```stata
1
2    cd "..."
3    cap log close
4    log using "log_cleaning", replace
5    cls
6    set more off
7    cd "..."
8    use "hypo_database_Oct.dta", clear
9    set seed 987654
10
11   /*data checking and cleaning*/
12   rename patid id
13   distinct id
14   rename townsend2001_5 imd
15
16   format %9.0g smk_date
17   foreach var of varlist *date {
18       replace `var' = (`var' - studyentry)/(365.24/12)
19       }
20   mdesc egfr_date-w_date
21
22   tabstat aspirin_date statin_date egfr_date hba1c_date ldl_date chol_date bp_date smk_date alc_date w_date, statistics(mean median p25 p75 p5
     p95) columns(statistics) format(%7.2f)
23
24   drop alc_week diastolic marital
25   mdesc imd af_date af0 alc_date alc_status aspirin_date bmi aspirin0 bp_date systolic chol_date cholesterol diagdate egfr_date egfr ethnic
     gender /*
26   */hba1c_date hba1c_last ldl_date ldl mean_hba1c median_hba1c sd_hba1c smk_date smk_status statin_date statin0 stroke_date stroke0 w_date weight
27   mdesc imd alc_date alc_status bmi bp_date systolic chol_date cholesterol diagdate egfr_date egfr ethnic gender /*
28   */hba1c_date hba1c_last ldl_date ldl mean_hba1c median_hba1c sd_hba1c smk_date smk_status w_date weight
29
30   rename alc_status alc
31   rename systolic sbp
32   rename cholesterol tchol
33   rename ethnic eth
34   rename gender sex
35   rename hba1c_last la1c
36   rename smk_status smk
37   rename aspirin0 asa0
38   rename statin0 stat0
39   gsort -sex
40   sencode sex, replace
41   sort id
42   mdesc imd alc bmi sbp tchol egfr eth sex la1c smk asa0 stat0 af0 stroke0 pad0 hf0 cancer0 mi0
43
44   tab eth, m
45   replace eth = "nonWhite" if (eth != "White" & eth != "")
```

```stata
46    tab eth, m
47
48    tab cause, sort m
49    rename cause ICD_code
50    merge m:1 ICD_code using "icd.dta"
51    drop description
52    drop if _merge == 2
53    gsort -death _merge
54    tab _merge if death == 1
55    order ICD_code, before(icd)
56    tab ICD_code if (_merge == 1 & death == 1), sort
57    cls
58    tab ICD_code if (_merge == 1 & death == 1)
59    rename cause_death type
60    replace type = "cvd" if type == "Cardiovascular"
61    replace type = "tum" if type == "Cancer"
62    replace type = "other" if type == "" & ICD_code != ""
63    drop _merge icd_version
64    rename ICD_code cause
65    replace studytime = studytime/365.24
66    rename studytime time
67
68    gen tcvd = time
69    gen dcvd = 1 if type == "cvd"
70    replace dcvd = 0 if type != "cvd"
71    gen ttum = time
72    gen dtum = 1 if type == "tum"
73    replace dtum = 0 if type != "tum"
74    gen tother = time
75    gen dother = 1 if type == "other"
76    replace dother = 0 if type != "other"
77    gen tall = time
78    gen dall = 1 if cause != ""
79    replace dall = 0 if cause == ""
80
81    gen day = runiform()
82    gen datebirth = yob + day
83    drop day
84    format studyentry %td
85    gen timezero = 2011 + runiform()/365.24
86    gen age0 = timezero-datebirth
87    sort eth
88    sencode eth, replace
89    sort id
90    mdesc age0 sex eth imd bmi smk alc sbp tchol ldl egfr la1c mean_hba1c median_hba1c sd_hba1c insulin metformin su othergld cancer0 mi0 pad0
          stroke0 hf0 af0 stat0 asa0
91    egen float glulow = rowtotal(insulin su metformin othergld)
```

```stata
 92    tab glulow
 93    egen float glumiss = rowmiss(insulin su metformin othergld)
 94    tab glumiss
 95    foreach var of varlist insulin su metformin othergld {
 96        replace `var' = 0 if `var' == .
 97        }
 98    mdesc age0 sex eth imd bmi smk alc sbp tchol ldl egfr la1c mean_hba1c median_hba1c sd_hba1c insulin metformin su othergld cancer0 mi0 pad0
       stroke0 hf0 af0 stat0 asa0
 99    drop glulow glumiss
100    save "db0", replace
101    log close
102
103
104    *###############################################################################
105    ///////////////////////////////////MAIN ANALYSIS//////////////////////////////////////////
106    *###############################################################################
107
108    cap log close
109    log using "log_analysis", replace
110
111    *#######################################################
112    *********************descriptive*********************
113    cls
114    use "db0", clear
115    describe, short
116
117    sum age0 sbp tchol la1c bmi egfr
118    drop if sbp == 0                          /*12  patients*/
119    drop if bmi == 0 | bmi <10 | bmi >70      /*735 patients*/
120    drop if tchol>10                          /*504 patients*/
121    drop if egfr>150                          /*210 patients*/
122
123    mdesc age0 sex eth smk alc sbp tchol la1c bmi egfr imd
124    describe, short
125    egen float miss = rowmiss(age0 sex eth smk alc sbp tchol la1c bmi egfr imd) /*key variables for primary analysis - base model*/
126    tab miss
127    keep if miss == 0
128    drop miss
129    describe, short
130
131    forvalues k = 1/3 {
132        gen tbef`k' = -(hypodate`k' - studyentry)/(365.24/12)
133    }
134    distplot tbef1, xlabel(0(6)156, labsize(vsmall) grid) xtitle("Last hypoglycaemia before study entry (months)", size(small)) /*
135    */            ylabel(#10, angle(horizontal) format(%7.1f) labsize(vsmall)) ytitle("Probability", size(small)) legend(position(5) ring(0))
       xsize(6.5) ysize(4.5)
136    graph save Graph "Results\distplot.gph", replace
```

```stata
137    graph close _all
138
139    tab N_hypo1, m
140    tab N_hypo2, m
141    tab N_hypo3, m
142    gen la1cm = (la1c - 2.15)*10.929
143
144    baselinetable                          /*
145    */  age0(cts tab("p50 (p25-p75)"))  /*
146    */  sex(cat)                          /*
147    */  eth(cat)                          /*
148    */  imd(cat)                          /*
149    */  smk(cat)                          /*
150    */  alc(cat)                          /*
151    */  sbp(cts tab("p50 (p25-p75)"))   /*
152    */  tchol(cts tab("p50 (p25-p75)")) /*
153    */  la1c(cts tab("p50 (p25-p75)"))  /*
154    */  la1cm(cts tab("p50 (p25-p75)")) /*
155    */  bmi(cts tab("p50 (p25-p75)"))   /*
156    */  egfr(cts tab("p50 (p25-p75)"))  /*
157    */  metformin(cat)                    /*
158    */  su(cat)                           /*
159    */  insulin(cat)                      /*
160    */  othergld(cat)                     /*
161    */  mi0(cat)                          /*
162    */  stroke0(cat)                      /*
163    */  pad0(cat)                         /*
164    */  hf0(cat)                          /*
165    */  af0(cat)                          /*
166    */  stat0(cat)                        /*
167    */  asa0(cat)                         /*
168    */  cancer0(cat)                      /*
169    */  dall(cat)                         /*
170    */  dcvd(cat)                         /*
171    */  dtum(cat)                         /*
172    */  dother(cat)                       /*
173    */  , by(hypo1, totalcolumn) notable exportexcel("Results\table_1", replace)
174
175    drop la1cm
176
177    forvalues k = 0/1 {
178        preserve
179        contract cause if type == "other" & hypo1 == `k', freq(freq`k')
180        gsort -freq`k'
181        tempfile other`k'
182        save `other`k'', replace
183        restore
```

```stata
184     }
185     preserve
186     use `other0', clear
187     merge 1:1 cause using `other1'
188     gsort -freq1 -freq0
189
190     forvalues k = 0/1 {
191         gen cum`k' = sum(freq`k')
192         egen float tot`k' = total(freq`k')
193         gen p`k' = freq`k'*100/tot`k', after(tot`k')
194         gen p_cum`k' = cum`k'*100/tot`k'
195     }
196     drop if p_cum0 >=75  /*no ties*/
197     forvalues k = 0/1 {
198         replace freq`k' = 0 if freq`k' == .
199         replace p`k'    = 0 if p`k'    == .
200     }
201     gen cruded = p1-p0
202     rename cause icd
203     drop _merge
204     merge 1:1 icd using "ICD10"
205     drop if _merge == 2
206     sort disease icd
207     replace disease = "Diarrhoea and gastroenteritis of presumed infectious origin" if icd == "A09.9"
208     replace disease = "Unspecified dementia"                          if icd == "F03"
209     replace disease = "Parkinson's disease"                          if icd == "G20"
210     replace disease = "Other secondary pulmonary hypertension"       if icd == "I27.2"
211     replace disease = "Unspecified atrial fibrillation and atrial flutter" if icd == "I48.9"
212     replace disease = "Unspecified acute lower respiratory infection" if icd == "J22"
213     replace disease = "Bronchiectasis"                               if icd == "J47"
214     replace disease = "Esophagitis"                                  if icd == "K20"
215     replace disease = "Indeterminate colitis"                        if icd == "K52.3"
216     replace disease = "Pyoderma gangrenosum"                         if icd == "L88"
217     replace disease = "Pressure ulcer"                               if icd == "L89"
218     replace disease = "Unspecified kidney failure"                   if icd == "N19"
219     replace disease = "Benign prostatic hyperplasia"                 if icd == "N40"

220     replace disease = "Senility"                                     if icd == "R54"
221     replace disease = "Other ill-defined and unspecified causes of mortality" if icd == "R99"
222     save "Results\bars_other", replace
223     restore
224
225     foreach var of varlist age0 sbp tchol la1c bmi egfr {
226         gen ln_`var' = ln(`var')
227     }
228
229     *###########################################################
```

```stata
230     ********************survival**************************
231     cls
232     tab sex, m
233     sdecode sex, replace
234     replace sex = "0" if sex == "F"
235     replace sex = "1" if sex == "M"
236     destring sex, replace
237
238     tab eth, m
239     sdecode eth, replace
240     replace eth = "0" if eth == "White"
241     replace eth = "1" if eth == "nonWhite"
242     destring eth, replace
243
244     tab smk, m
245     sdecode smk, replace
246     replace smk = "0" if smk == "no"
247     replace smk = "1" if smk == "ex"
248     replace smk = "2" if smk == "yes"
249     destring smk, replace
250
251     tab alc, m
252     sdecode alc, replace
253     replace alc = "0" if alc == "no"
254     replace alc = "1" if alc == "ex"
255     replace alc = "2" if alc == "yes"
256     destring alc, replace
257
258     tab imd, m
259
260     foreach var of varlist smk alc imd {
261         tab `var', gen(`var')
262     }
263     save "db1", replace
264
265     ********************Age-specific CC SURVIVAL at different times: stacked only, no CI********************
266
267     use "db1", clear
268     rcsgen age0, gen(age0s) orthog df(3)
269     global Kage `r(knots)'
270     matrix Mage = r(R)
271     foreach mod of varlist age0s* {
272         gen i_`mod' = `mod'*hypo1
273     }
274     foreach q in cvd tum other {
275         stset t`q', id(id) failure(d`q'==1)
276         stdescribe
```

```stata
277        stsum
278        strate hypo1, per(1000)
279        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5, scale(h) df(4)

280        estimates store `q'
281    }
282
283    display "$S_TIME  $S_DATE"
284    range tt 0 5 51
285    forvalues k = 50(10)80 {
286        preserve
287        rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
288        standsurv, crmodels(cvd tum other) cif timevar(tt) atvar(hno hyes) verbose                                /*
289        */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0    i_age0s2 0    i_age0s3 0)         /*
290        */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
291        keep tt hno* hyes*
292        drop if tt == .
293        gen age0 = `k'
294        tempfile r`k'
295        save `r`k'', replace
296        restore
297    }
298
299    display "$S_TIME  $S_DATE"
300    preserve
301    clear
302    forvalues k = 50(10)80 {
303        append using `r`k''
304    }
305    gen hno_stack0  = hno_cvd
306    gen hno_stack1  = hno_cvd  + hno_tum
307    gen hno_stack2  = hno_cvd  + hno_tum  + hno_other
308    gen hyes_stack0 = hyes_cvd
309    gen hyes_stack1 = hyes_cvd + hyes_tum
310    gen hyes_stack2 = hyes_cvd + hyes_tum + hyes_other
311    gen dif_stack0  = hyes_stack0 - hno_stack0
312    gen dif_stack1  = hyes_stack1 - hno_stack1
313    gen dif_stack2  = hyes_stack2 - hno_stack2
314    order age0, last
315    foreach var of varlist h* d* {
316        replace `var' = `var' * 100
317        }
318    save "Results\survage", replace
319    restore
320
321    ***************************Age-specific SURVIVAL at 5 years only: different CC models********************************
322    use "db1", clear
```

```
323    gen t5 = 5 in 1
324    display "$S_TIME  $S_DATE"
325
326    rcsgen age0, gen(age0s) orthog df(3)
327    global Kage `r(knots)'
328    matrix Mage = r(R)
329    foreach mod of varlist age0s* {
330        gen i_`mod' = `mod'*hypo1
331    }
332
333    *-------------------------------
334    ****base model CC - cpr*
335    foreach q in cvd tum other {
336        stset t`q', id(id) failure(d`q'==1)
337        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5, scale(h) df(4)
338        estimates store `q'
339    }
340    forvalues k = 50(10)80 {
341        preserve
342        rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
343        standsurv, crmodels(cvd tum other) cif timevar(t5) atvar(hno hyes) contrast(difference) contrastvar(dif) ci verbose /*
344        */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0    i_age0s2 0    i_age0s3 0)                    /*
345        */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
346        keep t5 hno* hyes* dif*
347        drop if t5 == .
348        gen age0 = `k'
349        tempfile r`k'
350        save `r`k'', replace
351        restore
352    }
353
354    clear
355    forvalues k = 50(10)80 {
356        append using `r`k''
357    }
358    order age0, last
359    gen model   = "baseCC"
360    save "Results\fplot_baseCC", replace
361    display "$S_TIME  $S_DATE"
362
363    *-------------------------------
364    ****other covs model CC - cpr*
365    foreach q in cvd tum other {
366        stset t`q', id(id) failure(d`q'==1)
367        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
368        */   metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
```

```stata
369          estimates store `q'
370      }
371      forvalues k = 50(10)80 {
372          preserve
373          rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
374          standsurv, crmodels(cvd tum other) cif timevar(t5) atvar(hno hyes) contrast(difference) contrastvar(dif) ci verbose /*
375          */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0     i_age0s2 0     i_age0s3 0)                      /*
376          */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
377          keep t5 hno* hyes* dif*
378          drop if t5 == .
379          gen age0 = `k'
380          tempfile r`k'
381          save `r`k'', replace
382          restore
383      }
384
385      clear
386      forvalues k = 50(10)80 {
387          append using `r`k''
388      }
389      order age0, last
390      gen model = "covsCC"
391      save "Results\fplot_covsCC", replace
392      display "$S_TIME  $S_DATE"
393      restore
394      log close
395
396
397      *###########################################################################
398      ***************************MULTIPLE IMPUTATIONS*****************************
399      *###########################################################################
400
401      cap log close
402      log using "log_MImputation", replace
403
404      *databases and estimations*
405      cls
406      use "db0", clear
407      describe, short
408      mdesc age0 sex eth smk alc sbp tchol la1c bmi egfr imd /*
409      */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0
410
411      drop if sbp == 0                     /*12  patients*/
412      drop if bmi == 0 | bmi <10 | bmi >70    /*735 patients*/
413      drop if tchol>10                     /*504 patients*/
414      drop if egfr>150                     /*210 patients*/
415
```

```
416    mdesc age0 sex eth smk alc sbp tchol la1c bmi egfr imd /*
417    */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0
418    describe, short
419
420    cls
421    tab sex, m
422    sdecode sex, replace
423    replace sex = "0" if sex == "F"
424    replace sex = "1" if sex == "M"
425    destring sex, replace
426    tab eth, m
427    sdecode eth, replace
428    replace eth = "0" if eth == "White"
429    replace eth = "1" if eth == "nonWhite"
430    destring eth, replace
431    tab smk, m
432    sdecode smk, replace
433    replace smk = "0" if smk == "no"
434    replace smk = "1" if smk == "ex"
435    replace smk = "2" if smk == "yes"
436    destring smk, replace
437    tab alc, m
438    sdecode alc, replace
439    replace alc = "0" if alc == "no"
440    replace alc = "1" if alc == "ex"
441    replace alc = "2" if alc == "yes"
442    destring alc, replace
443    tab imd, m
444
445    local u = 10        /*databases imputed*/
446
447    mi set mlong
448
449    mi register imputed eth smk alc sbp la1c imd                        /*   variables with missing data*/
450
451    mi register regular age0 sex tchol bmi egfr /*
452    */        metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0  /*   covariates included in the model without missing
       + outcomes
453    */        dcvd dtum dother tall hypo1                               /*   time is the same for all outcomes*/
454
455    mi impute chained (regress) sbp la1c (logit) eth (mlogit) smk alc imd =   /*   covariates needed to be imputed
456    */        age0 sex tchol bmi egfr                                   /*   all other covariates
457    */        metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0  /*
458    */        dcvd dtum dother tall hypo1, add(`u')                     /*   seed not defined as already defined above*/
459
460    foreach var of varlist smk alc imd {
461        tab `var', gen(`var')
```

```
462     }
463
464     forvalues j = 1/`u' {
465         display "$S_TIME  $S_DATE -- database MI: `j'"
466
467         preserve
468         *single dataset
469         mi extract `j', clear
470
471         *make spline & interactions
472         rcsgen age0, gen(age0s) orthog df(3)
473         global Kage `r(knots)'
474         matrix Mage = r(R)
475         foreach mod of varlist age0s* {
476             gen i_`mod' = `mod'*hypo1
477         }
478
479         *cmprisk - coeffs
480         foreach q in cvd tum other {
481             stset t`q', id(id) failure(d`q'==1)
482             stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
483             */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
484             estimates store `q'
485         }
486
487         *cmprisk - standsurv
488         gen t5 = 5 in 1
489         forvalues k = 50(10)80 {
490             rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
491             standsurv, crmodels(cvd tum other) cif timevar(t5) atvar(hno hyes) contrast(difference) contrastvar(dif) se ci verbose  /*
492             */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0     i_age0s2 0     i_age0s3 0)                        /*
493             */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
494             gen age = `k' in 1
495             gen db  = `j' in 1
496             tempfile c`k'_`j'
497             save `c`k'_`j'', replace
498             drop hno* hyes* dif* age db
499         }
500
501         *all death - coeffs
502         stset tall, id(id) failure(dall==1)
503         stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
504         */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
505
506         *all death - standsurv
507         forvalues k = 50(10)80 {
508             rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
```

```stata
509              standsurv, timevar(t5) atvar(hno_all hyes_all) contrast(difference) contrastvar(dif_all) ci se verbose  /*
510          */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0      i_age0s2 0      i_age0s3 0)          /*
511          */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
512              gen age = `k' in 1
513              gen db  = `j' in 1
514              tempfile a`k'_`j'
515              save `a`k'_`j'', replace
516              drop hno* hyes* dif* age db
517          }
518          restore
519      }
520
521      clear
522      tempfile cmpr
523      forvalues k = 50(10)80 {
524          forvalues j = 1/`u' {
525              append using `c`k'_`j''
526          }
527      }
528      keep t5 hno* hyes* dif* age db
529      drop if t5 == .
530      save `cmpr', replace
531
532      clear
533      tempfile alld
534      forvalues k = 50(10)80 {
535          forvalues j = 1/`u' {
536              append using `a`k'_`j''
537          }
538      }
539      keep t5 hno* hyes* dif* age db
540      drop if t5 == .
541      merge 1:1 db age using `cmpr'
542      drop _merge
543      order t5 db age, first
544      drop t5
545      display "$S_TIME  $S_DATE"
546      save "Results\MI", replace
547      log close
548
549      use "Results\MI", clear
550      keep db age dif*
551      drop *_lci *_uci
552      foreach var of varlist dif_all - dif_other_se {
553          replace `var' = `var' * 100
554      }
555      replace dif_all = -dif_all       /*for all-cause the estimate is survival, for cause-specific is cif*/
```

```stata
556    foreach k in all cvd tum other {
557        rename dif_`k' `k'
558        rename dif_`k'_se `k'_se
559    }
560    sort age db
561
562    preserve
563    clear
564    tempfile mim
565    save `mim', emptyok replace
566    restore
567
568    forvalues k = 50(10)80 {
569        foreach e in all cvd tum other {
570            preserve
571            keep if age == `k'
572            local m = _N
573            di `m'                      /*This is Rubin's rule on the survival difference*/
574            keep age `e' `e'_se
575            egen q  = mean(`e')
576            gen  u1 = `e'_se^2
577            egen u  = mean(u1)
578            gen  b1 = (`e'-q)^2
579            egen b2 = total(b1)
580            gen  b  = b2/(`m'-1)
581            gen  t  = u + b*(1+1/`m')
582            gen  se = t^0.5
583            keep in 1
584            keep age q se
585            gen  lb = q - 1.96*se
586            gen  ub = q + 1.96*se
587            rename q es
588            gen  end = "`e'"
589            append using `mim'
590            save `mim', replace
591            restore
592        }
593    }
594    use `mim', clear
595    sort end age
596    gen     s = 1 if end == "cvd"
597    replace s = 2 if end == "tum"
598    replace s = 3 if end == "other"
599    replace s = 4 if end == "all"
600    sort s age
601    foreach var of varlist es lb ub {
602        tostring `var', replace format(%7.1f) force
```

```stata
603    }
604    gen dif = es + " (" + lb + ", " + ub + ")"
605    keep age end dif
606    reshape wide dif, i(age) j(end) string
607    order age difcvd diftum difother difall
608    export excel using "Results\MI_results.xls", firstrow(variables) replace
609
610
611    *###########################################################################
612    ***********************GRAPHS***********************************************
613    *###########################################################################
614
615    ****BARS
616    cd "..."
617    use "Results\bars_other", clear
618    set scheme s2color
619    distinct disease
620    duplicates tag disease, generate(dupdis)
621    replace disease = disease + " (" + icd + ")" if dupdis == 2
622    replace disease = "COPD wth acute exacerbation, unspec" if disease == "Chron obstruct pulmonary dis wth acute exacerbation, unspec"
623    replace disease = "COPD with acute lower resp infec"    if disease == "Chronic obstruct pulmonary dis with acute lower resp infec"
624    replace disease = "COPD unspecified"                    if disease == "Chronic obstructive pulmonary disease, unspecified"
625    replace disease = "IDDM with renal complications"       if disease == "Insulin-dependent diabetes mellitus with renal complications"
626    replace disease = "NIDDM without complications"         if disease == "Non-insulin-depend diabetes mellitus without complication"
627    replace disease = "NIDDM with multiple complications"   if disease == "Non-insulin-dependent diabetes mellitus with multiple comps"
628    replace disease = "NIDDM with renal complications"      if disease == "Non-insulin-dependent diabetes mellitus with renal comps"
629    replace disease = "UDM with ketoacidosis"               if disease == "Unspecified diabetes mellitus with ketoacidosis"
630    replace disease = "UDM with multiple complications"     if disease == "Unspecified diabetes mellitus with multiple complications"
631    replace disease = "UDM with renal complications"        if disease == "Unspecified diabetes mellitus with renal complications"
632    replace disease = "UDM without complications"           if disease == "Unspecified diabetes mellitus without complications"
633    graph hbar (asis) p0 p1, over(disease, sort(cruded) label(labsize(tiny))) /*
634    */    bar(1, fcolor(forest_green) lcolor(forest_green) lwidth(none)) bar(2, fcolor(red) lcolor(red) lwidth(none)) /*
635    */    xsize(9) ysize(8) legend(order(1 "No hypoglycaemia" 2 "Hypoglycaemia") symysize(*0.5) symxsize(*0.5) cols(1) colgap(small) size(vsmall) /*
636    */    region(fcolor(none) lwidth(none)) position(5) ring(0)) ylabel(0(1)12, labsize(small)) ytitle("Other causes of death (%)")
637    graph save Graph "Results\bars_other.gph", replace
638    graph close _all
639
640    ****SURVAGE
641    use "Results\survage", clear
642    set scheme plottig
643    twoway  (area  hno_stack0 tt,             fcolor(green%30) lcolor(green) lwidth(none))        /*
644    */      (line  hno_stack0 tt,             lcolor(green)    lpattern(solid))                   /*
645    */      (rarea hno_stack1 hno_stack0 tt,  fcolor(green%50) lcolor(green) lwidth(none))        /*
646    */      (line  hno_stack1 tt,             lcolor(green)    lpattern(solid))                   /*
647    */      (rarea hno_stack2 hno_stack1 tt,  fcolor(green%70) lcolor(green) lwidth(none))        /*
648    */      (line  hno_stack2 tt,             lcolor(green)    lpattern(solid)),                  /*
649    */      xlabel(#5, grid labsize(small)) by(, legend(off) note("")) subtitle(, size(small)) ylabel(0(10)50, angle(h) labsize(small)) xsize(2)
```

```stata
      ysize(7) xtitle("") by(age0, cols(4)) name(st_no, replace) nodraw
650   twoway  (area  hyes_stack0 tt,                 fcolor(red%30)   lcolor(red) lwidth(none))          /*
651   */      (line  hyes_stack0 tt,                 lcolor(red)      lpattern(solid))                    /*
652   */      (rarea hyes_stack1 hyes_stack0 tt,  fcolor(red%50)   lcolor(red) lwidth(none))          /*
653   */      (line  hyes_stack1 tt,                 lcolor(red)      lpattern(solid))                    /*
654   */      (rarea hyes_stack2 hyes_stack1 tt,  fcolor(red%70)   lcolor(red) lwidth(none))          /*
655   */      (line  hyes_stack2 tt,                 lcolor(red)      lpattern(solid)),                   /*
656   */      xlabel(#5, grid labsize(small)) by(, legend(off) note("")) subtitle(, size(small)) ylabel(0(10)50, angle(h) labsize(small))  xsize(2)
      ysize(7) xtitle("") by(age0, cols(4)) name(st_yes, replace) nodraw
657   twoway  (area  dif_stack0 tt,                  fcolor(blue%30)  lcolor(blue) lwidth(none))         /*
658   */      (line  dif_stack0 tt,                  lcolor(blue)     lpattern(solid))                    /*
659   */      (rarea dif_stack1 dif_stack0 tt,    fcolor(blue%50)  lcolor(blue) lwidth(none))         /*
660   */      (line  dif_stack1 tt,                  lcolor(blue)     lpattern(solid))                    /*
661   */      (rarea dif_stack2 dif_stack1 tt,    fcolor(blue%70)  lcolor(blue) lwidth(none))         /*
662   */      (line  dif_stack2 tt,                  lcolor(blue)     lpattern(solid)),                   /*
663   */      xlabel(#5, grid labsize(small)) by(, legend(off) note("")) subtitle(, size(small)) ylabel(0(10)50, angle(h) labsize(small))  xsize(2)
      ysize(7) xtitle("") by(age0, cols(4)) name(st_dif, replace) nodraw
664   graph combine st_no st_yes st_dif, ycommon rows(4) xsize(6.5) ysize(6) nocopies
665   graph save Graph "Results\survage.gph", replace
666   graph close _all
667
668
669   ****GRADIENT FOREST PLOT
670   use "Results\fplot_baseCC", clear
671   append using "Results\fplot_covsCC"
672   drop t5
673   order model age0, first
674
675   foreach e in dif_cvd dif_tum dif_other {
676       replace `e' = -`e'                       /*model for all estimate the difference for survival while in cmprisk is the difference in cif*/
677   }
678   foreach e in dif_cvd dif_tum dif_other {
679       renames `e'_lci \ `e'_1
680       renames `e'_uci \ `e'_2
681   }
682   foreach e in dif_cvd dif_tum dif_other {
683       renames `e'_1 \ `e'_uci
684       renames `e'_2 \ `e'_lci
685   }
686
687   *Difference - normal scale
688   qui {
689       foreach m in baseCC covsCC {
690           forvalues a = 50(10)80 {
691               foreach e in dif_cvd dif_tum dif_other dif_all {
692                   preserve
693                   keep model age0 `e'*
```

```stata
694                     keep if age0  == `a'
695                     keep if model == "`m'"
696                     drop model age0
697                     gen se = (`e'_uci - `e'_lci)/3.92
698                     forvalues k = 1(1)95 {
699                         gen lb`k' = `e' - invnorm(1-(100-`k')/200)*se
700                         gen ub`k' = `e' + invnorm(1-(100-`k')/200)*se
701                     }
702                     rename `e' es
703                     keep es lb* ub*
704                     foreach var of varlist * {
705                         replace `var' = 100*`var'
706                     }
707                     gen p = "`e'_`a'"
708                     reshape long lb ub, i(p) j(ci)
709                     rename lb bl
710                     rename ub bu
711                     reshape long b, i(ci) j(conf) string
712                     gen seq = _n
713                     replace es = . if seq !=1
714                     gen m = "`m'"
715                     tempfile `m'_`e'_`a'
716                     save ``m'_`e'_`a'', replace
717                     restore
718                 }
719             }
720         }
721     }
722
723     preserve
724     clear
725     foreach m in baseCC covsCC {
726         forvalues a = 50(10)80 {
727             foreach e in dif_cvd dif_tum dif_other dif_all {
728                 append using ``m'_`e'_`a''
729             }
730         }
731     }
732     sum b
733
734     split p, p(_)
735     gen     m1 = "0" if m == "baseCC"
736     replace m1 = "1" if m == "covsCC"
737     gen g = m1+p2+p3
738     gen t = 1      if p2 == "cvd"
739     replace t = 2      if p2 == "tum"
740     replace t = 3      if p2 == "other"
```

```
741    replace t = 4    if p2 == "all"
742    sort t p3 ci m
743    destring p3, gen(age)
744    replace age = age + 1.5 if m == "covsCC"
745    sencode p, replace
746    sencode m, replace
747    sencode p2, replace
748    replace es = -es    /*to be consistent with graph of cumulative incidence above*/
749    replace b = -b
750    save "Results\covs", replace
751
752    *graph*
753    set scheme s2color
754    *set scheme plottig
755    local sug ""
756    local sag ""
757    local sup ""
758    local sap ""
759    forvalues k = 1/95 {
760        local i = (95-`k')/100
761        local sug "`sug' (scatter b  age if m == 1 & ci == `k', msymbol(square) msize(small) mcolor(blue*`i')   mlwidth(none))"
762        local sag "`sag' (scatter b  age if m == 2 & ci == `k', msymbol(square) msize(small) mcolor(orange*`i') mlwidth(none))"
763        local sup "`sup' (scatter es age if m == 1,            msymbol(circle) msize(small) mcolor(white)     mlwidth(thin) mlcolor(black))"
764        local sap "`sap' (scatter es age if m == 2,            msymbol(circle) msize(small) mcolor(white)     mlwidth(thin) mlcolor(black))"
765    }
766    twoway `sug' `sag' `sup' `sap', by(, legend(off)) by(p2, cols(4) note("")) subtitle(, size(small))  /*
767    */  ylabel(30(-5)-10, labsize(small) angle(horizontal)) xlabel(, labsize(small)) xtitle("") xsize(6.5) ysize(2) scale(1.3) yline(0, lwidth(
       vthin) lcolor(black) lpattern(solid))
768    graph save Graph "Results\covs.gph", replace
769    graph close _all
770    restore
771
772
773    *###############################################################################
774    *************************SENSITIVITY - TIME FROM HYPO*************************
775    *###############################################################################
776    cls
777    use "db1", clear
778    rcsgen age0, gen(age0s) orthog df(3)
779
780    foreach mod of varlist age0s* {
781        gen i_`mod' = `mod'*hypo1
782    }
783
784    replace tbef1 = 0 if hypo1 == 0
785    qladder tbef1
786    graph close _all
```

```stata
787
788    preserve
789    clear
790    tempfile res
791    save `res', emptyok replace
792    restore
793
794    foreach q in cvd tum other {
795        preserve
796        stset t`q', id(id) failure(d`q'==1)
797        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5, scale(h) df(4)
798        parmest, fast
799        gen outcome = "`q'"
800        gen model   = "base"
801        append using `res'
802        save `res', replace
803        restore
804        preserve
805        stset t`q', id(id) failure(d`q'==1)
806        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 tbef1, scale(h) df(4)
807        parmest, fast
808        gen outcome = "`q'"
809        gen model   = "timebefore"
810        append using `res'
811        save `res', replace
812        restore
813    }
814    use `res', clear
815    keep if (parm == "hypo1" | parm == "tbef1")
816    sort outcome model
817
818    gen hr = exp(estimate)
819    gen lb = exp(min95)
820    gen ub = exp(max95)
821    foreach var of varlist hr lb ub {
822        tostring `var', format(%7.2f) replace force
823    }
824    gen es = hr + " (" + lb + ", " + ub + ")"
825    export excel using "Results\timebefore.xls", firstrow(variables) replace
826
827
828    *##############################################################################
829    ************************SUMMARY RESULTS TABLE********************************
830    *##############################################################################
831    cls
832    use "Results\covs.dta", clear
```

```stata
833    keep if (ci == 1 | ci == 95)
834    sort p2 p3 m seq
835    by g, sort : egen float lb = min(b)
836    by g, sort : egen float ub = max(b)
837    sort p2 p3 m seq
838    drop if es == .
839    keep p es m lb ub
840    foreach var of varlist es lb ub {
841        tostring `var', replace force format(%7.1f)
842    }
843    gen dif = es + " (" + lb + ", " + ub + ")"
844    drop es lb ub
845    sdecode p, replace
846    split p, parse(_)
847    rename p2 out
848    keep m dif p3 out
849    rename p3 age
850    sdecode m, replace
851    sort m out age
852    gen c = m + "_" + age
853    drop age m
854    reshape wide dif, i(c) j(out) string
855    split c, parse(_)
856    rename c2 age
857    destring age, replace
858    sort age c1
859    order age c1 difc dift difo difa
860    rename c1 model
861    drop c
862
863    preserve
864    import excel "Results\MI_results.xls", sheet("Sheet1") firstrow clear
865    gen model = "mi"
866    tempfile mi
867    save `mi', replace
868    restore
869
870    append using `mi'
871    sort age model
872    export excel using "Results\compare_results.xls", firstrow(variables) replace
873
874
875
876
877    ****************************************************************************************************
878    ****************************************************************************************************
879    * R E V I S I O N --- R1 *
```

```stata
880     *******************************************************************************************************
881     *******************************************************************************************************
882
883     display "$S_TIME  $S_DATE"
884     set seed 987654321
885
886     *#############################################################################
887     ***************************MULTIPLE IMPUTATIONS R1***************************
888     *#############################################################################
889
890     *databases and estimations*
891     cls
892     use "db0", clear
893     describe, short
894     mdesc age0 sex eth smk alc sbp tchol la1c bmi egfr imd /*
895     */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0
896
897     drop if sbp == 0                          /*12  patients*/
898     drop if bmi == 0 | bmi <10 | bmi >70      /*735 patients*/
899     drop if tchol>10                          /*504 patients*/
900     drop if egfr>150                          /*210 patients*/
901
902     mdesc age0 sex eth smk alc sbp tchol la1c bmi egfr imd /*
903     */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0
904     describe, short
905
906     cls
907     tab sex, m
908     sdecode sex, replace
909     replace sex = "0" if sex == "F"
910     replace sex = "1" if sex == "M"
911     destring sex, replace
912     tab eth, m
913     sdecode eth, replace
914     replace eth = "0" if eth == "White"
915     replace eth = "1" if eth == "nonWhite"
916     destring eth, replace
917     tab smk, m
918     sdecode smk, replace
919     replace smk = "0" if smk == "no"
920     replace smk = "1" if smk == "ex"
921     replace smk = "2" if smk == "yes"
922     destring smk, replace
923     tab alc, m
924     sdecode alc, replace
925     replace alc = "0" if alc == "no"
926     replace alc = "1" if alc == "ex"
```

```stata
927     replace alc = "2" if alc == "yes"
928     destring alc, replace
929     tab imd, m
930
931     local u = 50            /*databases imputed*/
932
933     mi set mlong
934
935     mi register imputed eth smk alc sbp la1c imd                                    /*   variables with missing data*/
936
937     mi register regular age0 sex tchol bmi egfr /*
938     */         metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0   /*   covariates included in the model without missing
        + outcomes
939     */         dcvd dtum dother tall hypo1                                          /*   time is the same for all outcomes*/
940
941     mi impute chained (regress) sbp la1c (logit) eth (mlogit) smk alc imd =         /*   covariates needed to be imputed
942     */         age0 sex tchol bmi egfr                                              /*   all other covariates
943     */         metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0   /*
944     */         dcvd dtum dother tall hypo1, add(`u')                                /*   seed not defined as already defined above*/
945
946     foreach var of varlist smk alc imd {
947         tab `var', gen(`var')
948     }
949
950     forvalues j = 1/`u' {
951         display "$S_TIME  $S_DATE -- database MI: `j'"
952
953         preserve
954         *single dataset
955         mi extract `j', clear
956
957         *make spline & interactions
958         rcsgen age0, gen(age0s) orthog df(3)
959         global Kage `r(knots)'
960         matrix Mage = r(R)
961         foreach mod of varlist age0s* {
962             gen i_`mod' = `mod'*hypo1
963         }
964
965         *cmprisk - coeffs
966         foreach q in cvd tum other {
967             stset t`q', id(id) failure(d`q'==1)
968             stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
969             */   metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
970             estimates store `q'
971         }
972
```

```
973        *cmprisk - standsurv
974        gen t5 = 5 in 1
975        forvalues k = 50(10)80 {
976            rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
977            standsurv, crmodels(cvd tum other) cif timevar(t5) atvar(hno hyes) contrast(difference) contrastvar(dif) se ci verbose  /*
978            */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0     i_age0s2 0     i_age0s3 0)             /*
979            */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
980            gen age = `k' in 1
981            gen db  = `j' in 1
982            tempfile c`k'_`j'
983            save `c`k'_`j'', replace
984            drop hno* hyes* dif* age db
985        }
986
987        *all death - coeffs
988        stset tall, id(id) failure(dall==1)
989        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
990        */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
991
992        *all death - standsurv
993        forvalues k = 50(10)80 {
994            rcsgen, scalar(`k') knots(${Kage}) rmatrix(Mage) gen(v)
995            standsurv, timevar(t5) atvar(hno_all hyes_all) contrast(difference) contrastvar(dif_all) ci se verbose  /*
996            */  at1(hypo1 0 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 0     i_age0s2 0     i_age0s3 0)           /*
997            */  at2(hypo1 1 age0s1 `=v1' age0s2 `=v2' age0s3 `=v3' i_age0s1 `=v1' i_age0s2 `=v2' i_age0s3 `=v3')
998            gen age = `k' in 1
999            gen db  = `j' in 1
1000           tempfile a`k'_`j'
1001           save `a`k'_`j'', replace
1002           drop hno* hyes* dif* age db
1003       }
1004       restore
1005   }
1006
1007   clear
1008   tempfile cmpr
1009   forvalues k = 50(10)80 {
1010       forvalues j = 1/`u' {
1011           append using `c`k'_`j''
1012       }
1013   }
1014   keep t5 hno* hyes* dif* age db
1015   drop if t5 == .
1016   save `cmpr', replace
1017
1018   clear
1019   tempfile alld
```

```stata
1020     forvalues k = 50(10)80 {
1021         forvalues j = 1/`u' {
1022             append using `a`k'_`j''
1023         }
1024     }
1025     keep t5 hno* hyes* dif* age db
1026     drop if t5 == .
1027     merge 1:1 db age using `cmpr'
1028     drop _merge
1029     order t5 db age, first
1030     drop t5
1031
1032     keep db age dif*
1033     drop *_lci *_uci
1034     foreach var of varlist dif_all - dif_other_se {
1035         replace `var' = `var' * 100
1036     }
1037     replace dif_all = -dif_all          /*for all-cause the estimate is survival, for cause-specific is cif*/
1038     foreach k in all cvd tum other {
1039         rename dif_`k' `k'
1040         rename dif_`k'_se `k'_se
1041     }
1042     sort age db
1043
1044     preserve
1045     clear
1046     tempfile mim
1047     save `mim', emptyok replace
1048     restore
1049
1050     forvalues k = 50(10)80 {
1051         foreach e in all cvd tum other {
1052             preserve
1053             keep if age == `k'
1054             local m = _N
1055             di `m'                     /*This is Rubin's rule on the survival difference*/
1056             keep age `e' `e'_se
1057             egen q  = mean(`e')
1058             gen  u1 = `e'_se^2
1059             egen u  = mean(u1)
1060             gen  b1 = (`e'-q)^2
1061             egen b2 = total(b1)
1062             gen  b  = b2/(`m'-1)
1063             gen  t  = u + b*(1+1/`m')
1064             gen  se = t^0.5
1065             keep in 1
1066             keep age q se
```

```stata
1067            gen  lb = q - 1.96*se
1068            gen  ub = q + 1.96*se
1069            rename q es
1070            gen  end = "`e'"
1071            append using `mim'
1072            save `mim', replace
1073            restore
1074        }
1075    }
1076    use `mim', clear
1077    sort end age
1078    gen      s = 1 if end == "cvd"
1079    replace s = 2 if end == "tum"
1080    replace s = 3 if end == "other"
1081    replace s = 4 if end == "all"
1082    sort s age
1083    foreach var of varlist es lb ub {
1084        tostring `var', replace format(%7.1f) force
1085    }
1086    gen dif = es + " (" + lb + ", " + ub + ")"
1087    keep age end dif
1088    reshape wide dif, i(age) j(end) string
1089    order age difcvd diftum difother difall
1090    export excel using "MI_results_r1.xls", firstrow(variables) replace
1091    display "$S_TIME  $S_DATE"
1092
1093
1094    /****************************************************************************************************************************
        *********/
1095    /*INSULIN AND SU CAUSE-SPECIFIC HAZARD RATIO - COMPLETE CASE*/
1096
1097    cls
1098    use "db1", clear
1099
1100    rcsgen age0, gen(age0s) orthog df(3)
1101    global Kage `r(knots)'
1102    matrix Mage = r(R)
1103    foreach mod of varlist age0s* {
1104        gen i_`mod' = `mod'*hypo1
1105    }
1106
1107    preserve
1108    clear
1109    tempfile hrs
1110    save `hrs', emptyok replace
1111    restore
1112
```

```
1113    foreach q in cvd tum other {
1114        stset t`q', id(id) failure(d`q'==1)
1115        stpm2 hypo1 age0s1 age0s2 age0s3 i_age0s1 i_age0s2 i_age0s3 sbp tchol la1c bmi egfr sex eth smk2 smk3 alc2 alc3 imd2-imd5 /*
1116        */    metformin su insulin othergld mi0 stroke0 pad0 hf0 af0 cancer0 stat0 asa0, scale(h) df(4)
1117        preserve
1118        parmest, fast
1119        gen outcome = "`q'"
1120        append using `hrs'
1121        save `hrs', replace
1122        restore
1123    }
1124
1125    use `hrs', clear
1126    keep if parm == "insulin" | parm == "su"
1127    keep parm estimate min95 max95 outcome
1128    foreach var of varlist estimate-max95 {
1129        gen `var'_exp = exp(`var')
1130        tostring `var'_exp, format(%7.2f) force replace
1131    }
1132    export excel using "hrs_r1.xls", firstrow(variables) replace
```