.397	1791.475	2213.319
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1978.637	1772.293	2184.980	1904.071	1696.513	2111.629	1896.961	1686.686	2107.237
csc2	V7-V1	-67.377	-218.365	83.610	-84.192	-237.587	69.202	-105.435	-261.265	50.395
	Vis 1	2.870	2.666	3.073	2.962	2.759	3.165	2.919	2.705	3.132
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
imtareal	Vis 7	2.903	2.695	3.112	2.973	2.763	3.183	2.937	2.724	3.149
	V7-V1	0.034	-0.114	0.181	0.011	-0.139	0.161	0.018	-0.134	0.170
	Vis 1	17.474	16.506	18.442	18.045	17.077	19.014	17.944	16.935	18.953
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
n.pl(1)	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	17.579	16.601	18.558	18.029	17.047	19.011	17.795	16.787	18.803
	V7-V1	0.105	-0.327	0.538	-0.016	-0.457	0.424	-0.150	-0.596	0.297
	Vis 1	2.191	1.835	2.616	1.988	1.641	2.408	2.164	1.785	2.624
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
n.pl(1)	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.624	2.198	3.133	2.312	1.909	2.800	2.463	2.033	2.985
	V7-V1	1.198	1.105	1.298	1.163	1.067	1.268	1.138	1.043	1.242

> round(ftable(Eff[, "PP", "Prim", , , 1:3+3], col.vars=4:3), 3)

		Asp-Det			Asp-Bip			Det-Bip			
	par	Est	lo	hi	Est	lo	hi	Est	lo	hi	
var	hba1c	Vis 1	-0.115	-0.382	0.153	-0.098	-0.371	0.175	0.017	-0.257	0.290
		Vis 2	-0.122	-0.390	0.146	0.725	0.451	0.998	0.847	0.573	1.120
		Vis 3	0.121	-0.148	0.391	0.777	0.502	1.051	0.655	0.381	0.930
		Vis 4	0.117	-0.153	0.388	0.672	0.397	0.947	0.554	0.277	0.832
		Vis 5	0.116	-0.156	0.387	0.553	0.275	0.830	0.437	0.156	0.718
		Vis 6	0.206	-0.070	0.481	0.470	0.189	0.751	0.264	-0.022	0.550
		Vis 7	0.423	0.154	0.693	0.586	0.312	0.861	0.163	-0.112	0.438
weight	V7-V1	0.538	0.297	0.779	0.685	0.439	0.930	0.146	-0.099	0.392	
	Vis 1	1.120	-2.667	4.906	1.655	-2.212	5.523	0.535	-3.339	4.409	
	Vis 2	1.226	-2.561	5.013	-0.377	-4.245	3.491	-1.602	-5.477	2.272	
	Vis 3	1.478	-2.310	5.265	-0.260	-4.129	3.608	-1.738	-5.613	2.137	
	Vis 4	1.753	-2.037	5.543	0.242	-3.627	4.111	-1.511	-5.390	2.368	
	Vis 5	1.385	-2.407	5.176	0.324	-3.549	4.196	-1.061	-4.943	2.821	
	Vis 6	1.311	-2.483	5.105	0.671	-3.204	4.546	-0.640	-4.526	3.245	
bmi	Vis 7	1.020	-2.769	4.809	0.312	-3.557	4.182	-0.708	-4.583	3.168	
	V7-V1	-0.100	-1.019	0.819	-1.343	-2.278	-0.408	-1.243	-2.180	-0.306	
	Vis 1	0.230	-0.852	1.312	0.247	-0.858	1.352	0.017	-1.089	1.124	
	Vis 2	0.265	-0.817	1.347	-0.426	-1.531	0.679	-0.691	-1.798	0.416	
	Vis 3	0.364	-0.719	1.446	-0.383	-1.489	0.722	-0.747	-1.854	0.360	
	Vis 4	0.442	-0.641	1.525	-0.225	-1.331	0.880	-0.667	-1.776	0.441	
	Vis 5	0.336	-0.747	1.420	-0.195	-1.301	0.912	-0.531	-1.641	0.579	
whr	Vis 6	0.298	-0.786	1.383	-0.095	-1.203	1.012	-0.394	-1.505	0.717	
	Vis 7	0.170	-0.912	1.253	-0.211	-1.317	0.894	-0.382	-1.489	0.726	
	V7-V1	-0.059	-0.364	0.246	-0.459	-0.769	-0.148	-0.399	-0.710	-0.088	
	Vis 1	0.003	-0.016	0.023	0.012	-0.008	0.032	0.008	-0.012	0.028	
	Vis 2	0.009	-0.011	0.028	0.010	-0.010	0.030	0.001	-0.019	0.021	
	Vis 3	0.013	-0.007	0.032	0.011	-0.009	0.031	-0.002	-0.022	0.018	
	Vis 4	0.010	-0.010	0.030	0.007	-0.013	0.027	-0.003	-0.023	0.017	
whr	Vis 5	0.011	-0.009	0.031	0.009	-0.011	0.030	-0.002	-0.022	0.019	
	Vis 6	0.012	-0.008	0.032	0.013	-0.008	0.033	0.001	-0.020	0.021	

	Vis 7	0.016	-0.004	0.035	0.026	0.006	0.046	0.011	-0.009	0.031
	V7-V1	0.012	-0.002	0.026	0.015	0.000	0.029	0.003	-0.012	0.017
gluc	Vis 1	-0.826	-1.546	-0.107	-0.152	-0.886	0.581	0.674	-0.062	1.410
	Vis 2	-0.628	-1.366	0.110	-0.893	-1.644	-0.143	-0.265	-1.020	0.489
	Vis 3	-0.201	-0.954	0.551	-0.650	-1.408	0.108	-0.449	-1.213	0.315
	Vis 4	0.457	-0.296	1.210	-0.275	-1.034	0.484	-0.732	-1.505	0.040
	Vis 5	-0.411	-1.163	0.342	-1.494	-2.257	-0.732	-1.084	-1.864	-0.303
	Vis 6	-0.471	-1.240	0.297	-1.017	-1.801	-0.233	-0.546	-1.352	0.261
	Vis 7	-0.235	-0.963	0.493	-0.955	-1.696	-0.214	-0.720	-1.463	0.022
	V7-V1	0.592	-0.285	1.468	-0.803	-1.695	0.089	-1.395	-2.289	-0.500
ins(1)	Vis 1	1.276	1.011	1.611	1.092	0.861	1.385	0.856	0.675	1.085
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.764	0.601	0.970	0.609	0.477	0.777	0.797	0.625	1.016
	V7-V1	0.599	0.470	0.763	0.557	0.435	0.714	0.931	0.728	1.190
cpep(1)	Vis 1	1.189	0.972	1.453	1.191	0.970	1.462	1.002	0.816	1.231
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.969	0.791	1.188	0.831	0.676	1.022	0.857	0.697	1.055
	V7-V1	0.816	0.701	0.949	0.698	0.599	0.814	0.856	0.734	0.998
idos(1)	Vis 1	1.056	0.907	1.230	0.953	0.816	1.113	0.902	0.772	1.053
	Vis 2	1.255	1.078	1.461	1.355	1.160	1.583	1.080	0.924	1.261
	Vis 3	1.242	1.066	1.447	1.487	1.273	1.737	1.197	1.024	1.400
	Vis 4	1.250	1.073	1.457	1.550	1.326	1.811	1.239	1.059	1.450
	Vis 5	1.256	1.077	1.464	1.601	1.368	1.872	1.274	1.088	1.493
	Vis 6	1.219	1.044	1.422	1.619	1.383	1.895	1.328	1.133	1.558
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.154	1.033	1.288	1.699	1.520	1.900	1.473	1.314	1.651
ipkg(1)	Vis 1	1.043	0.909	1.196	0.937	0.814	1.077	0.898	0.780	1.033
	Vis 2	1.235	1.077	1.417	1.359	1.181	1.564	1.100	0.956	1.266
	Vis 3	1.223	1.066	1.404	1.494	1.298	1.719	1.221	1.060	1.406
	Vis 4	1.229	1.070	1.411	1.549	1.346	1.784	1.261	1.094	1.454
	Vis 5	1.233	1.073	1.416	1.597	1.386	1.841	1.296	1.123	1.496
	Vis 6	1.200	1.043	1.380	1.614	1.399	1.861	1.345	1.164	1.554
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.150	1.034	1.280	1.723	1.545	1.920	1.497	1.341	1.673
sys	Vis 1	0.817	-2.918	4.552	0.490	-3.319	4.300	-0.327	-4.143	3.490
	Vis 2	0.609	-3.122	4.339	-0.295	-4.095	3.505	-0.904	-4.715	2.907
	Vis 3	-0.729	-4.466	3.007	-0.744	-4.556	3.067	-0.015	-3.833	3.803
	Vis 4	0.005	-3.777	3.787	-0.048	-3.881	3.785	-0.053	-3.929	3.822
	Vis 5	-2.310	-6.104	1.485	-2.176	-6.052	1.700	0.134	-3.805	4.072
	Vis 6	-2.699	-6.552	1.154	-2.765	-6.699	1.168	-0.066	-4.083	3.950
	Vis 7	1.615	-2.198	5.428	3.853	-0.042	7.748	2.238	-1.711	6.187
	V7-V1	0.798	-3.157	4.754	3.363	-0.672	7.398	2.565	-1.524	6.653
dia	Vis 1	0.152	-1.997	2.300	-0.239	-2.431	1.953	-0.391	-2.586	1.805
	Vis 2	-0.030	-2.176	2.116	-0.910	-3.097	1.277	-0.880	-3.073	1.313
	Vis 3	-0.093	-2.243	2.056	0.226	-1.967	2.419	0.319	-1.877	2.516
	Vis 4	-0.001	-2.174	2.173	-0.275	-2.479	1.929	-0.274	-2.501	1.953
	Vis 5	-0.206	-2.386	1.974	-0.642	-2.868	1.585	-0.436	-2.696	1.825
	Vis 6	-1.385	-3.595	0.826	-1.989	-4.246	0.268	-0.605	-2.906	1.697
	Vis 7	0.637	-1.553	2.827	-0.428	-2.664	1.809	-1.065	-3.331	1.201
	V7-V1	0.485	-1.689	2.660	-0.189	-2.407	2.029	-0.674	-2.922	1.573
pulse	Vis 1	-1.498	-4.409	1.413	-0.454	-3.423	2.515	1.044	-1.935	4.022
	Vis 2	-0.966	-3.877	1.945	-2.068	-5.036	0.901	-1.101	-4.075	1.872
	Vis 3	-0.789	-3.710	2.133	-1.726	-4.701	1.248	-0.938	-3.922	2.047
	Vis 4	-1.718	-4.649	1.212	-1.459	-4.443	1.524	0.259	-2.748	3.266
	Vis 5	-1.148	-4.087	1.791	-0.404	-3.412	2.604	0.744	-2.296	3.783
	Vis 6	-1.232	-4.204	1.741	0.503	-2.526	3.532	1.735	-1.344	4.813
	Vis 7	-0.471	-3.433	2.491	-2.031	-5.053	0.992	-1.560	-4.613	1.493
	V7-V1	1.027	-1.442	3.496	-1.577	-4.089	0.936	-2.604	-5.157	-0.050

	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.070	-0.177	0.316	0.033	-0.215	0.281	-0.037	-0.285	0.212
	V7-V1	-0.023	-0.233	0.187	-0.016	-0.228	0.196	0.007	-0.207	0.220
imtareal	Vis 1	0.572	-0.535	1.678	0.470	-0.664	1.605	-0.101	-1.236	1.033
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.450	-0.676	1.576	0.216	-0.927	1.359	-0.234	-1.378	0.909
	V7-V1	-0.122	-0.739	0.496	-0.255	-0.876	0.367	-0.133	-0.760	0.494
n.pl(1)	Vis 1	0.907	0.737	1.117	0.988	0.800	1.219	1.088	0.876	1.352
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.881	0.716	1.084	0.939	0.761	1.158	1.065	0.858	1.323
	V7-V1	0.971	0.863	1.092	0.951	0.844	1.070	0.979	0.866	1.107
 > round(ftable(Eff[, "PP", "Rest",,,1:3], col.vars=4:3), 3)										
		Biph			AspD			Detm		
	var	Est	lo	hi	Est	lo	hi	Est	lo	hi
	hba1c									
	Vis 1	8.635	8.443	8.827	8.529	8.336	8.722	8.543	8.342	8.744
	Vis 2	8.150	7.958	8.343	8.037	7.844	8.230	8.881	8.680	9.082
	Vis 3	7.672	7.478	7.865	7.801	7.607	7.995	8.455	8.254	8.657
	Vis 4	7.706	7.513	7.899	7.831	7.635	8.027	8.385	8.182	8.587
	Vis 5	7.763	7.570	7.956	7.886	7.688	8.084	8.321	8.115	8.527
	Vis 6	7.702	7.507	7.896	7.915	7.713	8.116	8.176	7.966	8.385
	Vis 7	7.620	7.426	7.813	8.051	7.857	8.246	8.213	8.011	8.414
	V7-V1	-1.015	-1.185	-0.845	-0.478	-0.648	-0.307	-0.331	-0.507	-0.154
	weight									
	Vis 1	95.884	93.125	98.642	97.153	94.384	99.922	97.867	94.983	100.751
	Vis 2	97.394	94.635	100.153	98.770	96.000	101.539	97.346	94.461	100.230
	Vis 3	98.153	95.394	100.912	99.780	97.010	102.551	98.222	95.337	101.107
	Vis 4	98.558	95.799	101.317	100.460	97.687	103.234	99.130	96.243	102.016
	Vis 5	98.800	96.041	101.559	100.333	97.559	103.108	99.453	96.563	102.343
	Vis 6	99.031	96.270	101.792	100.491	97.713	103.268	100.030	97.138	102.922
	Vis 7	99.288	96.528	102.048	100.458	97.687	103.229	99.928	97.043	102.814
	V7-V1	3.404	2.756	4.053	3.305	2.653	3.956	2.061	1.388	2.735
	bmi									
	Vis 1	31.898	31.118	32.678	32.162	31.378	32.945	32.226	31.410	33.042
	Vis 2	32.399	31.619	33.179	32.698	31.915	33.481	32.054	31.238	32.870
	Vis 3	32.641	31.861	33.422	33.039	32.255	33.822	32.339	31.523	33.155
	Vis 4	32.781	32.001	33.562	33.257	32.472	34.042	32.637	31.820	33.454
	Vis 5	32.855	32.075	33.636	33.225	32.440	34.010	32.742	31.924	33.560
	Vis 6	32.939	32.158	33.720	33.271	32.484	34.057	32.924	32.105	33.743
	Vis 7	32.999	32.218	33.780	33.203	32.419	33.987	32.868	32.052	33.684
	V7-V1	1.101	0.885	1.316	1.041	0.825	1.258	0.642	0.418	0.866
	whr									
	Vis 1	0.999	0.985	1.013	1.003	0.989	1.016	1.011	0.997	1.026
	Vis 2	0.992	0.978	1.006	1.001	0.988	1.015	1.003	0.988	1.017
	Vis 3	0.993	0.980	1.007	1.007	0.993	1.020	1.005	0.990	1.019
	Vis 4	0.994	0.980	1.008	1.004	0.990	1.018	1.001	0.987	1.016
	Vis 5	0.997	0.983	1.011	1.008	0.994	1.023	1.007	0.992	1.022
	Vis 6	0.994	0.980	1.008	1.006	0.992	1.021	1.007	0.992	1.022
	Vis 7	0.995	0.981	1.009	1.011	0.997	1.025	1.022	1.008	1.037
	V7-V1	-0.003	-0.013	0.007	0.009	-0.001	0.019	0.011	0.001	0.022
	gluc									
	Vis 1	10.697	10.182	11.211	9.898	9.380	10.416	10.581	10.043	11.118
	Vis 2	9.122	8.596	9.648	8.530	7.998	9.062	8.275	7.726	8.825
	Vis 3	8.706	8.171	9.241	8.526	7.982	9.069	8.096	7.544	8.647
	Vis 4	8.138	7.608	8.668	8.625	8.075	9.174	7.906	7.348	8.463
	Vis 5	8.983	8.457	9.509	8.591	8.039	9.143	7.522	6.956	8.088
	Vis 6	8.749	8.216	9.283	8.300	7.732	8.867	7.764	7.177	8.352
	Vis 7	8.667	8.146	9.188	8.456	7.932	8.979	7.748	7.206	8.289
	V7-V1	-2.030	-2.648	-1.412	-1.442	-2.063	-0.821	-2.833	-3.476	-2.190

	Vis 7	0.894	0.724	1.104	0.946	0.765	1.171	1.059	0.850	1.319
	V7-V1	0.971	0.863	1.092	0.949	0.843	1.068	0.978	0.865	1.105
<code>> round(ftable(Eff[, "PP", "Conf",,,1:3], col.vars=4:3), 3)</code>										
		Biph Est	lo	hi	AspD Est	lo	hi	Detm Est	lo	hi
var	par									
hba1c	Vis 1	8.922	8.578	9.266	8.802	8.458	9.145	8.826	8.471	9.180
	Vis 2	8.438	8.094	8.782	8.310	7.966	8.653	9.164	8.810	9.519
	Vis 3	7.959	7.614	8.303	8.074	7.730	8.418	8.738	8.383	9.092
	Vis 4	7.993	7.648	8.337	8.104	7.759	8.449	8.666	8.311	9.022
	Vis 5	8.049	7.705	8.394	8.159	7.813	8.506	8.604	8.246	8.962
	Vis 6	7.987	7.642	8.332	8.187	7.839	8.536	8.459	8.099	8.819
	Vis 7	7.907	7.562	8.251	8.324	7.980	8.668	8.495	8.140	8.850
	V7-V1	-1.015	-1.185	-0.846	-0.477	-0.648	-0.307	-0.331	-0.508	-0.154
weight	Vis 1	89.018	83.706	94.330	89.760	84.459	95.062	90.252	84.784	95.721
	Vis 2	90.528	85.216	95.840	91.377	86.076	96.679	89.731	84.262	95.200
	Vis 3	91.287	85.975	96.599	92.388	87.086	97.689	90.607	85.138	96.076
	Vis 4	91.692	86.380	97.005	93.069	87.766	98.373	91.514	86.044	96.984
	Vis 5	91.934	86.621	97.246	92.942	87.638	98.246	91.838	86.366	97.310
	Vis 6	92.164	86.851	97.477	93.098	87.793	98.404	92.415	86.942	97.888
	Vis 7	92.422	87.109	97.735	93.065	87.763	98.367	92.313	86.844	97.782
	V7-V1	3.404	2.756	4.053	3.304	2.653	3.956	2.061	1.387	2.734
bmi	Vis 1	32.411	30.835	33.987	32.731	31.158	34.304	32.698	31.075	34.321
	Vis 2	32.912	31.336	34.489	33.267	31.694	34.840	32.526	30.903	34.149
	Vis 3	33.155	31.578	34.731	33.608	32.035	35.181	32.811	31.188	34.434
	Vis 4	33.294	31.718	34.871	33.826	32.252	35.400	33.109	31.485	34.732
	Vis 5	33.369	31.792	34.945	33.794	32.220	35.369	33.213	31.589	34.837
	Vis 6	33.452	31.875	35.029	33.840	32.265	35.415	33.396	31.771	35.020
	Vis 7	33.512	31.935	35.088	33.772	32.199	35.345	33.340	31.717	34.963
	V7-V1	1.101	0.885	1.316	1.041	0.825	1.258	0.642	0.419	0.866
whr	Vis 1	0.947	0.925	0.969	0.948	0.926	0.970	0.956	0.933	0.979
	Vis 2	0.941	0.918	0.963	0.947	0.925	0.969	0.948	0.925	0.971
	Vis 3	0.942	0.920	0.964	0.952	0.930	0.974	0.950	0.927	0.973
	Vis 4	0.942	0.920	0.964	0.950	0.928	0.972	0.946	0.923	0.969
	Vis 5	0.945	0.923	0.968	0.954	0.932	0.976	0.952	0.929	0.975
	Vis 6	0.942	0.920	0.964	0.952	0.929	0.974	0.952	0.929	0.975
	Vis 7	0.944	0.922	0.966	0.957	0.935	0.979	0.967	0.944	0.990
	V7-V1	-0.003	-0.013	0.007	0.009	-0.001	0.019	0.011	0.001	0.022
gluc	Vis 1	11.160	10.385	11.934	10.337	9.562	11.112	11.026	10.225	11.826
	Vis 2	9.595	8.812	10.378	8.969	8.186	9.752	8.717	7.910	9.524
	Vis 3	9.173	8.386	9.960	8.975	8.185	9.766	8.544	7.733	9.355
	Vis 4	8.605	7.820	9.389	9.059	8.265	9.854	8.346	7.531	9.161
	Vis 5	9.444	8.661	10.227	9.030	8.234	9.827	7.964	7.141	8.787
	Vis 6	9.215	8.429	10.002	8.746	7.936	9.556	8.211	7.373	9.050
	Vis 7	9.129	8.350	9.909	8.896	8.118	9.674	8.193	7.388	8.997
	V7-V1	-2.030	-2.648	-1.413	-1.441	-2.062	-0.819	-2.833	-3.476	-2.190
ins(l)	Vis 1	63.712	46.690	86.938	81.080	59.465	110.552	69.505	50.469	95.720
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	58.664	42.875	80.268	44.932	32.896	61.371	35.702	25.855	49.301
	V7-V1	0.921	0.775	1.094	0.554	0.468	0.657	0.514	0.430	0.613
cpep(l)	Vis 1	668.105	507.842	878.945	790.612	601.273	1039.573	795.846	599.992	1055.631
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	569.223	432.294	749.523	549.585	417.648	723.201	473.473	356.674	628.519
	V7-V1	0.852	0.766	0.948	0.695	0.624	0.774	0.595	0.533	0.664
idos(l)	Vis 1	40.578	33.016	49.871	42.756	34.801	52.530	38.430	31.074	47.528
	Vis 2	70.054	56.999	86.098	87.691	71.375	107.737	94.365	76.293	116.718
	Vis 3	77.212	62.818	94.903	95.673	77.853	117.573	114.160	92.292	141.211
	Vis 4	79.705	64.847	97.968	99.426	80.890	122.211	122.820	99.260	151.972

	Vis 7	0.743	0.637	0.867	0.782	0.671	0.911	0.787	0.671	0.923
	V7-V1	0.966	0.899	1.038	1.018	0.947	1.094	1.020	0.947	1.098
trig(l)	Vis 1	1.735	1.468	2.050	1.785	1.511	2.108	1.755	1.478	2.084
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.636	1.383	1.934	1.828	1.546	2.161	1.741	1.465	2.069
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.710	1.446	2.021	1.829	1.546	2.164	1.802	1.515	2.144
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.698	1.436	2.007	1.800	1.523	2.126	1.811	1.525	2.151
	V7-V1	0.979	0.910	1.053	1.008	0.938	1.084	1.032	0.957	1.112
fimtavg	Vis 1	0.721	0.674	0.767	0.727	0.681	0.773	0.724	0.676	0.771
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.712	0.665	0.758	0.727	0.681	0.774	0.712	0.665	0.760
	V7-V1	-0.009	-0.022	0.004	0.000	-0.012	0.013	-0.011	-0.025	0.002
fimtmax	Vis 1	0.870	0.818	0.923	0.871	0.819	0.924	0.876	0.822	0.930
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.860	0.808	0.913	0.873	0.820	0.925	0.861	0.807	0.916
	V7-V1	-0.010	-0.025	0.005	0.001	-0.014	0.017	-0.015	-0.030	0.001
iem	Vis 1	2012.277	1690.713	2333.841	1937.271	1618.506	2256.036	1958.331	1625.521	2291.141
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1945.203	1619.846	2270.560	1858.681	1537.492	2179.871	1854.539	1521.596	2187.481
	V7-V1	-67.073	-217.920	83.773	-78.589	-231.886	74.707	-103.793	-259.482	51.896
csc2	Vis 1	2.925	2.601	3.248	3.036	2.715	3.357	2.985	2.650	3.319
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	2.958	2.631	3.285	3.041	2.718	3.364	3.000	2.666	3.335
	V7-V1	0.033	-0.114	0.181	0.005	-0.145	0.154	0.016	-0.136	0.168
imtareal	Vis 1	15.223	13.697	16.749	15.763	14.252	17.275	15.623	14.050	17.196
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	15.330	13.796	16.863	15.760	14.244	17.276	15.472	13.898	17.045
	V7-V1	0.107	-0.326	0.540	-0.003	-0.443	0.438	-0.151	-0.598	0.295
n.pl(l)	Vis 1	1.433	1.064	1.930	1.283	0.936	1.760	1.392	1.024	1.893
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.718	1.276	2.313	1.495	1.090	2.050	1.586	1.167	2.155
	V7-V1	1.199	1.107	1.299	1.165	1.069	1.270	1.139	1.044	1.243

> round(ftable(Eff[, "PP", "Conf", , , 1:3+3], col.vars=4:3), 3)

		Asp-Det		Asp-Bip		Det-Bip				
var	par	Est	lo	hi	Est	lo	hi	Est	lo	hi
hba1c	Vis 1	-0.121	-0.389	0.148	-0.096	-0.370	0.178	0.024	-0.250	0.299
	Vis 2	-0.128	-0.397	0.141	0.726	0.453	1.000	0.854	0.580	1.129
	Vis 3	0.115	-0.155	0.386	0.779	0.503	1.054	0.663	0.388	0.939
	Vis 4	0.111	-0.161	0.383	0.674	0.398	0.949	0.563	0.284	0.841

	Vis 5	0.110	-0.163	0.382	0.555	0.277	0.833	0.445	0.163	0.727
	Vis 6	0.200	-0.076	0.476	0.472	0.190	0.753	0.272	-0.015	0.559
	Vis 7	0.418	0.147	0.688	0.588	0.313	0.864	0.171	-0.105	0.447
	V7-V1	0.538	0.297	0.779	0.685	0.439	0.930	0.147	-0.099	0.392
weight	Vis 1	0.743	-2.863	4.348	1.234	-2.443	4.911	0.492	-3.194	4.178
	Vis 2	0.849	-2.757	4.455	-0.797	-4.475	2.880	-1.646	-5.333	2.040
	Vis 3	1.101	-2.506	4.707	-0.680	-4.358	2.998	-1.781	-5.468	1.907
	Vis 4	1.377	-2.232	4.986	-0.179	-3.858	3.500	-1.556	-5.247	2.135
	Vis 5	1.008	-2.602	4.618	-0.096	-3.778	3.586	-1.104	-4.798	2.591
	Vis 6	0.934	-2.679	4.547	0.251	-3.434	3.936	-0.683	-4.381	3.015
	Vis 7	0.642	-2.966	4.251	-0.109	-3.788	3.570	-0.752	-4.440	2.936
	V7-V1	-0.100	-1.019	0.819	-1.344	-2.278	-0.409	-1.243	-2.180	-0.307
bmi	Vis 1	0.320	-0.753	1.392	0.287	-0.807	1.381	-0.033	-1.129	1.064
	Vis 2	0.355	-0.718	1.428	-0.386	-1.480	0.708	-0.741	-1.838	0.356
	Vis 3	0.453	-0.620	1.526	-0.344	-1.438	0.751	-0.797	-1.894	0.300
	Vis 4	0.532	-0.543	1.606	-0.186	-1.281	0.909	-0.717	-1.816	0.381
	Vis 5	0.426	-0.649	1.500	-0.155	-1.251	0.940	-0.581	-1.681	0.519
	Vis 6	0.388	-0.688	1.464	-0.056	-1.153	1.041	-0.444	-1.545	0.657
	Vis 7	0.260	-0.813	1.334	-0.172	-1.266	0.923	-0.432	-1.529	0.665
	V7-V1	-0.059	-0.364	0.246	-0.459	-0.769	-0.148	-0.399	-0.710	-0.088
whr	Vis 1	0.001	-0.016	0.018	0.009	-0.008	0.026	0.008	-0.009	0.025
	Vis 2	0.006	-0.010	0.023	0.007	-0.010	0.024	0.001	-0.017	0.018
	Vis 3	0.010	-0.007	0.027	0.008	-0.009	0.025	-0.002	-0.019	0.015
	Vis 4	0.008	-0.009	0.025	0.004	-0.013	0.021	-0.004	-0.021	0.014
	Vis 5	0.009	-0.008	0.026	0.007	-0.011	0.024	-0.002	-0.020	0.016
	Vis 6	0.010	-0.008	0.027	0.010	-0.008	0.027	0.000	-0.018	0.018
	Vis 7	0.013	-0.004	0.030	0.023	0.006	0.041	0.010	-0.007	0.028
	V7-V1	0.012	-0.002	0.026	0.015	0.000	0.029	0.003	-0.012	0.017
gluc	Vis 1	-0.823	-1.543	-0.103	-0.134	-0.868	0.599	0.689	-0.047	1.425
	Vis 2	-0.625	-1.364	0.113	-0.878	-1.628	-0.128	-0.252	-1.007	0.502
	Vis 3	-0.198	-0.950	0.555	-0.629	-1.387	0.129	-0.432	-1.195	0.332
	Vis 4	0.455	-0.299	1.208	-0.259	-1.017	0.500	-0.713	-1.486	0.060
	Vis 5	-0.414	-1.166	0.338	-1.480	-2.242	-0.718	-1.066	-1.847	-0.285
	Vis 6	-0.469	-1.237	0.300	-1.004	-1.787	-0.221	-0.535	-1.342	0.272
	Vis 7	-0.233	-0.961	0.495	-0.937	-1.677	-0.196	-0.704	-1.446	0.039
	V7-V1	0.590	-0.287	1.466	-0.803	-1.695	0.089	-1.392	-2.287	-0.498
ins(1)	Vis 1	1.273	1.009	1.605	1.091	0.861	1.383	0.857	0.676	1.087
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.766	0.603	0.972	0.609	0.477	0.776	0.795	0.624	1.012
	V7-V1	0.602	0.473	0.767	0.558	0.436	0.714	0.927	0.725	1.185
cpep(1)	Vis 1	1.183	0.974	1.438	1.191	0.976	1.453	1.007	0.825	1.229
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.966	0.793	1.176	0.832	0.681	1.017	0.862	0.705	1.053
	V7-V1	0.816	0.701	0.949	0.698	0.599	0.814	0.856	0.734	0.998
idos(1)	Vis 1	1.054	0.906	1.225	0.947	0.812	1.105	0.899	0.770	1.049
	Vis 2	1.252	1.076	1.456	1.347	1.155	1.571	1.076	0.922	1.256
	Vis 3	1.239	1.065	1.442	1.479	1.267	1.725	1.193	1.022	1.393
	Vis 4	1.247	1.072	1.452	1.541	1.320	1.799	1.235	1.057	1.444
	Vis 5	1.253	1.076	1.459	1.592	1.362	1.860	1.270	1.086	1.486
	Vis 6	1.216	1.042	1.417	1.609	1.376	1.882	1.324	1.130	1.551
	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.154	1.033	1.288	1.699	1.520	1.901	1.473	1.315	1.651
ipkg(1)	Vis 1	1.044	0.910	1.198	0.935	0.813	1.076	0.896	0.778	1.031
	Vis 2	1.237	1.078	1.419	1.357	1.179	1.561	1.097	0.953	1.263
	Vis 3	1.225	1.067	1.406	1.491	1.296	1.717	1.218	1.057	1.403
	Vis 4	1.230	1.071	1.413	1.547	1.344	1.781	1.258	1.091	1.450
	Vis 5	1.234	1.074	1.418	1.595	1.384	1.839	1.293	1.120	1.493
	Vis 6	1.201	1.044	1.382	1.611	1.397	1.859	1.341	1.161	1.550

	Vis 7	NA	NA	NA	NA	NA	NA	NA	NA	NA
	V7-V1	1.150	1.034	1.280	1.723	1.545	1.921	1.498	1.341	1.673
sys	Vis 1	0.697	-3.037	4.431	0.358	-3.447	4.164	-0.339	-4.153	3.475
	Vis 2	0.496	-3.233	4.226	-0.422	-4.218	3.374	-0.918	-4.727	2.890
	Vis 3	-0.845	-4.581	2.891	-0.866	-4.673	2.942	-0.020	-3.837	3.796
	Vis 4	-0.101	-3.882	3.680	-0.173	-4.002	3.655	-0.072	-3.946	3.801
	Vis 5	-2.416	-6.210	1.377	-2.289	-6.161	1.583	0.127	-3.810	4.064
	Vis 6	-2.803	-6.654	1.048	-2.879	-6.808	1.051	-0.076	-4.090	3.939
	Vis 7	1.514	-2.298	5.326	3.717	-0.174	7.608	2.203	-1.745	6.150
	V7-V1	0.817	-3.139	4.772	3.358	-0.677	7.394	2.542	-1.547	6.631
dia	Vis 1	-0.029	-2.162	2.103	-0.239	-2.412	1.934	-0.210	-2.388	1.969
	Vis 2	-0.211	-2.341	1.919	-0.910	-3.078	1.258	-0.699	-2.875	1.476
	Vis 3	-0.281	-2.415	1.852	0.227	-1.947	2.402	0.509	-1.671	2.688
	Vis 4	-0.188	-2.346	1.970	-0.271	-2.457	1.915	-0.083	-2.293	2.127
	Vis 5	-0.392	-2.556	1.773	-0.629	-2.838	1.579	-0.238	-2.482	2.006
	Vis 6	-1.561	-3.756	0.634	-1.977	-4.217	0.262	-0.416	-2.701	1.869
	Vis 7	0.451	-1.723	2.624	-0.419	-2.638	1.800	-0.870	-3.119	1.380
	V7-V1	0.480	-1.695	2.655	-0.180	-2.398	2.038	-0.660	-2.908	1.588
pulse	Vis 1	-1.659	-4.547	1.230	-0.371	-3.313	2.571	1.287	-1.666	4.241
	Vis 2	-1.127	-4.015	1.761	-1.986	-4.928	0.956	-0.859	-3.808	2.089
	Vis 3	-0.955	-3.854	1.944	-1.644	-4.592	1.304	-0.689	-3.649	2.270
	Vis 4	-1.887	-4.795	1.021	-1.375	-4.332	1.582	0.513	-2.470	3.495
	Vis 5	-1.314	-4.230	1.602	-0.318	-3.300	2.664	0.996	-2.019	4.011
	Vis 6	-1.393	-4.343	1.557	0.590	-2.413	3.592	1.983	-1.072	5.037
	Vis 7	-0.639	-3.578	2.300	-1.937	-4.933	1.060	-1.297	-4.326	1.731
	V7-V1	1.019	-1.450	3.488	-1.566	-4.078	0.947	-2.585	-5.138	-0.032
chol	Vis 1	0.107	-0.113	0.327	0.008	-0.216	0.232	-0.099	-0.324	0.126
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.156	-0.069	0.381	0.057	-0.171	0.286	-0.099	-0.328	0.131
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	-0.040	-0.266	0.186	0.011	-0.219	0.241	0.051	-0.182	0.284
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-0.021	-0.244	0.201	0.022	-0.204	0.248	0.043	-0.183	0.270
	V7-V1	-0.128	-0.326	0.070	0.014	-0.188	0.216	0.142	-0.060	0.344
ldl	Vis 1	0.158	-0.037	0.353	0.067	-0.131	0.265	-0.091	-0.290	0.108
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	0.172	-0.027	0.371	0.110	-0.092	0.312	-0.063	-0.266	0.141
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	0.062	-0.138	0.262	0.099	-0.104	0.303	0.037	-0.168	0.243
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.048	-0.148	0.245	0.066	-0.135	0.267	0.018	-0.183	0.219
	V7-V1	-0.110	-0.277	0.057	-0.001	-0.171	0.169	0.109	-0.061	0.279
hdl	Vis 1	-0.071	-0.153	0.011	-0.079	-0.163	0.004	-0.009	-0.093	0.075
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	-0.092	-0.175	-0.009	-0.098	-0.182	-0.013	-0.006	-0.091	0.079
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	-0.098	-0.181	-0.014	-0.089	-0.174	-0.005	0.008	-0.077	0.094
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-0.113	-0.195	-0.030	-0.125	-0.209	-0.041	-0.012	-0.096	0.072
	V7-V1	-0.042	-0.094	0.009	-0.045	-0.098	0.007	-0.003	-0.056	0.049
vldl(l)	Vis 1	0.999	0.890	1.121	1.004	0.892	1.129	1.005	0.893	1.131
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.102	0.974	1.246	1.124	0.994	1.272	1.021	0.900	1.157
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.120	0.989	1.269	1.112	0.981	1.262	0.993	0.874	1.129
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.053	0.937	1.183	1.059	0.941	1.193	1.006	0.894	1.134
	V7-V1	1.054	0.952	1.167	1.056	0.952	1.170	1.002	0.903	1.110
trig(l)	Vis 1	1.029	0.909	1.165	1.012	0.891	1.149	0.983	0.866	1.116
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	1.117	0.984	1.269	1.065	0.936	1.211	0.953	0.837	1.085
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	1.070	0.942	1.215	1.054	0.926	1.200	0.985	0.864	1.123
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	1.060	0.935	1.202	1.067	0.939	1.212	1.006	0.886	1.143
	V7-V1	1.030	0.929	1.142	1.054	0.949	1.170	1.023	0.922	1.136

fimtavg	Vis 1	0.006	-0.026	0.038	0.003	-0.030	0.036	-0.003	-0.036	0.030
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.016	-0.016	0.048	0.001	-0.032	0.034	-0.015	-0.048	0.018
	V7-V1	0.010	-0.009	0.028	-0.002	-0.021	0.016	-0.012	-0.030	0.007
fimtmax	Vis 1	0.001	-0.036	0.037	0.006	-0.032	0.043	0.005	-0.032	0.042
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.012	-0.024	0.049	0.001	-0.036	0.039	-0.011	-0.049	0.026
	V7-V1	0.012	-0.010	0.033	-0.004	-0.026	0.018	-0.016	-0.038	0.006
iem	Vis 1	-75.006	-308.097	158.086	-53.945	-293.455	185.565	21.061	-218.992	261.113
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	-86.522	-329.524	156.481	-90.665	-334.719	153.390	-4.143	-248.927	240.641
	V7-V1	-11.516	-226.583	203.551	-36.719	-253.490	180.051	-25.204	-243.684	193.277
csc2	Vis 1	0.111	-0.122	0.345	0.060	-0.180	0.300	-0.051	-0.291	0.189
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.082	-0.161	0.325	0.042	-0.202	0.286	-0.040	-0.285	0.205
	V7-V1	-0.029	-0.239	0.181	-0.018	-0.229	0.194	0.011	-0.202	0.224
imtareal	Vis 1	0.540	-0.516	1.597	0.400	-0.681	1.482	-0.140	-1.222	0.943
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.430	-0.646	1.507	0.142	-0.949	1.233	-0.289	-1.381	0.804
	V7-V1	-0.110	-0.727	0.508	-0.258	-0.880	0.363	-0.149	-0.776	0.478
n.pl(1)	Vis 1	0.896	0.731	1.098	0.972	0.791	1.193	1.085	0.878	1.341
	Vis 2	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 3	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 4	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 5	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 6	NA	NA	NA	NA	NA	NA	NA	NA	NA
	Vis 7	0.870	0.711	1.066	0.923	0.753	1.133	1.061	0.859	1.310
	V7-V1	0.972	0.864	1.093	0.950	0.844	1.070	0.978	0.865	1.106

```

> #for( vv in dimnames(Eff)[[1]] )
> # {
> #   cat( "-----\n", vv, "\n" )
> #   dec <- 3 - ( max(Eff[vv,,,,1:3])>100 ) -
> #             ( max(Eff[vv,,,,1:3])>1000 )
> #   print( round( ftable( Eff[vv,,,,1:3 ], col.vars=5:4 ), dec ) )
> #   print( round( ftable( Eff[vv,,,,1:3+3], col.vars=5:4 ), dec ) )
> # }

```

and the tests in those table:

```

> for( vv in dimnames(Tst)[[1]] )
+ {
+   cat( "-----\n", vv, "\n" )
+   print( round( ftable( Tst[vv,,, "Pval"], row.vars=3 ), 4 ) )
+ }

```

hba1c

			ana	IT		PP			
			mod	Prim	Rest	Conf	Prim	Rest	Conf
test									
	All equal	AspD vs. Biph	0.0001	0.0001	0.0001	0.0001	0.0002	0.0002	0.0002
	All equal	Detm vs. Biph	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
	All equal	Detm vs. AspD	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Visit 7	equal	AspD vs. Biph	0.0019	0.0019	0.0020	0.0021	0.0021	0.0020	0.0025
Visit 7	equal	Detm vs. Biph	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Visit 7	equal	Detm vs. AspD	0.1074	0.1110	0.0995	0.2454	0.2590	0.2249	0.2249
Change	equal	AspD vs. Biph	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Change	equal	Detm vs. Biph	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Change	equal	Detm vs. AspD	0.1304	0.1310	0.1297	0.2430	0.2410	0.2422	0.2422
		Biph change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		AspD change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		Detm change=0	0.0034	0.0033	0.0034	0.0002	0.0002	0.0002	0.0002

weight									
			ana	IT		PP			
			mod	Prim	Rest	Conf	Prim	Rest	Conf
test									
	All equal	AspD vs. Biph	0.7468	0.7433	0.7905	0.8203	0.8125	0.8414	0.8414
	All equal	Detm vs. Biph	0.0005	0.0005	0.0005	0.0011	0.0010	0.0011	0.0011
	All equal	Detm vs. AspD	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Visit 7	equal	AspD vs. Biph	0.3618	0.3539	0.4764	0.5978	0.5578	0.7272	0.7272
Visit 7	equal	Detm vs. Biph	0.4699	0.4398	0.5984	0.8743	0.7533	0.9535	0.9535
Visit 7	equal	Detm vs. AspD	0.8514	0.8789	0.8538	0.7205	0.7953	0.6895	0.6895
Change	equal	AspD vs. Biph	0.8102	0.8112	0.8150	0.8316	0.8318	0.8307	0.8307
Change	equal	Detm vs. Biph	0.0026	0.0027	0.0026	0.0049	0.0049	0.0048	0.0048
Change	equal	Detm vs. AspD	0.0055	0.0057	0.0054	0.0093	0.0093	0.0093	0.0093
		Biph change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		AspD change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		Detm change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

bmi									
			ana	IT		PP			
			mod	Prim	Rest	Conf	Prim	Rest	Conf
test									
	All equal	AspD vs. Biph	0.7147	0.7104	0.6786	0.7557	0.7499	0.7301	0.7301
	All equal	Detm vs. Biph	0.0008	0.0008	0.0007	0.0012	0.0012	0.0012	0.0012
	All equal	Detm vs. AspD	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Visit 7	equal	AspD vs. Biph	0.5557	0.5410	0.4561	0.7577	0.7172	0.6346	0.6346
Visit 7	equal	Detm vs. Biph	0.9372	0.8905	0.8825	0.7078	0.8207	0.7588	0.7588
Visit 7	equal	Detm vs. AspD	0.6103	0.6365	0.5510	0.4991	0.5617	0.4405	0.4405
Change	equal	AspD vs. Biph	0.7037	0.7043	0.7014	0.7028	0.7031	0.7036	0.7036
Change	equal	Detm vs. Biph	0.0021	0.0022	0.0021	0.0038	0.0038	0.0038	0.0038
Change	equal	Detm vs. AspD	0.0071	0.0073	0.0070	0.0118	0.0118	0.0118	0.0118
		Biph change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		AspD change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
		Detm change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

whr									
			ana	IT		PP			
			mod	Prim	Rest	Conf	Prim	Rest	Conf
test									
	All equal	AspD vs. Biph	0.6510	0.6415	0.6754	0.6884	0.6766	0.7159	0.7159
	All equal	Detm vs. Biph	0.2192	0.2114	0.2443	0.1406	0.1334	0.1621	0.1621
	All equal	Detm vs. AspD	0.5185	0.5196	0.5343	0.4821	0.4846	0.4925	0.4925
Visit 7	equal	AspD vs. Biph	0.0936	0.0894	0.1075	0.1223	0.1129	0.1368	0.1368
Visit 7	equal	Detm vs. Biph	0.0226	0.0206	0.0205	0.0100	0.0087	0.0083	0.0083
Visit 7	equal	Detm vs. AspD	0.5378	0.5286	0.4713	0.2899	0.2856	0.2396	0.2396
Change	equal	AspD vs. Biph	0.0926	0.0918	0.0901	0.0902	0.0904	0.0913	0.0913
Change	equal	Detm vs. Biph	0.0484	0.0469	0.0431	0.0446	0.0444	0.0453	0.0453
Change	equal	Detm vs. AspD	0.7516	0.7447	0.7252	0.7293	0.7269	0.7297	0.7297
		Biph change=0	0.4875	0.4802	0.4766	0.5097	0.5092	0.5151	0.5151
		AspD change=0	0.0914	0.0926	0.0912	0.0821	0.0824	0.0820	0.0820
		Detm change=0	0.0371	0.0365	0.0327	0.0310	0.0308	0.0311	0.0311

AspD change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
Detm change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000

ipkg(1)								
	ana	IT			PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf	
test								
All equal AspD vs. Biph		0.0004	0.0005	0.0003	0.0006	0.0008	0.0006	
All equal Detm vs. Biph		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
All equal Detm vs. AspD		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Visit 7 equal AspD vs. Biph		0.0123	0.0163	0.0120	0.0106	0.0139	0.0104	
Visit 7 equal Detm vs. Biph		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Visit 7 equal Detm vs. AspD		0.0000	0.0000	0.0000	0.0001	0.0002	0.0001	
Change equal AspD vs. Biph		0.0064	0.0067	0.0063	0.0099	0.0101	0.0099	
Change equal Detm vs. Biph		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Change equal Detm vs. AspD		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Biph change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
AspD change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Detm change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	

sys								
	ana	IT			PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf	
test								
All equal AspD vs. Biph		0.3440	0.3539	0.3447	0.3704	0.3774	0.3675	
All equal Detm vs. Biph		0.0741	0.0765	0.0771	0.0818	0.0838	0.0836	
All equal Detm vs. AspD		0.9303	0.9302	0.9319	0.9189	0.9189	0.9222	
Visit 7 equal AspD vs. Biph		0.3373	0.3365	0.3629	0.4064	0.3982	0.4364	
Visit 7 equal Detm vs. Biph		0.0262	0.0262	0.0299	0.0525	0.0524	0.0612	
Visit 7 equal Detm vs. AspD		0.2064	0.2069	0.2081	0.2667	0.2725	0.2741	
Change equal AspD vs. Biph		0.7282	0.7190	0.7215	0.6925	0.6935	0.6858	
Change equal Detm vs. Biph		0.1249	0.1221	0.1265	0.1024	0.1025	0.1029	
Change equal Detm vs. AspD		0.2391	0.2393	0.2451	0.2189	0.2186	0.2231	
Biph change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
AspD change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
Detm change=0		0.0165	0.0159	0.0155	0.0228	0.0224	0.0223	

dia								
	ana	IT			PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf	
test								
All equal AspD vs. Biph		0.8251	0.8216	0.8188	0.8310	0.8265	0.8223	
All equal Detm vs. Biph		0.6053	0.6443	0.6121	0.6628	0.6999	0.6667	
All equal Detm vs. AspD		0.9043	0.9217	0.9329	0.9491	0.9610	0.9600	
Visit 7 equal AspD vs. Biph		0.5282	0.5262	0.6290	0.5685	0.5568	0.6846	
Visit 7 equal Detm vs. Biph		0.6088	0.7015	0.6347	0.7077	0.8691	0.7112	
Visit 7 equal Detm vs. AspD		0.2635	0.3192	0.3482	0.3569	0.4646	0.4485	
Change equal AspD vs. Biph		0.6996	0.6908	0.7234	0.6617	0.6628	0.6653	
Change equal Detm vs. Biph		0.8795	0.9242	0.8642	0.8675	0.8783	0.8735	
Change equal Detm vs. AspD		0.5998	0.6309	0.6080	0.5565	0.5667	0.5649	
Biph change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
AspD change=0		0.0002	0.0002	0.0002	0.0002	0.0002	0.0002	
Detm change=0		0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	

pulse								
	ana	IT			PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf	
test								
All equal AspD vs. Biph		0.9840	0.9850	0.9820	0.9507	0.9571	0.9323	
All equal Detm vs. Biph		0.3460	0.3585	0.3580	0.3598	0.3810	0.3690	
All equal Detm vs. AspD		0.1496	0.1501	0.1574	0.1542	0.1533	0.1542	
Visit 7 equal AspD vs. Biph		0.9893	0.9697	0.9595	0.7553	0.7872	0.6699	
Visit 7 equal Detm vs. Biph		0.2080	0.2321	0.2454	0.1878	0.2273	0.2052	
Visit 7 equal Detm vs. AspD		0.2074	0.2219	0.2712	0.3166	0.3506	0.4012	
Change equal AspD vs. Biph		0.5168	0.5116	0.5393	0.4149	0.4162	0.4184	
Change equal Detm vs. Biph		0.1852	0.1935	0.1827	0.2187	0.2198	0.2220	

Change equal Detm vs. AspD	0.0532	0.0553	0.0565	0.0457	0.0462	0.0472	
Biph change=0	0.1222	0.1158	0.1255	0.0947	0.0939	0.0946	
AspD change=0	0.5528	0.5431	0.5297	0.6302	0.6251	0.6239	
Detm change=0	0.0011	0.0011	0.0011	0.0012	0.0012	0.0012	

chol							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.2625	0.2532	0.2461	0.2542	0.2423	0.2532	
All equal Detm vs. Biph	0.9900	0.9870	0.9846	0.9912	0.9888	0.9873	
All equal Detm vs. AspD	0.3782	0.3756	0.3834	0.4099	0.4137	0.4237	
Visit 7 equal AspD vs. Biph	0.9721	0.9962	0.9384	0.9120	0.9504	0.8500	
Visit 7 equal Detm vs. Biph	0.9218	0.8682	0.8058	0.9372	0.8793	0.8496	
Visit 7 equal Detm vs. AspD	0.8939	0.8640	0.7465	0.8515	0.8314	0.7075	
Change equal AspD vs. Biph	0.2323	0.2309	0.2121	0.2135	0.2101	0.2053	
Change equal Detm vs. Biph	0.8254	0.8079	0.8318	0.8883	0.8920	0.8925	
Change equal Detm vs. AspD	0.1603	0.1527	0.1474	0.1729	0.1715	0.1676	
Biph change=0	0.0175	0.0180	0.0141	0.0095	0.0093	0.0090	
AspD change=0	0.4832	0.4938	0.4803	0.4039	0.4058	0.4108	
Detm change=0	0.0083	0.0078	0.0068	0.0069	0.0069	0.0067	

ldl							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.3604	0.3564	0.3801	0.2698	0.2565	0.2962	
All equal Detm vs. Biph	0.9178	0.9029	0.8753	0.8984	0.8769	0.8561	
All equal Detm vs. AspD	0.5429	0.5468	0.5372	0.5397	0.5467	0.5574	
Visit 7 equal AspD vs. Biph	0.6380	0.6289	0.7122	0.5492	0.5229	0.6300	
Visit 7 equal Detm vs. Biph	0.6228	0.5843	0.5477	0.5895	0.5454	0.5194	
Visit 7 equal Detm vs. AspD	0.9782	0.9443	0.8125	0.9624	0.9830	0.8636	
Change equal AspD vs. Biph	0.2634	0.2659	0.2548	0.2038	0.2030	0.1978	
Change equal Detm vs. Biph	0.9012	0.8884	0.8639	0.9789	0.9756	0.9914	
Change equal Detm vs. AspD	0.2187	0.2148	0.1945	0.2222	0.2229	0.2101	
Biph change=0	0.0097	0.0100	0.0090	0.0056	0.0055	0.0053	
AspD change=0	0.3114	0.3124	0.3115	0.3328	0.3324	0.3353	
Detm change=0	0.0069	0.0067	0.0052	0.0084	0.0085	0.0075	

hdl							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.0575	0.0604	0.0611	0.0773	0.0834	0.0795	
All equal Detm vs. Biph	0.0346	0.0337	0.0415	0.0475	0.0426	0.0560	
All equal Detm vs. AspD	0.9592	0.9599	0.9627	0.9560	0.9525	0.9615	
Visit 7 equal AspD vs. Biph	0.0043	0.0046	0.0047	0.0071	0.0078	0.0073	
Visit 7 equal Detm vs. Biph	0.0018	0.0018	0.0022	0.0030	0.0026	0.0036	
Visit 7 equal Detm vs. AspD	0.7709	0.7546	0.8047	0.7417	0.6840	0.7823	
Change equal AspD vs. Biph	0.1112	0.1129	0.1117	0.1086	0.1103	0.1095	
Change equal Detm vs. Biph	0.0840	0.0818	0.0845	0.0887	0.0897	0.0913	
Change equal Detm vs. AspD	0.8722	0.8567	0.8725	0.8995	0.8976	0.9072	
Biph change=0	0.0840	0.0847	0.0841	0.1072	0.1094	0.1092	
AspD change=0	0.6036	0.6082	0.6057	0.5109	0.5113	0.5087	
Detm change=0	0.4671	0.4543	0.4693	0.4178	0.4163	0.4237	

vldl(1)							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.1419	0.1357	0.1453	0.1699	0.1616	0.1738	
All equal Detm vs. Biph	0.1267	0.1084	0.1145	0.1579	0.1380	0.1451	
All equal Detm vs. AspD	0.9922	0.9903	0.9928	0.9943	0.9926	0.9943	
Visit 7 equal AspD vs. Biph	0.2480	0.2535	0.2342	0.4063	0.4080	0.3892	
Visit 7 equal Detm vs. Biph	0.1895	0.1739	0.1793	0.3577	0.3211	0.3402	
Visit 7 equal Detm vs. AspD	0.8669	0.8194	0.8698	0.9175	0.8581	0.9150	

Change equal AspD vs. Biph	0.2821	0.2834	0.2985	0.3038	0.3043	0.3110
Change equal Detm vs. Biph	0.3111	0.3014	0.3119	0.3006	0.3032	0.3030
Change equal Detm vs. AspD	0.9578	0.9765	0.9848	0.9840	0.9876	0.9760
Biph change=0	0.2789	0.2794	0.2983	0.3386	0.3440	0.3417
AspD change=0	0.6615	0.6636	0.6674	0.6179	0.6115	0.6288
Detm change=0	0.7221	0.6996	0.6927	0.6071	0.6053	0.6079

trig(l)							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.3584	0.3544	0.3225	0.4523	0.4478	0.4347	
All equal Detm vs. Biph	0.6407	0.6038	0.6135	0.7484	0.7130	0.7377	
All equal Detm vs. AspD	0.8993	0.9045	0.8983	0.8918	0.9030	0.8939	
Visit 7 equal AspD vs. Biph	0.2149	0.2146	0.1840	0.3920	0.3864	0.3628	
Visit 7 equal Detm vs. Biph	0.1759	0.1619	0.1604	0.3392	0.2967	0.3224	
Visit 7 equal Detm vs. AspD	0.8993	0.8645	0.9296	0.9076	0.8464	0.9238	
Change equal AspD vs. Biph	0.5826	0.5862	0.6116	0.5620	0.5687	0.5720	
Change equal Detm vs. Biph	0.3541	0.3391	0.3653	0.3149	0.3190	0.3231	
Change equal Detm vs. AspD	0.6989	0.6735	0.6843	0.6631	0.6622	0.6647	
Biph change=0	0.4538	0.4522	0.5057	0.5468	0.5569	0.5633	
AspD change=0	0.9801	0.9882	0.9603	0.8280	0.8271	0.8251	
Detm change=0	0.5731	0.5474	0.5384	0.4149	0.4133	0.4147	

fimtavg							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.3843	0.4124	0.3849	0.4671	0.4878	0.4643	
All equal Detm vs. Biph	0.6784	0.7385	0.7292	0.9590	0.9773	0.9665	
All equal Detm vs. AspD	0.3979	0.3901	0.3852	0.4194	0.4061	0.3994	
Visit 7 equal AspD vs. Biph	0.2136	0.2494	0.2152	0.3418	0.3889	0.3365	
Visit 7 equal Detm vs. Biph	0.5332	0.5988	0.5975	0.9063	0.9875	0.9571	
Visit 7 equal Detm vs. AspD	0.5382	0.5344	0.4799	0.4164	0.3905	0.3748	
Change equal AspD vs. Biph	0.3369	0.3276	0.3343	0.3030	0.2981	0.3038	
Change equal Detm vs. Biph	0.6934	0.6983	0.6918	0.8267	0.8340	0.8187	
Change equal Detm vs. AspD	0.1793	0.1755	0.1769	0.2192	0.2188	0.2160	
Biph change=0	0.1715	0.1672	0.1708	0.1639	0.1580	0.1650	
AspD change=0	0.9945	0.9954	0.9985	0.9443	0.9483	0.9434	
Detm change=0	0.0590	0.0585	0.0583	0.1001	0.0988	0.0979	

fimtmax							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.4679	0.4787	0.4637	0.5279	0.5324	0.5241	
All equal Detm vs. Biph	0.6003	0.6552	0.6540	0.9040	0.9321	0.9135	
All equal Detm vs. AspD	0.2720	0.2683	0.2727	0.3601	0.3572	0.3511	
Visit 7 equal AspD vs. Biph	0.3446	0.3824	0.3418	0.5204	0.5663	0.5043	
Visit 7 equal Detm vs. Biph	0.5411	0.6021	0.6135	0.8926	0.9972	0.9464	
Visit 7 equal Detm vs. AspD	0.7415	0.7275	0.6588	0.6211	0.5770	0.5573	
Change equal AspD vs. Biph	0.2935	0.2847	0.2902	0.2801	0.2757	0.2808	
Change equal Detm vs. Biph	0.5734	0.5776	0.5723	0.7120	0.7200	0.7033	
Change equal Detm vs. AspD	0.1095	0.1066	0.1075	0.1534	0.1538	0.1506	
Biph change=0	0.1860	0.1811	0.1847	0.1785	0.1717	0.1799	
AspD change=0	0.8690	0.8592	0.8640	0.8518	0.8576	0.8506	
Detm change=0	0.0375	0.0370	0.0369	0.0707	0.0698	0.0688	

iem							
	ana	IT		PP			
	mod	Prim	Rest	Conf	Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.8983	0.8594	0.8831	0.8259	0.7700	0.7559	
All equal Detm vs. Biph	0.6861	0.6061	0.6720	0.8078	0.7053	0.7671	
All equal Detm vs. AspD	0.8931	0.8304	0.8759	0.9814	0.9589	0.9715	
Visit 7 equal AspD vs. Biph	0.6465	0.5828	0.6181	0.5497	0.4904	0.4853	

Visit 7 equal Detm vs. Biph	0.4617	0.3842	0.4395	0.5147	0.4045	0.4665
Visit 7 equal Detm vs. AspD	0.7833	0.7502	0.7864	0.9549	0.8822	0.9735
Change equal AspD vs. Biph	0.7692	0.8115	0.7958	0.8783	0.9018	0.9164
Change equal Detm vs. Biph	0.4414	0.3948	0.4376	0.7310	0.6794	0.7399
Change equal Detm vs. AspD	0.6356	0.5425	0.6068	0.8490	0.7729	0.8211
Biph change=0	0.3803	0.3867	0.3817	0.3818	0.3851	0.3835
AspD change=0	0.2001	0.2334	0.2187	0.2820	0.3042	0.3150
Detm change=0	0.0510	0.0400	0.0503	0.1848	0.1564	0.1913

csc2

	ana mod	IT Prim	Rest	Conf	PP Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.8582	0.7925	0.8136	0.7429	0.6853	0.6433	
All equal Detm vs. Biph	0.8718	0.7975	0.8502	0.9243	0.8548	0.8861	
All equal Detm vs. AspD	0.9010	0.8507	0.8813	0.9378	0.9565	0.9137	
Visit 7 equal AspD vs. Biph	0.6942	0.6145	0.6619	0.5793	0.5086	0.5069	
Visit 7 equal Detm vs. Biph	0.6027	0.5057	0.5693	0.7933	0.6362	0.7354	
Visit 7 equal Detm vs. AspD	0.8999	0.8730	0.8971	0.7731	0.8551	0.7478	
Change equal AspD vs. Biph	0.8863	0.8645	0.8507	0.8326	0.8305	0.7885	
Change equal Detm vs. Biph	0.7610	0.6959	0.7634	0.8815	0.9405	0.8690	
Change equal Detm vs. AspD	0.6565	0.5766	0.6266	0.9520	0.8913	0.9200	
Biph change=0	0.5970	0.6116	0.5993	0.6529	0.6594	0.6569	
AspD change=0	0.7475	0.7932	0.7987	0.8839	0.8941	0.9516	
Detm change=0	0.3416	0.2928	0.3456	0.8195	0.7466	0.8409	

imtareal

	ana mod	IT Prim	Rest	Conf	PP Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.4277	0.5343	0.4275	0.5930	0.6986	0.6026	
All equal Detm vs. Biph	0.1694	0.2070	0.1907	0.5951	0.6439	0.6255	
All equal Detm vs. AspD	0.7114	0.6844	0.6903	0.8782	0.8638	0.8300	
Visit 7 equal AspD vs. Biph	0.3205	0.4042	0.3132	0.4335	0.5324	0.4333	
Visit 7 equal Detm vs. Biph	0.3681	0.4529	0.4387	0.7116	0.8344	0.7988	
Visit 7 equal Detm vs. AspD	0.9256	0.9336	0.8138	0.6879	0.6851	0.6045	
Change equal AspD vs. Biph	0.6346	0.6534	0.6636	0.6994	0.7164	0.7274	
Change equal Detm vs. Biph	0.1978	0.1916	0.1936	0.4215	0.4111	0.4149	
Change equal Detm vs. AspD	0.4196	0.3947	0.3902	0.6771	0.6478	0.6422	
Biph change=0	0.5265	0.5217	0.5315	0.6332	0.6321	0.6277	
AspD change=0	0.9660	0.9988	0.9948	0.9422	0.9688	0.9900	
Detm change=0	0.2363	0.2293	0.2267	0.5111	0.4960	0.5058	

n.pl(1)

	ana mod	IT Prim	Rest	Conf	PP Prim	Rest	Conf
test							
All equal AspD vs. Biph	0.4705	0.5257	0.3718	0.4828	0.5667	0.4040	
All equal Detm vs. Biph	0.4982	0.4696	0.5032	0.6564	0.6596	0.6039	
All equal Detm vs. AspD	0.2700	0.2765	0.2497	0.7409	0.7683	0.7457	
Visit 7 equal AspD vs. Biph	0.2212	0.2602	0.1596	0.2319	0.2971	0.1794	
Visit 7 equal Detm vs. Biph	0.9865	0.9311	0.8729	0.5550	0.6120	0.4451	
Visit 7 equal Detm vs. AspD	0.2238	0.2353	0.2207	0.5656	0.6119	0.5826	
Change equal AspD vs. Biph	0.6514	0.6517	0.6622	0.6238	0.6184	0.6325	
Change equal Detm vs. Biph	0.2616	0.2512	0.2481	0.4020	0.3854	0.3997	
Change equal Detm vs. AspD	0.5139	0.4983	0.4848	0.7345	0.7183	0.7226	
Biph change=0	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	
AspD change=0	0.0004	0.0003	0.0003	0.0006	0.0006	0.0005	
Detm change=0	0.0087	0.0091	0.0084	0.0036	0.0038	0.0034	

8.3 Graphs of trajectories

Finally we want to plot the estimates, so we put the plotting of a single variable into a function. But first we need a convenience function to place text on the graph:

```
> source( "cnr.R" )
> cnr
function (xf, yf)
{
  cn <- par()$usr
  xf <- ifelse(xf > 1, xf/100, xf)
  yf <- ifelse(yf > 1, yf/100, yf)
  xx <- (1 - xf) * cn[1] + xf * cn[2]
  yy <- (1 - yf) * cn[3] + yf * cn[4]
  if (par()$xlog)
    xx <- 10^xx
  if (par()$ylog)
    yy <- 10^yy
  list(x = xx, y = yy)
}

> pleff <-
+ function( var,
+          ytxt = var,
+          yl = NULL, # yaxis limits
+          yt = NULL, # yaxis major ticks
+          ym = NULL, # yaxis minor ticks
+          hl = ym )
+ {
+ # Get the estimates, but only for the times where they are, otherwise
+ # the the points will not be connected (a feature)
+ var <- dimnames(Eff)$var[grep(var,vnam <- dimnames(Eff)$var)]
+ eff <- Eff[var,"IT","Prim",,,]
+ pef <- cbind( eff[-8,,ilev[1]],
+              eff[-8,,ilev[2]],
+              eff[-8,,ilev[3]] )
+ pef <- pef[complete.cases(pef),]
+ tim <- (as.numeric( gsub("Vis ", "",rownames(pef) ) )-1)*3
+
+ if( is.null(yl) ) yl <- range(pef)*c(0.9,1.2)
+ matplot( tim, pef, type="n",
+          xlab="Months since trial entry", xaxt="n", xlim=c(0,19.5),
+          ylab=ytxt, ylim=yl, yaxs="i", yaxt="n", bty="n" )
+ if( !is.null(hl) ) abline( h=hl, col=gray(0.8) )
+ axis( side=1, at=0:6*3, col=clr[4] )
+ axis( side=2, if(!is.null(yt)) at=yt, col=clr[4] )
+ axis( side=2, if(!is.null(ym)) at=ym, labels=rep("",length(ym)), col=clr[4] )
+ text( cnr(c(98,98,98),c(98,92,86)), iN, col=iclr[1:3],
+       font=2, adj=c(1,1), cex=1.2 )
+ if( ltrf[match(var,vnam)] ) { text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+                                   "% change\nfrom baseline", col=clr[4], adj=c(1,0.5) )
+ } else {
+                                   text( cnr(98,74)[[1]], cnr(98,74)[[2]],
+                                   "Change\nfrom baseline", col=clr[4], adj=c(1,0.5) ) }
+ EF <- eff[8,"Est",ilev]
+ # It might not be vist 7 that is the last non-missing, so find that
+ ends <- eff[1:7,"Est",ilev]
+ ends <- ends[max(which(!is.na(ends[,1]))),]
+ # dv <- ends-mean(ends) ; dv <- dv/abs(dv)
+ oe <- order( ends )
+ eo <- c(mean(ends),ends[oe])
+ de <- diff(eo)
+ nd <- de[-1]/abs(de[-1])*pmax( abs(de[-1]), diff(yl)/30 )
+ de <- c(de[1]+nd[1]-de[2],nd)
+ eo <- eo[1] + cumsum(de)
+ ends <- eo[order(oe)]
+ if( ltrf[match(var,vnam)] ) EF <- (EF-1)*100
```

```

+ # print( c(EF, ends ) )
+ text( c(20,20,20), ends,
+       paste( formatC( EF, format="f", digits=1 ), sep="" ),
+       col=iclr[1:3], adj=1, font=2 )
+ matlines( tim, pef, type="l", lwd=c(5,1,1), lty=1, col=rep(iclr[1:3],each=3) )
+ }

```

So we can draw two example graphs, groomed to look nice:

```

> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
> pleff( "hba1c", expression("Hb"*A[1][c]*" (%) [Mean (95% CI)]"),
+       yl = c(7,10),
+       yt = 7:10,
+       ym = seq(7,10,0.5) )

```

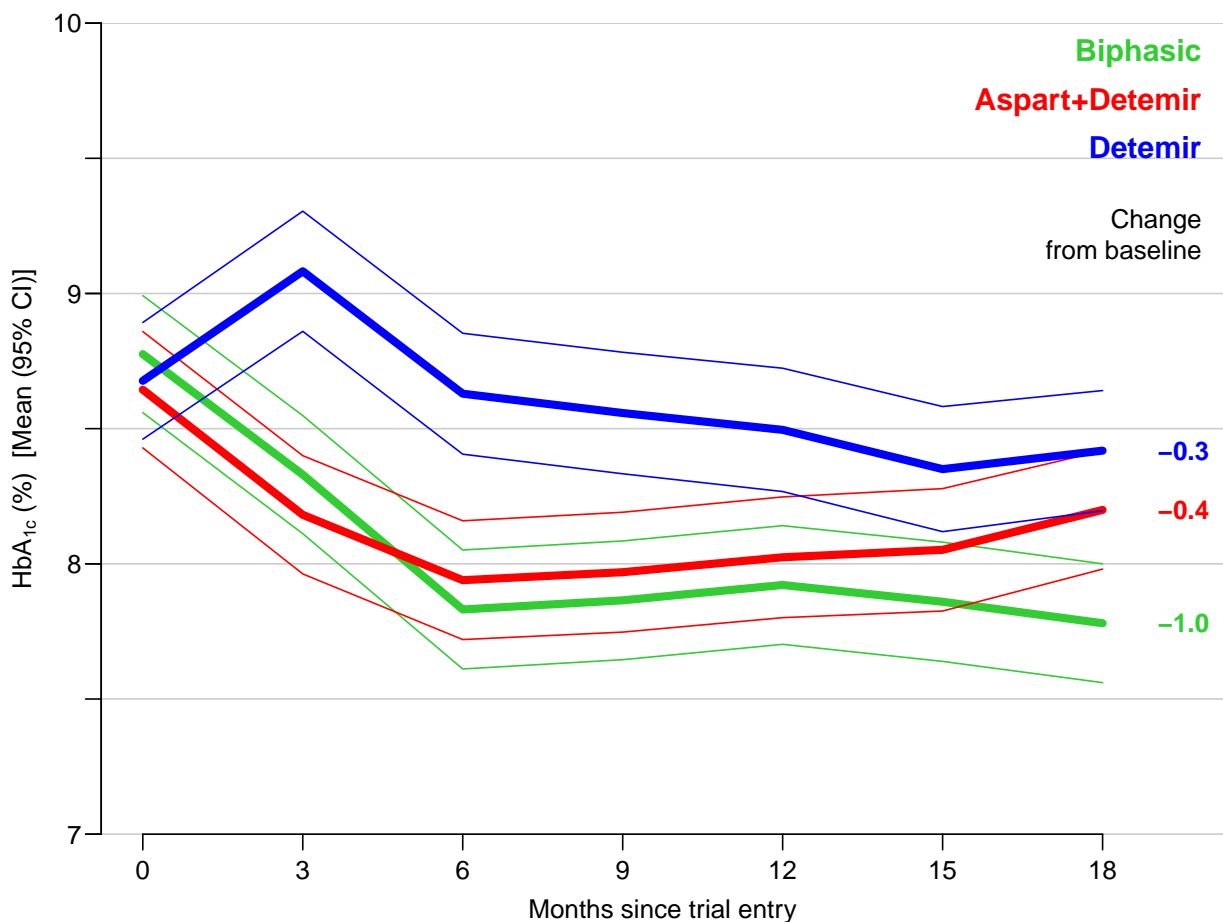


Figure 8.2: Trajectories for HbA_{1c} , illustrating how parameters translate into the graph.

```

> par( mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
> pleff("trig", "Triglycerides (mmol/l) [Mean (95% CI)]",
+       yl = c(1,2.5), # yaxis limits
+       yt = 0:4, # yaxis major ticks
+       ym = seq(1,3,0.25) ) # yaxis minor ticks

```

With this function in place it is now simple to produce plots for all the variables, as a first guide to how they should be individually adjusted to look sensible:

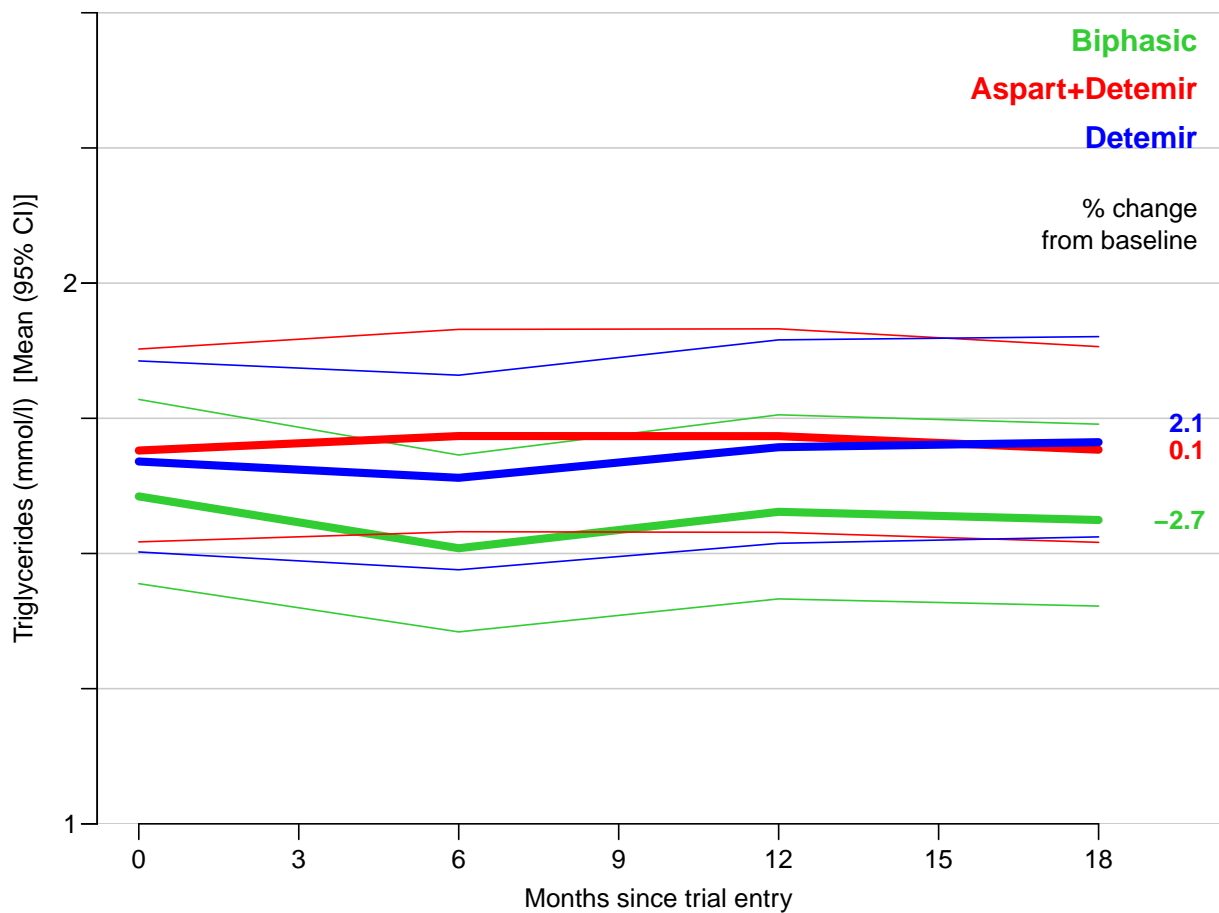


Figure 8.3: Trajectories for Triglycerides, illustrating how parameters translate into the graph.

```
> tmpl <-
+ function()
+ {
+ par( mfrow=c(2,2), mar=c(3,3,1,1), mgp=c(3,1,0)/1.6, las=1 )
+ # HbA1c:
+ pleff( "hba1c",
+       expression("Hb"*A[1][c]*" (%) [Mean (95% CI)]"),
+       yl = c(7,10),
+       yt = 7:10,
+       ym = seq(7,10,0.5) )
+ text( cnr(2,98), "a", adj=c(0,1), font=2, cex=1.5 )
+ # Gluc
+ pleff("gluc","Fasting p-glucose (mmol/L) [Mean (95% CI)]",
+       yl = c(7,12), # yaxis limits
+       yt = seq(7,13,2), # yaxis major ticks
+       ym = seq(7,13,1) ) # yaxis minor ticks
+ text( cnr(2,98), "b", adj=c(0,1), font=2, cex=1.5 )
+ # Insulin dose
+ pleff("ipkg","Insulin dose (IU/day/kg) [Mean (95% CI)]",
+       yl = c(0.0,2.4), # yaxis limits
+       yt = seq(0.0,2.0,1.0), # yaxis major ticks
+       ym = seq(0.0,2.4,0.2) ) # yaxis minor ticks
+ text( cnr(2,98), "c", adj=c(0,1), font=2, cex=1.5 )
+ # Weight:
+ pleff("weight","Weight (kg) [Mean (95% CI)]",
+       yl = c(90,120), # yaxis limits
```

```

+           yt = seq(90,120,10), # yaxis major ticks
+           ym = seq(90,120,5) ) # yaxis minor ticks
+ text( cnr(2,98), "d", adj=c(0,1), font=2, cex=1.5 )
+ }
> tml()

```

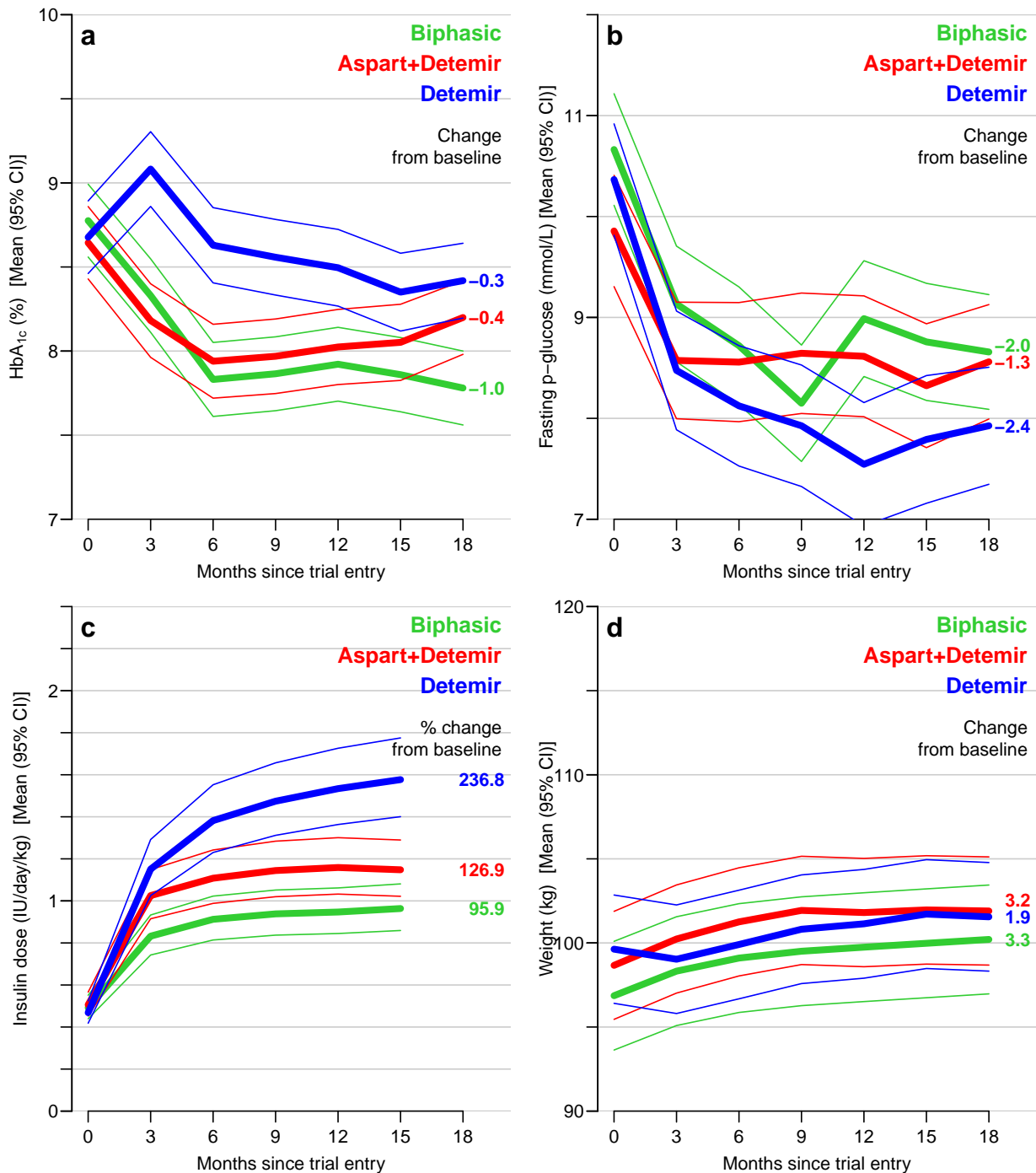


Figure 8.4: Trajectory plots for the first 4 variables.

```

> win.metafile( "./results/first4-ins.emf", height=9, width=8 )
> tml()
> dev.off()

```

null device
1