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

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**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

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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
*/

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loc model M2a_HR

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***Combination Graphs

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*Species (SpeciesX)

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use "C:\data\malaria\results\efron 8 Oct 2015 16_30_08\M2a_HR.dta", clear
/*smooth scaled Schoenfeld residuals with running mean line smoother*/
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
/*exponentiate smoothed scaled Schoenfeld residuals for plotting*/
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 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)

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

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*Age (AGR4_4b)

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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)

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    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:  $\chi^2$  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 /* 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(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 " $\chi^2$ : 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:  $\chi^2$ :P.vivax relative to  $\chi^2$ :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

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loc outc Adm
loc v_name DHP
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(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)) ///
ytile("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
*/

loc model M3b_HR
/*smooth scaled Schoenfeld residuals with running mean line smoother*/
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
/*exponentiate smoothed scaled Schoenfeld residuals for plotting*/
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") || ///

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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)

```

* 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 excludid: 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 /* 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") || ///
line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2") || /// /*Plot exp smth Sch residual CI area */
function y = 1, lpattern(solid) range(_t) lc("27 158 119") || /// /* plot exp smth Sch residual estimate */
function y = 1.46, lpattern(shortdash) range(_t) lc(black) || /// /*plot null / baseline value of 1 */
name(M3_PH_Died_vivax, replace) /// /* plot estimated HR for variable */
legend(order(2 "smoothed residuals (95 %CI)" 3 "{it:P.falciparum}" (reference)) /// /* graph options */
    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") || ///
line `v'_smooth_e _t, sort clpattern(solid) lc("217 95 2") || /// /*Plot exp smth Sch residual CI area */
function y = 1, lpattern(solid) range(_t) lc("27 158 119") || /// /* plot exp smth Sch residual estimate */
function y = 0.97, lpattern(shortdash) range(_t) lc(black) || /// /*plot null / baseline value of 1 */
name(M3_PH_Died_DHP, replace) /// /* plot estimated HR for variable */
legend(order(2 "smoothed residuals (95 %CI)" 3 "oral quinine (reference)" /// /* graph options */
    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)) ///
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

```
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
```

```
/*smooth scaled Schoenfeld residuals with running mean line smoother*/
```

```
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
```

```
/*exponentiate smoothed scaled Schoenfeld residuals for plotting*/
```

```
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
```

```
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:  $\chi^2$  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 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 ///
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

```