SUPPLEMENTAL MATERIAL

Appendix B - STATA code for calculating the cumulative incidence of major amputation using non-parametric survival methods (standard: Kaplan-Meier and competing risk: Aalen-Johansen), and for estimating the 2-year risk ratio of major amputation using unadjusted and adjusted semi-parametric models (standard: Cox proportional hazard Cox regression a competing risk: Fine-Gray regression) and the corresponding mean of the 2-year probability of major amputation.

```
ssc install stcompet

use "cohort_CLTI.dta", clear

/*
* timemo_cens denotes the survival time as the time (in months) from index procedure
to 1st occurrence of major amputation or death or end of follow-up or 2 years, whatever
occurred first.

* event_cr is the corresponding event indicator, i.e. patient's status at the end of
the follow-up as:
        - 1: major amputation
        - 0: alive without major amputation at the end of the follow-up
        - 2: deceased without major amputation

* indexproc_id is the ID of the index procedure (unique value for each row)

* age_cat75 is the variable for age groups as 0 if age <75 years and 1 if ≥75 years
```

indexproc_id	event_cr	timemo_cens	age_cat75
ID1	6	0	0
ID2	20	1	0
ID3	18	2	1
ID4	24	0	0
ID5	8	2	1

```
* The regression model are adjusted for the following list of covariates: sex race3
ethnicity regionid primaryinsurer_2cl preop_livinghome ib2.hx_smk preop_gdmt hx_htn
hx_chf hx_cad hx_cabg hx_pci hx_diab hx_ckd_2cl hx_cvd hx_ceacas hx_amp hx_bypendarpvi
urgency2
*/

save "cohort_CLTI.dta", replace


/********************************************************************************
1) Non-parametric survival methods: standard survival using Kaplan-Meier estimators
vs. competing risk using Aalen-Johansen estimator
********************************************************************************/

* Standard survival using Kaplan-Meier estimators
```

```
stset timemo_cens, id(indexproc_id) failure(event_cr==1) exit(time 24)
sts list, by(age_cat75) failure at(6 12 24)
sts generate mamp_cifkm = f ///
            mamp_cifkm_lci = lb(f) ///
            mamp_cifkm_uci = ub(f) ///
            mamp_sekm = se(f), by(age_cat75)
sts test age_cat75, logrank
foreach var in mamp_cifkm mamp_cifkm_lci mamp_cifkm_uci {
      replace `var' = 100 * `var'
}




* Competing risk using Aalen-Johansen estimator

stset timemo_cens, id(indexproc_id) failure(event_cr==1) exit(time 24)
stcompet cif = ci uci = hi lci = lo, compet1(2) by(age_cat75)
generate mamp_cifaj = cif if event_cr == 1
generate mamp_cifaj_se = se if event_cr == 1
generate mamp_cifaj_lci = lci if event_cr == 1
generate mamp_cifaj_uci = uci if event_cr == 1
drop cif lci uci se
stcrreg i.age_cat75, compete(event_cr==2)
foreach var in mamp_cifaj mamp_cifaj_lci mamp_cifaj_uci {
      replace `var' = 100 * `var'
}


* Relative Difference

gen mamp_reldiff = abs(mamp_cifkm-mamp_cifaj)/mamp_cifaj



replace _t = _t/12

* Graphs of cumulative incidence in patients < 75 years old

twoway (line mamp_cifaj _t if age_cat75 == 0 & event_cr == 1,sort lpattern(solid)  ///
            lcolor(red) lwidth(medium))                                            ///
      (rarea mamp_cifaj_lci mamp_cifaj_uci _t if age_cat75 == 0  & event_cr == 1, ///
            sort fcolor(red%10) lpattern(solid) lcolor(red%20) lwidth(medium))    ///
      (line mamp_cifkm _t if age_cat75 == 0 & event_cr == 1, sort lpattern(dash)  ///
            lcolor(red) lwidth(medium))                                            ///
      (rarea mamp_cifkm_lci mamp_cifkm_uci _t if age_cat75 == 0 & event_cr == 1,  ///
            sort fcolor(red%10) lpattern(dash) lcolor(red%20) lwidth(medium)),    ///
      xlabel(0(0.5)2, valuelabel labsize(medium)) xmtick(0(1)2)                    ///
      ylabel(0(5)20, labels valuelabel labsize(medium) glcolor(gs15)              ///
            angle(horizontal) gmax) ymtick(0(1)20)                                 ///
      xtitle("{bf:Years Since PVI}", size(medium) margin(small))                   ///
      ytitle("{bf:Cumulative Incidence Function (%)}", size(medium)               ///
            margin(small))                                                         ///
      title("{bf: Major Amputation In Age < 75 years}", size(medium) margin(small)
color(black))      ///
```

```
        plotregion(margin(zero) fcolor(white) ilcolor(white) lcolor(white))        ///
        graphregion(margin(zero) ilcolor(white) lcolor(white) fcolor(white))        ///
                yoverhangs xoverhangs                                               ///
        legend(order(1 " Alaen-Johansen" 3 " Kaplan-Meier")                         ///
                    span col(2) pos(6) size(medsmall) colgap(vsmall)        ///
                    keygap(vsmall) just(center) rowgap(2))                          ///
                    name("cif_gph_agelo75 ", replace)                      ///
graph display, xsize(20) ysize(20) margin(vsmall)
graph export "cif_gph_agelo75.png", replace name("cif_gph_agelo75")


* Graphs of cumulative incidence in patients ≥ 75 years old

twoway (line mamp_cifaj _t if age_cat75 == 1 & event_cr == 1,sort lpattern(solid)  ///
            lcolor(red) lwidth(medium))                                              ///
        (rarea mamp_cifaj_lci mamp_cifaj_uci _t if age_cat75 == 1  & event_cr == 1, ///
            sort fcolor(red%10) lpattern(solid) lcolor(red%20) lwidth(medium))   ///
        (line mamp_cifkm _t if age_cat75 == 1 & event_cr == 1, sort lpattern(dash)  ///
            lcolor(red) lwidth(medium))                                             ///
        (rarea mamp_cifkm_lci mamp_cifkm_uci _t if age_cat75 == 1 & event_cr == 1,  ///
            sort fcolor(red%10) lpattern(dash) lcolor(red%20) lwidth(medium)),   ///
        xlabel(0(0.5)2, valuelabel labsize(medium)) xmtick(0(1)2)                    ///
        ylabel(0(5)20, labels valuelabel labsize(medium) glcolor(gs15)              ///
            angle(horizontal) gmax) ymtick(0(1)20)                                  ///
        xtitle("{bf:Years Since PVI}", size(medium) margin(small))                 ///
        ytitle("{bf:Cumulative Incidence Function (%)}", size(medium)              ///
            margin(small))                                                          ///
        title("{bf: Major Amputation In Age ≥ 75 years}", size(medium) margin(small)
color(black))       ///
        plotregion(margin(zero) fcolor(white) ilcolor(white) lcolor(white))        ///
        graphregion(margin(zero) ilcolor(white) lcolor(white) fcolor(white))        ///
                yoverhangs xoverhangs                                               ///
        legend(order(1 " Alaen-Johansen" 3 " Kaplan-Meier")                         ///
                    span col(2) pos(6) size(medsmall) colgap(vsmall)        ///
                    keygap(vsmall) just(center) rowgap(2))                          ///
                    name("cif_gph_ageup75", replace)                         ///
graph display, xsize(20) ysize(20) margin(vsmall)
graph export "cif_gph_ageup75.png", replace name("cif_gph_ageup75")




/*******************************************************************************
2) Semi-parametric survival regression models: standard Cox proportional hazard
regression model vs. Fine-Gray competing risk regression model
********************************************************************************/



use "cohort_CLTI.dta", clear
stset timemo_cens, id(indexproc_id) failure(event_cr==1) exit(time 24)


* Standard Cox proportional hazard regression model

*Unadjusted model and the mean 2-year probability of major amputation
stcox i.age_cat75, hr
predict bhazcox_unadj, basechaza
```

```
predictnl cifcox_unadj = 100*(1 - (1 -
bhazcox_unadj)^exp((age_cat75==0)*_b[0.age_cat75] + (age_cat75==1)*_b[1.age_cat75]))


*Adjusted model and the mean 2-year probability of major amputation
stcox i.age_cat75 i.sex i.race3 i.ethnicity regionid i.primaryinsurer_2cl
i.preop_livinghome ib2.hx_smk i.preop_gdmt i.hx_htn i.hx_chf i.hx_cad i.hx_cabg
i.hx_pci i.hx_diab i.hx_ckd_2cl i.hx_cvd i.hx_ceacas i.hx_amp i.hx_bypendarpvi
i.urgency2
predict bhazcox_adj, basechaza
margins age_cat75, predict(xb) atmeans post
predictnl cifcox_adj = 100*(1 - (1 - bhazcox_adj)^exp((age_cat75==0)*_b[0.age_cat75] +
(age_cat75==1)*_b[1.age_cat75]))


* Fine-Gray competing risk regression model

*Unadjusted model and the mean 2-year probability of major amputation
stcrreg i.age_cat75, compete(event_cr==2)
predict bciffg_unadj, basecif
predict xbffg_unadj, xb
predictnl ciffg_unadj = 100*(1 - (1 - bciffg_unadj)^exp(xbffg_unadj))

*Adjusted model and the mean 2-year probability of major amputation
stcrreg  i.age_cat75 i.sex i.race3 i.ethnicity regionid i.primaryinsurer_2cl
i.preop_livinghome ib2.hx_smk i.preop_gdmt i.hx_htn i.hx_chf i.hx_cad i.hx_cabg
i.hx_pci i.hx_diab i.hx_ckd_2cl i.hx_cvd i.hx_ceacas i.hx_amp i.hx_bypendarpvi
i.urgency2, compete(event_cr==2)
predict bciffg_adj, basecif
margins age_cat75, predict(xb) atmeans post
predictnl ciffg_adj = 100*(1 - (1 - bciffg_adj)^exp((age_cat75==0)*_b[0.age_cat75] +
(age_cat75==1)*_b[1.age_cat75]))
```