```
/*****************************
*
*Proportional Hazards Assessment
*
****************************/




**M2AHR
***Model for hazard ratio of admission in outpatients on oral treatment (ie. risk of admission after
first day of follow up)
*** Variables are Species (omitting Ovale), Age group (4 categories), Ethnic group, combined sex
and pregnancy status, and oral treatment

use "C:\data\malaria\results\efron  8 Oct 2015 16_30_08\M2a_HR.dta", clear
stset AdmFU15, fail(AdmNext14)
/*  STORED MODEL WITH GENERATED SCALED SCHOENFELD RESIDUALS
loc model M2a_HR
loc cond if ip==0
stcox i.SpeciesX i.AGR4_4b i.EthnicX i.sexPreg i.oral_v_dhp `cond', allbaselevels vsquish
cluster(hrn) efron cformat(%6.2f) nolog
predict `i'*, scaledsch
*/

loc model M2a_HR

***Combination Graphs
        *Species (SpeciesX)
        use "C:\data\malaria\results\efron  8 Oct 2015 16_30_08\M2a_HR.dta", clear

        running sch1 _t if _d == 1,  gen(smooth_sch1 ) nodraw
        running sch2 _t if _d == 1,  gen(smooth_sch2 ) nodraw
        running sch3 _t if _d == 1,  gen(smooth_sch3 ) nodraw
        running sch4 _t if _d == 1,  gen(smooth_sch4 ) nodraw
        running sch5 _t if _d == 1,  gen(smooth_sch5 ) nodraw
        running sch6 _t if _d == 1,  gen(smooth_sch6 ) nodraw
        running sch7 _t if _d == 1,  gen(smooth_sch7 ) nodraw
        running sch8 _t if _d == 1,  gen(smooth_sch8 ) nodraw
        running sch9 _t if _d == 1,  gen(smooth_sch9 ) nodraw
        running sch10 _t if _d == 1, gen(smooth_sch10) nodraw
        running sch11 _t if _d == 1, gen(smooth_sch11) nodraw
        running sch12 _t if _d == 1, gen(smooth_sch12) nodraw
        running sch13 _t if _d == 1, gen(smooth_sch13) nodraw
        running sch14 _t if _d == 1, gen(smooth_sch14) nodraw
        running sch15 _t if _d == 1, gen(smooth_sch15) nodraw
        running sch16 _t if _d == 1, gen(smooth_sch16) nodraw
        gen smooth_esca1  = exp(smooth_sch1 )
        gen smooth_esca2  = exp(smooth_sch2 )
        gen smooth_esca3  = exp(smooth_sch3 )
        gen smooth_esca4  = exp(smooth_sch4 )
        gen smooth_esca5  = exp(smooth_sch5 )
        gen smooth_esca6  = exp(smooth_sch6 )
        gen smooth_esca7  = exp(smooth_sch7 )
        gen smooth_esca8  = exp(smooth_sch8 )
        gen smooth_esca9  = exp(smooth_sch9 )
        gen smooth_esca10 = exp(smooth_sch10)
        gen smooth_esca11 = exp(smooth_sch11)
```

```stata
gen smooth_esca12 = exp(smooth_sch12)
gen smooth_esca13 = exp(smooth_sch13)
gen smooth_esca14 = exp(smooth_sch14)
gen smooth_esca15 = exp(smooth_sch15)
gen smooth_esca16 = exp(smooth_sch16)

loc model M2a_HR
loc var Species
tw  line smooth_esca1 _t, sort lwidth(0.5) lc("27 158 119")  ||    ///
    line smooth_esca3 _t, sort lwidth(0.5) lc("117 112 179") ||    ///
    line smooth_esca4 _t, sort lwidth(0.5) lc("231 41 138")||     ///
    line smooth_esca2 _t, sort lwidth(0.5) lc("217 95 2")       ///
    name(`var'_PHtest, replace) ///
legend(order(1 "{it: P.falciparum} (ref.)" 4 "{it: P.vivax} (p < 0.0001)" 2 "{it: P.
malariae} (p = 0.458)" 3 "mixed (p = 0.044)") pos(3) col(1) textwidth(20) forcesize)
///
    xtitle("time (days following presentation)", margin(medsmall))
    ytitle("exponentiated scaled Schoenfeld residuals", margin(medsmall))  subtitle("
    `var'") xmtick(2(1)15) graphr(color(white) lc(white)) plotr(color(white)
    lc(white)) ylab(, angle(h) labsize(medsmall) nogrid format(%9.1f)) xlab(2 "1" 8
    "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20) ysize(12) xsca(nofextend)
    ylab(1, add)

    * graph export "C:\data\malaria\figures\PH test/`var'PHtest_`model'.png",
    as(png) replace width(800) height(600)


*Age (AGR4_4b)
loc var Age group
loc vars AGR4
tw  line smooth_esca6 _t, sort lwidth(0.5) lc("27 158 119") ||    ///
    line smooth_esca7 _t, sort lwidth(0.5) lc("217 95 2")    ||   ///
    line smooth_esca8 _t, sort lwidth(0.5) lc("117 112 179")||    ///
    line smooth_esca5 _t, sort lwidth(0.5) lc("231 41 138")      ///
    name(`vars'_PHtest, replace) ///
legend(order(1 "0 to < 1 year (p = 0.131)" 2 "1 to < 5 years (p = 0.010)" 3 "5 to <15
 (p = 0.0008 )" 4 "15+ (ref.)") pos(3) col(1) textwidth(20) forcesize) ///
    xtitle("time (days following presentation)", margin(medsmall)) ytitle("  ",
    margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
    lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
    format(%9.1f)) xlab(2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20)
    ysize(12) xsca(nofextend)  ylab(1, add)

    * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
    as(png) replace width(800) height(600)
*Ethnic
loc var Ethnic group
loc vars EthnicX
tw  line smooth_esca9  _t, sort lwidth(0.5) lc("27 158 119")    ||    ///
    line smooth_esca10 _t, sort lwidth(0.5) lc("217 95 2")      ||    ///
    line smooth_esca11 _t, sort lwidth(0.5) lc("117 112 179")        ///
    name(`vars'_PHtest, replace) ///
legend(order(1 "Highland (ref.)" 2 "Lowland (p = 0.272)" 3 "non-Papuan (p < 0.0001)")
 pos(3) col(1) textwidth(20) forcesize) ///
    xtitle("time (days following presentation)", margin(medsmall)) ytitle("  ",
    margin(medsmall)) subtitle("`var'") xmtick(2(1)15) graphr(color(white) lc(white))
     plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid format(%9
    .1f)) xlab(2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20) ysize(12)
```

```
                   xsca(nofextend)  ylab(1, add)


               * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
               as(png) replace width(800) height(600)
       *Sex and Pregnancy
       loc var Sex and pregnancy status
       loc vars sexPreg
       tw  line smooth_esca12  _t, sort lwidth(0.5) lc("27 158 119")   ||     ///
           line smooth_esca13  _t, sort lwidth(0.5) lc("217 95 2")     ||     ///
           line smooth_esca14  _t, sort lwidth(0.5) lc("117 112 179")         ///
           name(`vars'_PHtest, replace) ///
           legend(order(1 "Female (not pregnant; ref.)" 2 "Female (pregnant; p = 0.013)" 3
           "Male (p = 0.001)") pos(3) col(1) textwidth(20) forcesize)  ///
           xtitle("time (days following presentation)", margin(medsmall)) ytitle("  ",
           margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
           lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
            format(%9.1f)) xlab(2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20)
            ysize(12) xsca(nofextend)  ylab(1, add)


               * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
               as(png) replace width(800) height(600)
       *Oral treatment
       loc var Oral treatment
       loc vars oralDHP
       tw  line smooth_esca15  _t, sort lwidth(0.5) lc("27 158 119") ||     ///
           line smooth_esca16  _t, sort lwidth(0.5) lc("217 95 2")          ///
           name(`vars'_PHtest, replace) ///
               legend(order(1 "oral quinine (ref.)" 2 "DHP (p = 0.378)") pos(3) col(1)
               textwidth(20) forcesize) ///
           xtitle("time (days following presentation)", margin(medsmall)) ytitle("  ",
           margin(medsmall)) subtitle("`var'") xmtick(2(1)15) graphr(color(white) lc(white))
            plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid format(%9
           .1f)) xlab(2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20) ysize(12)
            xsca(nofextend)  ylab(1, add)


               * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
               as(png) replace width(800) height(600)
       loc model M2a_HR
       graph combine Species_PHtest AGR4_PHtest sexPreg_PHtest EthnicX_PHtest
       oralDHP_PHtest, col(1) graphr(color(white) lc(white)) plotr(color(white)) xcommon
       ysize(20) xsize(12) name(PH_`model',replace) note("Global PH test: {&chi} 133.04, df
       = 11, p < 0.0001", size(tiny)) iscale(0.4)
loc model M2a_HR
       graph export "C:\data\malaria\figures\PH test\PH_`model'.emf", as(emf) replace



       *Illustrative PH test with 95% CI  - following Royston Parmar in Flexible Parametric
       Survival Analysis (chapter 7 "Cox with model time-dependent effects")
               ***Vivax
               use "C:\data\malaria\results\efron  8 Oct 2015 16_30_08\M2a_HR.dta", clear
               loc model M2a_HR
               loc v sch2
               loc outc Adm
               loc v_name vivax
               * running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se)
               nodraw              /* generate smoothed Schoenfeld residual and associated
               SE */
```

```
* gen `v'_smooth_e =
exp(`v'_smooth)                                                      /* gen
exponentiated smoothed Schoenfeld residual */
* gen `v'_smooth_e_lci = exp(`v'_smooth -
1.96*`v'_smooth_se)                      /* lower 95% CI for exp. smth. Sch.
residuals */
* gen `v'_smooth_e_uci = exp(`v'_smooth +
1.96*`v'_smooth_se)                      /* upper 95% CI for exp. smth.
Sch. residuals */
    tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort fc("253
    205 172")   lc("253 205 172")   ||  ///      /*Plot exp smth Sch residual
    CI area */
    line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")
    ||  ///      /* plot exp smth Sch residual estimate */
    function y = 1, lpattern(solid) range(2 15) lc("27 158 119")
                  ||  ///      /*plot null / baseline value of 1 */
    function y = 0.92, lpattern(shortdash) range(2 15) lc(black)
    ///      /* plot estimated HR  for variable */
    name(M2_PH_Adm_vivax, replace)
                                                  ///      /* graph
    options */
    legend(order(2 "smoothed residuals (95 %CI)" 3 "{it: P.falciparum}
    (reference)"                              ///
        4 "estimated HR 0.92 (95% CI 0.85, 1.00)") colfirst notextfirst
        nostack cols(1) size(small)      ///
        nobox region(fcolor(white) margin(zero) lcolor(white)) position(12)
        ring(1))              ///
    ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))
    ///
    title("Species: {it:P.vivax} relative to {it:P.falciparum}",
                  ///
        size(medsmall) )                  ///
    xtitle("Time (days) since presentation with malaria")
                              ///
    ylabel(, nogrid angle(h) labsize(small))
                                              ///
    xlab(2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)
    yscale(log)      ///
    graphr(color(white) lc(white)) plotr(color(white) lc(white))

graph export "C:\data\malaria\figures\PH test\focusPH_`model'_pv.emf",
as(emf) replace


**OralDHP
loc model M2a_HR
loc v sch16
loc outc Adm
loc v_name DHP
* running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se)
nodraw              /* generate smoothed Schoenfeld residual and associated
SE */
* gen `v'_smooth_e =
exp(`v'_smooth)                                                      /* gen
exponentiated smoothed Schoenfeld residual */
* gen `v'_smooth_e_lci = exp(`v'_smooth -
1.96*`v'_smooth_se)                      /* lower 95% CI for exp. smth. Sch.
residuals */
```

```
* gen `v'_smooth_e_uci = exp(`v'_smooth +
1.96*`v'_smooth_se)                        /* upper 95% CI for exp. smth.
Sch. residuals */
        tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort fc("253
        205 172")    lc("253 205 172")  ||  ///      /*Plot exp smth Sch residual
        CI area */
        line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")      ||
        ///    /* plot exp smth Sch residual estimate */
        function y = 1, lpattern(solid) range(2 15) lc("27 158 119")      ||
        ///    /*plot null / baseline value of 1 */
        function y = 0.60, lpattern(shortdash) range(2 15) lc(black)
                                            ///    /* plot estimated HR  for
        variable */
        name(M2_PH_Adm_DHP, replace)
                                                    ///    /* graph
        options */
        legend(order(2 "smoothed residuals (95 %CI)" 3 "oral quinine(reference)"
                                    ///
            4 "estimated HR 0.60  (95% CI 0.55, 0.66)") colfirst notextfirst
            nostack cols(1) size(small)       ///
            nobox region(fcolor(white) margin(zero) lcolor(white)) position(12)
            ring(1))            ///
        ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))
        ///
        title("Oral treatment, DHP relative to quinine",            ///
            size(medsmall) )                ///
        xtitle("Time (days) since presentation with malaria")
                                        ///
        ylabel(, nogrid angle(h) labsize(small))
                                            ///
        xlab(2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)
        yscale(log)       ///
        graphr(color(white) lc(white)) plotr(color(white) lc(white))

    graph export "C:\data\malaria\figures\PH test\focusPH_`model'_DHP.emf",
    as(emf) replace
    graph combine M2_PH_Adm_vivax M2_PH_Adm_DHP, col(1) graphr(color(white)
    lc(white)) plotr(color(white)) ysize(20) xsize(12)
    name(PH_M2combo_PvDHP,replace) xcommon
    loc model M2a_HR
    graph export "C:\data\malaria\figures\PH test/`model'_combo_PvDHP.emf",
    as(emf) replace
```

```
*M3BHR
*** risk of death by day 15 in those who were not initially admitted, including oral / dhp first
treatment
*** Variables are Species (omitting Ovale), Age group (4 categories), Ethnic group (omitting
non-Papuans), combined sex and pregnancy status, and oral treatment
stset DiedFU15, fail(DiedNext14) id(obsno)

use "C:\data\malaria\results\efron  8 Oct 2015 21_14_52\M3b_HR.dta", clear

/*  STORED MODEL WITH GENERATED SCALED SCHOENFELD RESIDUALS
loc model M3b_HR
stcox i.SpeciesX i.AGR4_4b i.EthnicX i.sexPreg i.oral_v_dhp if ip==0 ,  allbaselevels
vsquish cluster(hrn) efron cformat(%6.2f) nolog
predict `i'*, scaledsch
```

```stata
*/

loc model M3b_HR
        running sch_`model'1 _t if _d == 1,  gen(smooth_sch1 ) nodraw
        running sch_`model'2 _t if _d == 1,  gen(smooth_sch2 ) nodraw
        running sch_`model'3 _t if _d == 1,  gen(smooth_sch3 ) nodraw
        running sch_`model'4 _t if _d == 1,  gen(smooth_sch4 ) nodraw
        running sch_`model'5 _t if _d == 1,  gen(smooth_sch5 ) nodraw
        running sch_`model'6 _t if _d == 1,  gen(smooth_sch6 ) nodraw
        running sch_`model'7 _t if _d == 1,  gen(smooth_sch7 ) nodraw
        running sch_`model'8 _t if _d == 1,  gen(smooth_sch8 ) nodraw
        running sch_`model'9 _t if _d == 1,  gen(smooth_sch9 ) nodraw
        running sch_`model'10 _t if _d == 1, gen(smooth_sch10) nodraw
        running sch_`model'11 _t if _d == 1, gen(smooth_sch11) nodraw
        running sch_`model'12 _t if _d == 1, gen(smooth_sch12) nodraw
        running sch_`model'13 _t if _d == 1, gen(smooth_sch13) nodraw
        running sch_`model'14 _t if _d == 1, gen(smooth_sch14) nodraw
        running sch_`model'15 _t if _d == 1, gen(smooth_sch15) nodraw
        running sch_`model'16 _t if _d == 1, gen(smooth_sch16) nodraw
    gen smooth_esca1  = exp(smooth_sch1 )
    gen smooth_esca2  = exp(smooth_sch2 )
    gen smooth_esca3  = exp(smooth_sch3 )
    gen smooth_esca4  = exp(smooth_sch4 )
    gen smooth_esca5  = exp(smooth_sch5 )
    gen smooth_esca6  = exp(smooth_sch6 )
    gen smooth_esca7  = exp(smooth_sch7 )
    gen smooth_esca8  = exp(smooth_sch8 )
    gen smooth_esca9  = exp(smooth_sch9 )
    gen smooth_esca10 = exp(smooth_sch10)
    gen smooth_esca11 = exp(smooth_sch11)
    gen smooth_esca12 = exp(smooth_sch12)
    gen smooth_esca13 = exp(smooth_sch13)
    gen smooth_esca14 = exp(smooth_sch14)
    gen smooth_esca15 = exp(smooth_sch15)
    gen smooth_esca16 = exp(smooth_sch16)




loc model M3b_HR
***Combinable Graphs
        *Species (SpeciesX)
        loc var Species
        tw  line smooth_esca1 _t, sort lwidth(0.5) lc("27 158 119")  ||    ///
            line smooth_esca2 _t, sort lwidth(0.5) lc("217 95 2")    ||    ///
            line smooth_esca3 _t, sort lwidth(0.5) lc("117 112 179") ||    ///
            line smooth_esca4 _t, sort lwidth(0.5) lc("231 41 138")        ///
        name(`var'_PHtest, replace) ///
    legend(order(1 "{it: P.falciparum} (ref.)" 2 "{it: P.vivax} (p =  0.303)" 3 "{it: P.
    malariae}  (p = 0.424)" 4 "mixed  (p = 0.021)") pos(3) col(1) textwidth(20)
    forcesize) ///
        xtitle("time (days following presentation)", margin(medsmall))
        ytitle("exponentiated scaled Schoenfeld residuals", margin(medsmall))  subtitle("
        `var'") xmtick(2(1)15) graphr(color(white) lc(white)) plotr(color(white)
        lc(white)) ylab(, angle(h) labsize(medsmall) nogrid format(%9.1f)) xlab(1 "0" 2
        "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20) ysize(12)
        xsca(nofextend)  ylab(1, add)
```

```stata
    * graph export "C:\data\malaria\figures\PH test/`var'PHtest_`model'.png",
    as(png) replace width(800) height(600)


*Age (AGR4_4b)
loc var Age group
loc vars AGR4
tw  line smooth_esca6 _t, sort lwidth(0.5) lc("27 158 119") ||    ///
    line smooth_esca7 _t, sort lwidth(0.5) lc("217 95 2")   ||    ///
    line smooth_esca8 _t, sort lwidth(0.5) lc("117 112 179")||    ///
    line smooth_esca5 _t, sort lwidth(0.5) lc("231 41 138")       ///
    name(`vars'_PHtest, replace) ///
legend(order(1 "0 to < 1 year  (p =  0.426)" 2 "1 to < 5 years  (p = 0.026)" 3 "5 to
<15  (p =  0.452)" 4 "15+ (ref.)")  pos(3) col(1) textwidth(20) forcesize) ///
    xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
    margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
    lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
     format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
    xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


    * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
    as(png) replace width(800) height(600)
*Ethnic
loc var Ethnic group
loc vars EthnicX
tw  line smooth_esca9  _t, sort lwidth(0.5) lc("27 158 119")    ||    ///
    line smooth_esca10 _t, sort lwidth(0.5) lc("217 95 2")           ///
    non-Papuans exlcuded:   line smooth_esca11 _t, sort lwidth(0.5) lc("117 112
    179")
    name(`vars'_PHtest, replace) ///
    legend(order(1 "Highland (ref.)" 2 "Lowland  (p =  0.345)" 3 "non-Papuan (no
    deaths)")  pos(3) col(1) textwidth(20) forcesize) ///
    xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
    margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
    lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
     format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
    xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


        * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
        as(png) replace width(800) height(600)
*Sex and Pregnancy
loc var Sex and pregnancy status
loc vars sexPreg
tw  line smooth_esca12 _t, sort lwidth(0.5) lc("27 158 119")  ||    ///
    line smooth_esca13 _t, sort lwidth(0.5) lc("217 95 2")    ||    ///
    line smooth_esca14 _t, sort lwidth(0.5) lc("117 112 179")       ///
    name(`vars'_PHtest, replace) ///
    legend(order(1 "Female (not pregnant; ref.)" 2 "Female (pregnant; p =  0.446)" 3
    "Male  (p = 0.615)")  pos(3) col(1) textwidth(20) forcesize) ///
    xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
    margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
    lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
     format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
    xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


    * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
    as(png) replace width(800) height(600)
*Oral treatment
```

```
loc var Oral treatment
loc vars oralDHP
tw line smooth_esca15  _t, sort lwidth(0.5) lc("27 158 119") ||      ///
   line smooth_esca16  _t, sort lwidth(0.5) lc("217 95 2")          ///
   name(`vars'_PHtest, replace) ///
   legend(order(1 "oral quinine (ref.)" 2 "DHP  (p = 0.145)")  pos(3) col(1)
   textwidth(20) forcesize) ///
   xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
   margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
   lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
    format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
   xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)

       * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
       as(png) replace width(800) height(600)


loc model M3b_HR
graph combine Species_PHtest AGR4_PHtest sexPreg_PHtest EthnicX_PHtest
oralDHP_PHtest, col(1) graphr(color(white) lc(white)) plotr(color(white)) xcommon
ysize(20) xsize(12) name(PH_`model',replace) note("Global PH test: {&chi} 20.20, df =
 10, p < 0.0274", size(tiny)) iscale(0.4)
loc model M3b_HR
graph export "C:\data\malaria\figures\PH test\PH_`model'.emf", as(emf) replace


*Illustrative PH test with 95% CI  - following Royston Parmar in Flexible Parametric
Survival Analysis (chapter 7 "Cox with model time-dependent effects")
     ***Vivax
     use "C:\data\malaria\results\efron  8 Oct 2015 21_14_52\M3b_HR.dta", clear
     loc model M3b_HR
     loc v sch_`model'2
     loc outc Died
     loc v_name vivax
     running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se) nodraw
                  /* generate smoothed Schoenfeld residual and associated SE */
     gen `v'_smooth_e = exp(`v'_smooth)
                                        /* gen exponentiated
     smoothed Schoenfeld residual */
     gen `v'_smooth_e_lci = exp(`v'_smooth - 1.96
     *`v'_smooth_se)                /* lower 95% CI for exp. smth. Sch.
     residuals */
     gen `v'_smooth_e_uci = exp(`v'_smooth + 1.96
     *`v'_smooth_se)                /* upper 95% CI for exp. smth. Sch.
     residuals */
        tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort fc("253
        205 172")    lc("253 205 172")  ||  ///     /*Plot exp smth Sch residual
        CI area */
        line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")
        || ///     /* plot exp smth Sch residual estimate */
        function y = 1, lpattern(solid) range(_t) lc("27 158 119")
        || ///     /*plot null / baseline value of 1 */
        function y = 1.46, lpattern(shortdash) range(_t) lc(black)
        ///     /* plot estimated HR  for variable */
        name(M3_PH_Died_vivax, replace)
                                        ///     /* graph
        options */
```

```
        legend(order(2 "smoothed residuals (95 %CI)" 3 "{it: P.falciparum}
        (reference)"                                      ///
            4 "estimated HR 1.46 (95% CI 0.85, 2.51)") colfirst notextfirst
            nostack cols(1) size(small)      ///
            nobox region(fcolor(white) margin(zero) lcolor(white)) position(12)
            ring(1))            ///
        ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))
        ///
        title("Species: {it:P.vivax} relative to {it:P.falciparum}",
                        ///
            size(medsmall) )                    ///
        xtitle("Time (days) since presentation with malaria")
                                    ///
        ylabel(10(10)36.6 0.2 "0.2" 0.5 "0.5" 1 2 3 5, add nogrid angle(h)
        labsize(small))        ///
        xlab(1 "0" 2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)
        yscale(log)        ///
        graphr(color(white) lc(white)) plotr(color(white) lc(white))

    graph export "C:\data\malaria\figures\PH test\focusPH_`model'_pv.emf",
    as(emf) replace

    **OralDHP
    loc model M3b_HR
    loc v sch_`model'16
    loc outc Died
    loc v_name DHP
    running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se) nodraw
                /* generate smoothed Schoenfeld residual and associated SE */
    gen `v'_smooth_e = exp(`v'_smooth)
                                            /* gen exponentiated
    smoothed Schoenfeld residual */
    gen `v'_smooth_e_lci = exp(`v'_smooth - 1.96
    *`v'_smooth_se)              /* lower 95% CI for exp. smth. Sch.
    residuals */
    gen `v'_smooth_e_uci = exp(`v'_smooth + 1.96
    *`v'_smooth_se)              /* upper 95% CI for exp. smth. Sch.
    residuals */
        tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort fc("253
        205 172")    lc("253 205 172")   || ///        /*Plot exp smth Sch residual
        CI area */
        line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")       ||
        ///     /* plot exp smth Sch residual estimate */
        function y = 1, lpattern(solid) range(_t) lc("27 158 119")       ||
        ///     /*plot null / baseline value of 1 */
        function y = 0.97, lpattern(shortdash) range(_t) lc(black)
                                    ///     /* plot estimated HR  for
        variable */
        name(M3_PH_Died_DHP, replace)
                                            ///     /* graph
        options */
        legend(order(2 "smoothed residuals (95 %CI)" 3 "oral quinine (reference)"
                            ///
            4 "estimated HR 0.97  (95% CI 0.50, 1.86)") colfirst notextfirst
            nostack cols(1) size(small)      ///
            nobox region(fcolor(white) margin(zero) lcolor(white)) position(12)
            ring(1))          ///
```

```stata
                    ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))
                    ///
                    title("Oral treatment: DHP relative to quinine",             ///
                        size(medsmall) )                          ///
                    xtitle("Time (days) since presentation with malaria")
                                                ///
                    ylabel(10(10)24.7 0.003 "0.003" 0.1 "0.1" 0.5 "0.5" 1 2 3 5, add nogrid
                    angle(h) labsize(small))        ///
                    xlab(1 "0" 2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)
                    yscale(log)        ///
                    graphr(color(white) lc(white)) plotr(color(white) lc(white))

            graph export "C:\data\malaria\figures\PH test\focusPH_`model'_DHP.emf",
            as(emf) replace
            graph combine M3_PH_Died_vivax M3_PH_Died_DHP, col(1) graphr(color(white)
            lc(white)) plotr(color(white)) ysize(20) xsize(12)
            name(PH_M3combo_PvDHP,replace) xcommon
            loc model M3b_HR
            graph export "C:\data\malaria\figures\PH test/`model'_combo_PvDHP.emf",
            as(emf) replace
```

*M4AHR:
***risk of death by day 15 limited to those who were admitted immediately & rx'd IV treatment first
*** Variables are Species (omitting Ovale), Age group (4 categories), Ethnic group, combined sex and pregnancy status, and IV treatment

```stata
use "C:\data\malaria\results\efron  8 Oct 2015 21_14_52\M4a_HR.dta", clear

/*  STORED MODEL WITH GENERATED SCALED SCHOENFELD RESIDUALS
loc model M4a_HR
stcox i.SpeciesX i.AGR4_4b i.EthnicX i.sexPreg i.ivArt if ip==1 , allbaselevels vsquish
cluster(hrn) efron cformat(%6.2f) nolog
predict `i'*, scaledsch
*/
loc model M4a_HR

        running sch_`model'1 _t if _d == 1,  gen(smooth_sch1 ) nodraw
        running sch_`model'2 _t if _d == 1,  gen(smooth_sch2 ) nodraw
        running sch_`model'3 _t if _d == 1,  gen(smooth_sch3 ) nodraw
        running sch_`model'4 _t if _d == 1,  gen(smooth_sch4 ) nodraw
        running sch_`model'5 _t if _d == 1,  gen(smooth_sch5 ) nodraw
        running sch_`model'6 _t if _d == 1,  gen(smooth_sch6 ) nodraw
        running sch_`model'7 _t if _d == 1,  gen(smooth_sch7 ) nodraw
        running sch_`model'8 _t if _d == 1,  gen(smooth_sch8 ) nodraw
        running sch_`model'9 _t if _d == 1,  gen(smooth_sch9 ) nodraw
        running sch_`model'10 _t if _d == 1, gen(smooth_sch10) nodraw
        running sch_`model'11 _t if _d == 1, gen(smooth_sch11) nodraw
        running sch_`model'12 _t if _d == 1, gen(smooth_sch12) nodraw
        running sch_`model'13 _t if _d == 1, gen(smooth_sch13) nodraw
        running sch_`model'14 _t if _d == 1, gen(smooth_sch14) nodraw
        running sch_`model'15 _t if _d == 1, gen(smooth_sch15) nodraw
        running sch_`model'16 _t if _d == 1, gen(smooth_sch16) nodraw
        gen smooth_esca1  = exp(smooth_sch1 )
        gen smooth_esca2  = exp(smooth_sch2 )
        gen smooth_esca3  = exp(smooth_sch3 )
        gen smooth_esca4  = exp(smooth_sch4 )
```

```
gen smooth_esca5  = exp(smooth_sch5 )
gen smooth_esca6  = exp(smooth_sch6 )
gen smooth_esca7  = exp(smooth_sch7 )
gen smooth_esca8  = exp(smooth_sch8 )
gen smooth_esca9  = exp(smooth_sch9 )
gen smooth_esca10 = exp(smooth_sch10)
gen smooth_esca11 = exp(smooth_sch11)
gen smooth_esca12 = exp(smooth_sch12)
gen smooth_esca13 = exp(smooth_sch13)
gen smooth_esca14 = exp(smooth_sch14)
gen smooth_esca15 = exp(smooth_sch15)
gen smooth_esca16 = exp(smooth_sch16)


loc model M4a_HR

***Combinable Graphs
    *Species (SpeciesX)
    loc var Species
    tw  line smooth_esca1 _t, sort lwidth(0.5) lc("27 158 119")  ||    ///
        line smooth_esca2 _t, sort lwidth(0.5) lc("217 95 2")    ||   ///
        line smooth_esca3 _t, sort lwidth(0.5) lc("117 112 179") ||    ///
        line smooth_esca4 _t, sort lwidth(0.5) lc("231 41 138")        ///
        name(`var'_PHtest, replace) ///
legend(order(1 "{it: P.falciparum} (ref.)" 2 "{it: P.vivax}  (p = 0.792)" 3 "{it: P.
malariae}  (p = 0.170)" 4 "mixed (p = 0.395)") pos(3) col(1) textwidth(20) forcesize)
 ///
        xtitle("time (days following presentation)", margin(medsmall))
        ytitle("exponentiated scaled Schoenfeld residuals", margin(medsmall))  subtitle("
        `var'") xmtick(2(1)15) graphr(color(white) lc(white)) plotr(color(white)
        lc(white)) ylab(, angle(h) labsize(medsmall) nogrid format(%9.1f)) xlab(2 "1" 8
        "7"  15 "14", labsize(medsmall)) ysca(log) xsize(20) ysize(12) xsca(nofextend)
        ylab(1, add)

        * graph export "C:\data\malaria\figures\PH test/`var'PHtest_`model'.png",
        as(png) replace width(800) height(600)

    *Age (AGR4_4b)
    loc var Age group
    loc vars AGR4
    tw  line smooth_esca6 _t, sort lwidth(0.5) lc("27 158 119") ||    ///
        line smooth_esca7 _t, sort lwidth(0.5) lc("217 95 2")    ||   ///
        line smooth_esca8 _t, sort lwidth(0.5) lc("117 112 179")||    ///
        line smooth_esca5 _t, sort lwidth(0.5) lc("231 41 138")       ///
        name(`vars'_PHtest, replace) ///
legend(order(1 "0 to < 1 year  (p = 0.080)" 2 "1 to < 5 years  (p = 0.129)" 3 "5 to <
15  (p = 0.0005)" 4 "15+ (ref.)")  pos(3) col(1) textwidth(20) forcesize) ///
        xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
        margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
        lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
         format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
        xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)

        * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
        as(png) replace width(800) height(600)
    *Ethnic
    loc var Ethnic group
```

```stata
        loc vars EthnicX
        tw  line smooth_esca9  _t, sort lwidth(0.5) lc("27 158 119")    ||    ///
            line smooth_esca10 _t, sort lwidth(0.5) lc("217 95 2")       ||    ///
            line smooth_esca11 _t, sort lwidth(0.5) lc("117 112 179")          ///
            name(`vars'_PHtest, replace) ///
            legend(order(1 "Highland (ref.)" 2 "Lowland  (p = 0.517)" 3 "non-Papuan (p = 0.
            115)")  pos(3) col(1) textwidth(20) forcesize) ///
            xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
            margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
            lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
             format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
            xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


            * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
            as(png) replace width(800) height(600)
    *Sex and Pregnancy
        loc var Sex and pregnancy status
        loc vars sexPreg
        tw  line smooth_esca12  _t, sort lwidth(0.5) lc("27 158 119")   ||    ///
            line smooth_esca13  _t, sort lwidth(0.5) lc("217 95 2")      ||    ///
            line smooth_esca14  _t, sort lwidth(0.5) lc("117 112 179")         ///
            name(`vars'_PHtest, replace) ///
            legend(order(1 "Female (not pregnant; ref.)" 2 "Female (pregnant, p = 0.629)" 3
            "Male  (p = 0.106)") pos(3) col(1) textwidth(20) forcesize) ///
            xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
            margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
            lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
             format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
            xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


            * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
            as(png) replace width(800) height(600)
    *Oral treatment
        loc var IV treatment
        loc vars ivArt
        tw  line smooth_esca15  _t, sort lwidth(0.5) lc("27 158 119") ||     ///
            line smooth_esca16  _t, sort lwidth(0.5) lc("217 95 2")          ///
            name(`vars'_PHtest, replace) ///
            legend(order(1 "IV quinine (ref.)" 2 "IV artesunate  (p = 0.965)") pos(3) col(1)
            textwidth(20) forcesize) ///
            xtitle("time (days following presentation)", margin(medsmall)) ytitle(" ",
            margin(medsmall))  subtitle("`var'") xmtick(2(1)15) graphr(color(white)
            lc(white)) plotr(color(white) lc(white)) ylab(, angle(h) labsize(medsmall) nogrid
             format(%9.1f)) xlab(1 "0" 2 "1" 8 "7"  15 "14", labsize(medsmall)) ysca(log)
            xsize(20) ysize(12) xsca(nofextend)  ylab(1, add)


            * graph export "C:\data\malaria\figures\PH test/`vars'PHtest_`model'.png",
            as(png) replace width(800) height(600)
loc model M4a_HR
        graph combine Species_PHtest AGR4_PHtest sexPreg_PHtest EthnicX_PHtest ivArt_PHtest,
        col(1) graphr(color(white) lc(white)) plotr(color(white)) xcommon ysize(20) xsize(12)
         name(PH_`model',replace) note("Global PH test: {&chi} 24.48, df = 11, p < 0.0108",
        size(tiny)) iscale(0.4)
        loc model M4a_HR
        graph export "C:\data\malaria\figures\PH test\PH_`model'.emf", as(emf) replace


*Illustrative PH test with 95% CI  - following Royston Parmar in Flexible Parametric Survival
```

```stata
Analysis (chapter 7 "Cox with model time-dependent effects")
***Vivax
use "C:\data\malaria\results\efron  8 Oct 2015 21_14_52\M4a_HR.dta", clear
loc model M4a_HR
loc v sch_`model'2
loc outc Adm
loc v_name vivax
running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se) nodraw /* gen smoothed
Schoenfeld residual and associated SE */
gen `v'_smooth_e = exp(`v'_smooth)                              /* gen exponentiated
smoothed Schoenfeld residual */
gen `v'_smooth_e_lci = exp(`v'_smooth - 1.96*`v'_smooth_se)        /* lower 95% CI for exp.
smth. Sch. residuals */
gen `v'_smooth_e_uci = exp(`v'_smooth + 1.96*`v'_smooth_se)        /* upper 95% CI for exp.
smth. Sch. residuals */
    tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort fc("253 205 172")
    lc("253 205 172")   ||  ///       /*Plot exp smth Sch residual CI area */
    line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")              ||  ///      /*
    plot exp smth Sch residual estimate */
    function y = 1, lpattern(solid) range(_t) lc("27 158 119")              ||  ///
    /*plot null / baseline value of 1 */
    function y = 1.26, lpattern(shortdash) range(_t) lc(black)          ///      /* plot
    estimated HR  for variable */
    name(M4_PH_Died_vivax, replace)                                      ///
    /* graph options */
    legend(order(2 "smoothed residuals (95 %CI)" 3 "{it: P.falciparum} (reference)"
                                    ///
        4 "estimated HR 1.26 (95% CI 0.97,  1.64)") colfirst notextfirst nostack cols(1)
        size(small)        ///
        nobox region(fcolor(white) margin(zero) lcolor(white)) position(12) ring(1))
                ///
    ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))   ///
    title("Species: {it:P.vivax} relative to {it:P.falciparum}",             ///
        size(medsmall) )              ///
    xtitle("Time (days) since presentation with malaria")                    ///
    ylabel(2(2)6 0.4 "0.4" 1, nogrid angle(h) labsize(small))
                                    ///
    xlab(1 "0" 2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)   yscale(log)
    ///
    graphr(color(white) lc(white)) plotr(color(white) lc(white))

graph export "C:\data\malaria\figures\PH test\focusPH_`model'_pv.emf", as(emf) replace


**ivArt
loc model M4a_HR
loc v sch_`model'16
loc outc Died
loc v_name ivArt
running `v' _t if _d==1, gen(`v'_smooth) gense(`v'_smooth_se) nodraw /* gen smoothed
Schoenfeld residual and associated SE */
gen `v'_smooth_e = exp(`v'_smooth)                              /* gen exponentiated
smoothed Schoenfeld residual */
gen `v'_smooth_e_lci = exp(`v'_smooth - 1.96*`v'_smooth_se)          /* lower 95% CI
for exp. smth. Sch. residuals */
gen `v'_smooth_e_uci = exp(`v'_smooth + 1.96*`v'_smooth_se)          /* upper 95% CI
for exp. smth. Sch. residuals */
tw rarea `v'_smooth_e_lci `v'_smooth_e_uci _t, pstyle(ci) sort          ///
```

```stata
        fc("253 205 172")   lc("253 205 172")   ||                 ///      /*Plot exp
        smth Sch residual CI area */
    line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2")       ||  ///      /* plot exp
    smth Sch residual estimate */
    function y = 1, lpattern(solid) range(_t) lc("27 158 119")         ||  ///      /*plot null /
    baseline value of 1 */
    function y = 2.64, lpattern(shortdash) range(_t) lc(black)         ///      /* plot
    estimated HR  for variable */
    name(M4_PH_Died_ivArt, replace)                                   ///      /* graph
    options */
    legend(order(2 "smoothed residuals (95 %CI)" 3 "IV quinine (reference)"
                        ///
        4 "estimated HR 2.64  (95% CI 1.83, 3.82)") colfirst notextfirst nostack cols(1)
            ///
        size(small) nobox region(fcolor(white) margin(zero) lcolor(white)) position(12)
        ring(1)) ///
    ytitle("Exponentiated scaled Schoenfeld residuals", margin(medsmall))
                        ///
    title("Intravenous treatment: artesunate relative to quinine",
                            ///
        size(medsmall) )
                                                                     ///
    xtitle("Time (days) since presentation with malaria")
                            ///
    ylabel(2(2)10 0.5 "0.5" 1 15, nogrid angle(h) labsize(small))
                        ///
    xlab(1 "0" 2 "1" 8 "7"  15 "14") xmtick(1(1)15)  xscale(nofextend)    yscale(log)
            ///
    graphr(color(white) lc(white)) plotr(color(white) lc(white))


graph export "C:\data\malaria\figures\PH test\focusPH_`model'_ivArt.emf", as(emf) replace


graph combine M4_PH_Died_vivax M4_PH_Died_ivArt, col(1) graphr(color(white) lc(white))
        ///
        plotr(color(white)) ysize(20) xsize(12) name(PH_M4combo_PvArt,replace) xcommon
loc model M4a_HR
graph export "C:\data\malaria\figures\PH test/`model'_combo_PvArt.emf", as(emf) replace
```