Design and Analysis of Nest Survival Studies
Part 3
Proportional Hazard Models

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Outline I

Proportional hazard models in *R*

Proportional hazard models

- Specialized type of survival analysis commonly used in medical trials
- Relaxes an assumption about the DSR over time
- Most useful for determining RELATIVE effects of covariates on DSR rather than estimating the DSR
- Need to load a function and preprocess the data.
- Need to have a deep understanding of *R* to use effectively.
- Relatively easy to add random effects.

Nur et al (2004) have an introduction to the use of survival models in nest survival studies.

Proportional hazard models in R

What is the **hazard**??

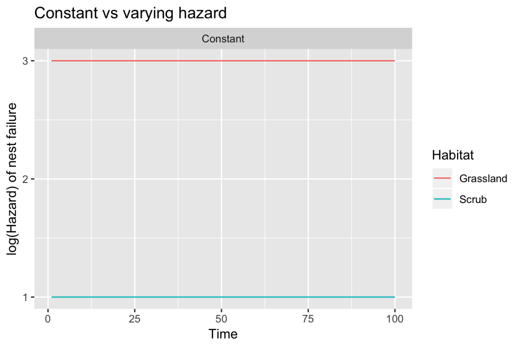
$h(t) =$ instantaneous risk of failure at T conditional on survival to that ti

$$h(t) = \lim_{\Delta t \to 0} \frac{P(fail\ in\ T \to T + \Delta t)}{\Delta t}$$

For example, for a constant DSR over time, then
$h(t) \approx log(-DSR)$

Common to model $\log h(t)$ to keep hazard from going below 0.

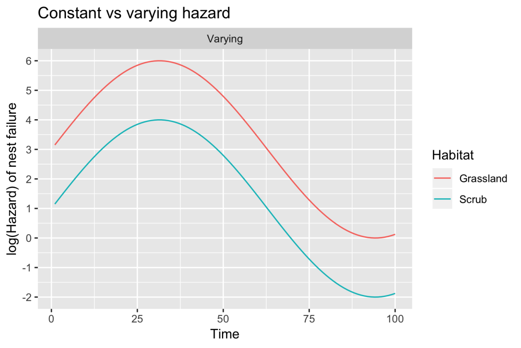
What is meant by proportional hazard?



This is the key assumption made when fitting nest survival models with covariates.

Proportional hazard models in *R*

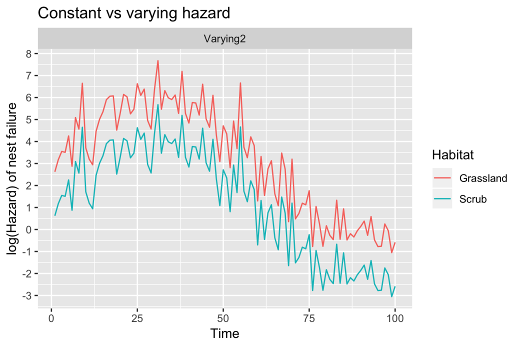
What is meant by proportional hazard?



You could fit a time trend to capture variation in hazard over time?

Proportional hazard models in *R*

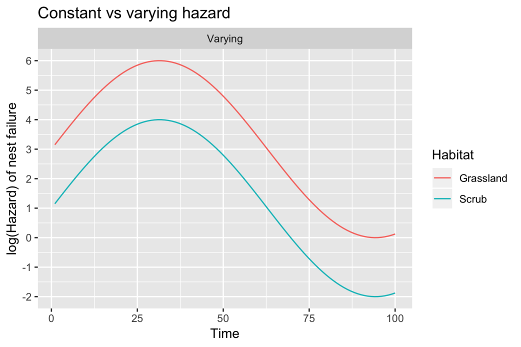
What is meant by proportional hazard?



Cox proportional hazard makes no assumption about underlying hazard but only assumes that hazards are proportional (on log-scale).

Proportional hazard models in *R*

What is meant by proportional hazard?



You could fit a time trend to capture variation in hazard over time?

Proportional hazard models in *R*

More formally, let $logh(t)$ be the arbitrary baseline hazard function. Then

$$logh_{covariate}(t) = logh(t) + \beta \times covariate$$

The β is the log(*hazard ratio*) due to the covariate.

- Fit using method of partial likelihood (Cox, 1972).
- Not as fully efficient compared to model where you model the baseline hazard function, but loss of efficiency is rather small.
- Usual AIC methods for model selection.
- Possible to estimate the baseline hazard (and DSR, and nest survival) but not focus of the study.
- Need to expand the nest data in similar fashion as before.
- Use *coxph()* in *survival* package.

Covariates

Often the influence of covariates on the DSR is of interest.

Covariates can be:

- **Categorical** e.g. habitat type
- **Continuous**, e.g. distance from water

Covariates can operate at the

- **Nest level** are are fixed for the duration of the nest, e.g. distance from water
- **Day level** and are common to all nests, e.g. linear trend in DSR
- **Nest x Day** level where each nest's covariates vary over the days, e.g. nest-age, mowing

The **Nest x Day** covariates are easier to implement with Cox PH models compared to *MARK* and *RMark*.

Covariates

Hypotheses about covariates

- Is there evidence of an effect? Look at estimates/se and model selection table
- Not clear how to estimate DSR in Cox PH models, i.e. average DSR, DSR at certain points in time not sensible since hazard is 0 when no failure occur.

Covariates

Nest-level covariates.

- Continuous covariates
  - Enter as a numeric columns in the nest data frame.
  - Specify variable name in formula, e.g. $Surv \sim Distance$).
- Categorical covariates
  - Enter as an alphanumeric columns in the nest data frame and declare as a factor.
  - Specify variable name in formula, e.g. $Surv \sim Treatment$).

Read in the **mallard** dataset.

```
malldata <- readxl::read_excel("mallard.xlsx",
                                 sheet="mallard")
head(malldata)
malldata <- as.data.frame(malldata) #avoid tibble problems

mallard3 <- expand.nest.data.ph(malldata)

malldata3$Habitat <- factor(malldata3$Habitat)
```

Not necessary that categorical variables be declared as factors

Nest level categorical covariates - Cox PH models I

Look at the data format for the Cox PH models

	First Found	Last Present	Last Checked	Fate	Start	End	Fail	Surv
1	73	89	89	0	73	74	0	(73,74+]
2	73	89	89	0	74	75	0	(74,75+]
...								
15	73	89	89	0	87	88	0	(87,88+]
16	73	89	89	0	88	89	0	(88,89+]
17	63	90	90	0	63	64	0	(63,64+]
18	63	90	90	0	64	65	0	(64,65+]
...								
43	63	90	90	0	89	90	0	(89,90+]
44	70	70	76	1	70	76	1	(70,76]

Nest level categorical covariates - Cox PH models II

```
45    63    81    85    1    63  64    0 (63,64+]
46    63    81    85    1    64  65    0 (64,65+]
...
62    63    81    85    1    80  81    0 (80,81+]
63    63    81    85    1    81  85    1  (81,85]
```

Notice how each day when nest is alive is separated in to individual record.

The *Surv* variable is a special variable created that indicates if the data are censored or a failure occured.

Nest level categorical covariates - Cox PH models I

Use the categorical variable in the model

```
mod.hab.ph <-  coxph(Surv~Habitat, data=malldata3)
summary(mod.hab.ph)
```

Nest level categorical covariates - Cox PH models II

```
             coef  exp(coef)  se(coef)      z  Pr(>|z|)
HabitatP -0.1996     0.8190    0.1249  -1.598     0.110
HabitatR -0.2059     0.8139    0.2300  -0.895     0.371
HabitatW -0.0697     0.9327    0.2403  -0.290     0.772

         exp(coef) exp(-coef) lower .95 upper .95
HabitatP    0.8190      1.221    0.6412     1.046
HabitatR    0.8139      1.229    0.5185     1.278
HabitatW    0.9327      1.072    0.5824     1.494

Concordance= 0.518  (se = 0.014 )
Likelihood ratio test= 2.73  on 3 df,   p=0.4
Wald test            = 2.78  on 3 df,   p=0.4
Score (logrank) test = 2.79  on 3 df,   p=0.4
```

Each value of habitat is compared to the baseline habitat so it makes it difficult to interpret. Refer to the CLD output.

Nest level categorical covariates -logexp() models I

DO NOT TRUST the output from the summary table as it depends on the (hidden) contrast matrix used to set up the indicator variables.
Values can change depending on user's configuration without warning.

- Use the *emmeans* package (with some modification for the custom link function) as the results are independent of the (hidden) contrast matrix or reference level used.

This is preferred when need to average levels of other factors (i.e. marginal estimates)

Nest level categorical covariates - Cox PH models I

Using the *emmeans* package

- Set up the reference grid (the emmeans object)
- Get the Pairwise differences on log-hazard scale
- Get the pairwise hazard ratios

Nest level categorical covariates - Cox PH models II

```
mod.hab.ph.emmo <- emmeans::emmeans(mod.hab.ph, ~Habitat)
summary(pairs(mod.hab.ph.emmo), infer=TRUE)
summary(pairs(mod.hab.ph.emmo, type="response"), infer=TRU
```

```
> summary(pairs(mod.hab.ph.emmo), infer=TRUE)
 contrast estimate    SE df asymp.LCL asymp.UCL z.ratio p.v
 N - P     0.19964 0.125 NA    -0.121     0.521  1.598  0.3
 N - R     0.20588 0.230 NA    -0.385     0.797  0.895  0.8
 N - W     0.06970 0.240 NA    -0.548     0.687  0.290  0.9
 P - R     0.00624 0.224 NA    -0.568     0.581  0.028  1.0
 P - W    -0.12993 0.234 NA    -0.731     0.471 -0.556  0.9
 R - W    -0.13618 0.304 NA    -0.917     0.645 -0.448  0.9

Results are given on the log (not the response) scale.
Confidence level used: 0.95 ...
```

Nest level categorical covariates - Cox PH models III

```
> summary(pairs(mod.hab.ph.emmo, type="response"), infer=TI
 contrast ratio    SE df asymp.LCL asymp.UCL z.ratio p.valu
 N / P    1.221 0.153 NA     0.886      1.68  1.598  0.3795
 N / R    1.229 0.283 NA     0.680      2.22  0.895  0.8075
 N / W    1.072 0.258 NA     0.578      1.99  0.290  0.9915
 P / R    1.006 0.225 NA     0.567      1.79  0.028  1.0000
 P / W    0.878 0.205 NA     0.482      1.60 -0.556  0.9450
 R / W    0.873 0.265 NA     0.400      1.91 -0.448  0.9700

Confidence level used: 0.95
Conf-level adjustment: tukey method for comparing a family
Intervals are back-transformed from the log scale
P value adjustment: tukey method for comparing a family of
Tests are performed on the log scale
```

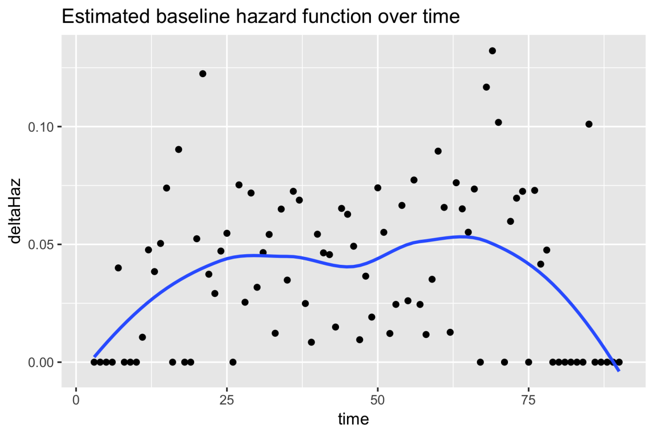
These are the difference in log(*hazard*) and hazard ratios respectively.

Nest level categorical covariates - Cox PH models I

Get the baseline hazard and plot

```
cumhaz <- basehaz(mod.hab.ph)
# estimate change in cumulative hazard and plot
cumhaz$deltaHaz <- c(NA,diff(cumhaz$hazard))
basehaz.plot <- ggplot(data=cumhaz, aes(x=time, y=deltaHaz)
  ggtitle("Estimated baseline hazard function over time")+
  geom_point()+
  geom_smooth(se=FALSE)
basehaz.plot
```

Nest level categorical covariates - Cox PH models



Appears to be general increase in hazard over time.
Dips at start/end are artefacts of the data.

Nest level categorical covariates - Cox PH models I

Testing for assumption of proportional hazards.

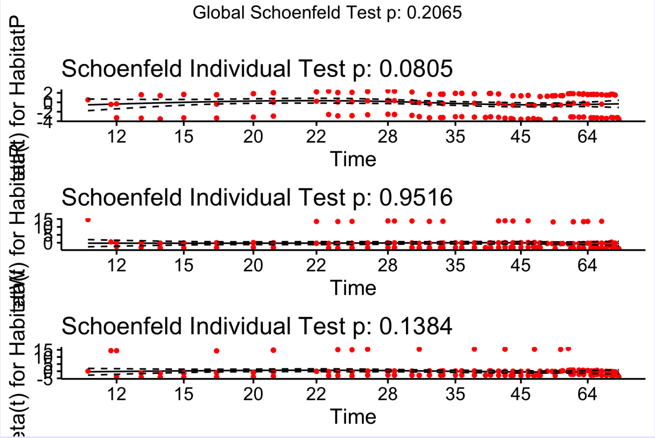
```
cox.zph(mod.hab.ph)
ggcoxzph(cox.zph(mod.hab.ph))
```

Nest level categorical covariates - Cox PH models II

```
> cox.zph(mod.hab.ph)
              rho   chisq      p
HabitatP -0.09736 3.05475 0.0805
HabitatR  0.00341 0.00368 0.9516
HabitatW -0.08343 2.19603 0.1384
GLOBAL         NA 4.56614 0.2065
```

No evidence of lack of fit.

Nest level categorical covariates - Cox PH models III



Look for flatness of curves.

Curves appear to be relatively flat.

Nest level categorical covariates - Cox PH models I

"Testing" for covariate effects (standard null hypothesis testing) is NOT recommended as does not provide useful information.

Better to get estimates use AIC with a null model to see the weight of evidence, followed by model averaging.

Nest level categorical covariates - Cox PH models I

a null model and do AIC.

```
mod.null.ph <- coxph(Surv~1, data=malldata3)

AICcmodavg::aictab( list(mod.hab.ph, mod.null.ph))
```

Nest level categorical covariates - Cox PH models II

	K	AICc	Delta_AICc	AICcWt	Cum.Wt	LL
Mod2	0	2962.64	0.00	0.84	0.84	-1481.32
Mod1	3	2965.91	3.27	0.16	1.00	-1479.95

Rather odd a model with 0 parameters (!)
Not much evidence for an impact of habitat on the DSR relative to the null model.
While model averaging is possible, it is not clear if these model averaged estimates are useful?

Nest level categorical covariates - Cox PH models III

logexp() model gives

	K	AICc	Delta_AICc	AICcWt	Cum.Wt	LL
Mod2	1	1569.12	0.00	0.81	0.81	-783.56
Mod1	4	1571.96	2.84	0.19	1.00	-781.98

Nest level continuous covariates I

Use the continuous variable in the model directly.
You may wish to standardize covariates that take large values.

Example, effect of cover (Robel height) on hazard

```
mod.rob.ph <-  coxph(Surv~Robel,data=malldata3)
summary(mod.rob.ph)
```

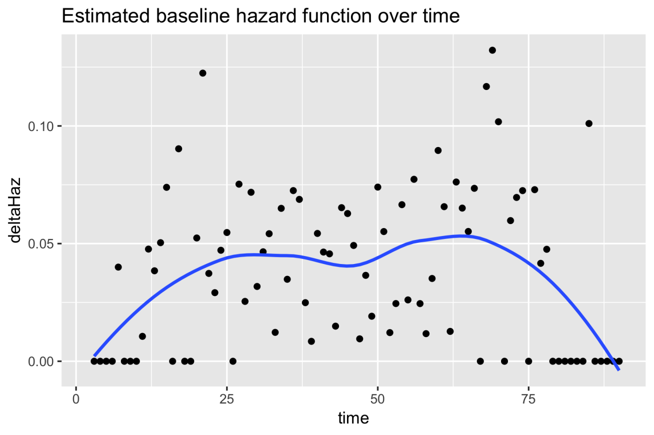
Nest level continuous covariates II

```
         coef exp(coef) se(coef)      z Pr(>|z|)
Robel -0.03877   0.96197  0.04888 -0.793    0.428

      exp(coef) exp(-coef) lower .95 upper .95
Robel     0.962       1.04    0.8741     1.059

Concordance= 0.512  (se = 0.014 )
Likelihood ratio test= 0.63  on 1 df,   p=0.4
Wald test            = 0.63  on 1 df,   p=0.4
Score (logrank) test = 0.63  on 1 df,   p=0.4
```

Estimated slope (on difference in log hazard) of failure is -0.0387 (SE .048) and 95% ci for slope includes zero.
So a decrease hazard of failure with increase in Robel height.

Nest level continuous covariates - Cox PH models

Baseline hazard will be same as for habitat model



Appears to be general increase in hazard over time.
Dips at start/end are artefacts of the data.

Nest level continuous covariates - Cox PH models I

Testing for assumption of proportional hazards.

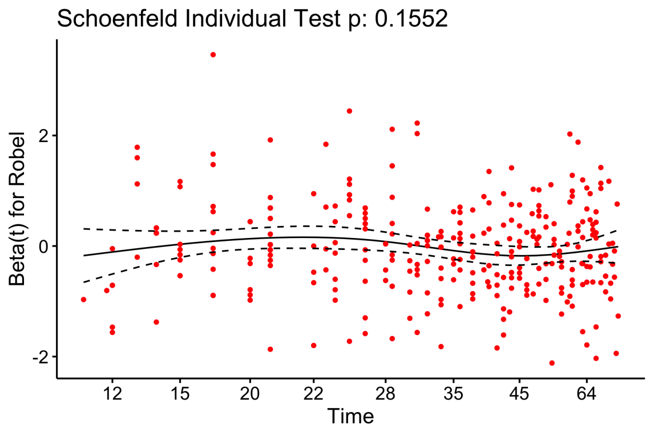
```
cox.zph(mod.rob.ph)
ggcoxzph(cox.zph(mod.rob.ph))
```

Nest level continuous covariates - Cox PH models II

```
> cox.zph(mod.rob.ph)
          rho chisq     p
Robel -0.0829  2.02 0.155
```

No evidence of lack of fit.

Nest level continuous covariates - Cox PH models III



Look for flatness of curves.
Curves appear to be relatively flat.

Nest level continuous covariates - Cox PH model I

"Testing" for covariate effects (standard null hypothesis testing) is NOT recommended as does not provide useful information.

Better to get estimates use AIC with a null model to see the weight of evidence, followed by model averaging.

Nest level continuous covariates - Cox PH model I

Fit a null model and do AIC in the usual way.

```
     K    AICc Delta_AICc AICcWt Cum.Wt       LL
Mod2 0 2962.64       0.00   0.66   0.66 -1481.32
Mod1 1 2964.01       1.37   0.34   1.00 -1481.00
```

logexp() model gives

```
 collect.models(type="Nest")
     model npar     AICc DeltaAICc    weight Deviance
1     S(~1)    1 1569.117  0.000000 0.6961759 1567.116
2 S(~Robel)    2 1570.775  1.658307 0.3038241 1566.773
```

Not much evidence for an impact of Robel height on the DSR relative to the null model.

Sampling occasion covariates - Cox PH model

These covariates apply to the sample occasions for all nests.

Add these to the data frame in the usual way for each nest and proceed similarly.

Journal of Avian Biology 46: 559–569, 2015
doi: 10.1111/jav.00536

Subject Editor: Peter Arcese. Editor-in-Chief: Thomas Alerstam. Accepted 5 April 2015

Impacts of nest predators and weather on reproductive success and population limitation in a long-distance migratory songbird

Thomas W. Sherry, Scott Wilson, Sarah Hunter and Richard T. Holmes

Exercise - Sherry - 2 - Cox PH models I

1. Refer to Table 1a.
    - Create a similarTable 1a.
    - Examine hazard ratio for Baffle Status for top ranked model.

Exercise - Sherry - 2 - Cox PH models II

Results from Cox PH model

```
Model selection based on AICc:

                               K    AICc Delta_AICc AICcWt Cum.
~DBH+YearF+BaffleStatus.3 11 1566.57       0.00      1
~DBH+YearF.2              10 1581.10      14.54      0
~DBH.1                     1 1602.46      35.89      0
```

Exercise - Sherry - 2 - Cox PH models III

```
> summary(pairs(fit.emmo, type="response"), infer=TRUE)
 contrast ratio    SE df asymp.LCL asymp.UCL z.ratio p.valu
 N / Y      2.5 0.623 NA      1.53      4.07 3.670   0.0002

Results are averaged over the levels of: YearF
Confidence level used: 0.95
Intervals are back-transformed from the log scale
Tests are performed on the log scale
```

Baffle status (N) has a higher hazard of failure than baffled trees.

Nest x Time covariates - Cox PH models

These covariates vary by nest for each day of the study. These are unlikely to be used in nest studies except for **Nest Age**.

Much simpler in the Cox PH models because you have a record for each day in the study for each nest (after expansion).

Some approximation is done for last interval where failure of a nest occurs but the time of the failure is unknown. The midpoint of the interval is used for the time of the study and nest age.

CAUTION:: Nest Age and Time are highly correlated so unless you have high contrast, you will be unable to distinguish between the two effects. You may wish to replace Time by NestAge in the *Surv* variable.

Age effects - Cox PH models

The variable **AgeDay1** for the age of the nest on the first day of the season. The variable **AgeDay1** in the datafile.is then used to generate a variable **NestAge** for every day for every nest when the data is expanded. in the modelling.

Including age effects - Cox PH models

Open the *killdeer.xlsx* workbook.
Open the *killdeer-age.R* script.

We read in the raw data and expand the data
Notice the fieldnames MUST match exactly as given. but the order of columns can differ. The *id* column is optional.

```
killdata <- readxl::read_excel("Killdeer.xlsx",
                               sheet="killdeer-age")
head(killdata)

killdata2 <- expand.nest.data.ph(killdata)
```

Note that age assigned to midpoint of last interval.

Including age effects - Cox PH models I

Fit a model with nest age as an additional covariate

```
mod.age <-  coxph(Surv~NestAge, data=killdata2)
summary(mod.age)
```

Including age effects - Cox PH models II

This gives the output

```
             coef exp(coef) se(coef)      z Pr(>|z|)
NestAge -0.3359    0.7147   0.1728 -1.944   0.0519 .
-
        exp(coef) exp(-coef) lower .95 upper .95
NestAge    0.7147      1.399    0.5094     1.003

Concordance= 0.815  (se = 0.084 )
Likelihood ratio test= 6.95  on 1 df,   p=0.008
Wald test            = 3.78  on 1 df,   p=0.05
Score (logrank) test = 5.53  on 1 df,   p=0.02
```

Data set is likely too small to use Nest Age as useful covariate.

Articles

Editor's Choice

Journal of Avian Biology 46: 559–569, 2015
doi: 10.1111/jav.00536

Subject Editor: Peter Arcese. Editor-in-Chief: Thomas Alerstam. Accepted 5 April 2015

Impacts of nest predators and weather on reproductive success and population limitation in a long-distance migratory songbird

Thomas W. Sherry, Scott Wilson, Sarah Hunter and Richard T. Holmes

Refer to Table 1b.

1. Make similar Table 1b
2. Look at estimated beta from top model and contrast to results in paper.
3. Check baseline hazard.
4. Check proportion assumption

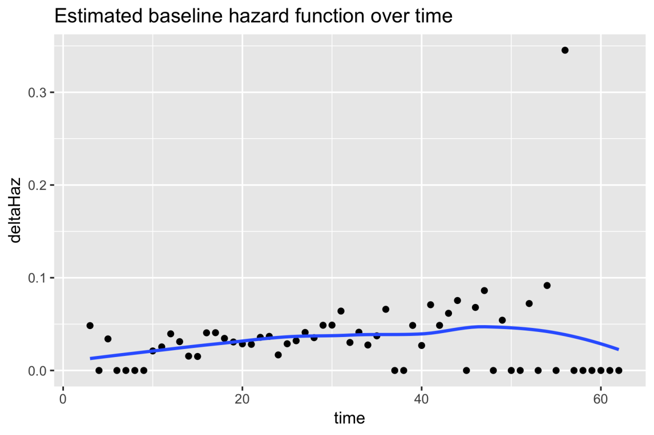
Results from Cox PH model for best model

```
Model selection based on AICc:

                                  K    AICc Delta_AICc AICcWt
2.~DBH+Pred+ MT +JR +NAge         5 2010.66       0.00   0.25
6.~DBH+Pred+ MT +JR               4 2010.75       0.10   0.24
3.~DBH+Pred+ MT +MR +JR +NAge     6 2011.49       0.83   0.17
4.~DBH+Pred+ MT +JT +JR  +NAge    6 2012.33       1.67   0.11
5.~DBH+Pred+ MT +JR +NAge +Den    6 2012.48       1.82   0.10
7.~DBH+Pred+ MT +MR +NAge         5 2013.88       3.22   0.05
8.~DBH+Pred+ MT +NAge             4 2014.20       3.54   0.04
9.~DBH+Pred+ MT +MR +NAge +Den    6 2015.19       4.53   0.03
1.~DBH
```

Estimates from best fitting model

```
          coef exp(coef)  se(coef)      z Pr(>|z|)
DBH  -0.021668  0.978565  0.005399 -4.013 5.99e-05 ***
Pred  0.080875  1.084236  0.031459  2.571  0.01015 *
MT   -0.186446  0.829904  0.063393 -2.941  0.00327 **
JR   -0.003219  0.996786  0.001353 -2.380  0.01732 *
NAge -0.019749  0.980445  0.013571 -1.455  0.14560

      exp(coef) exp(-coef) lower .95 upper .95
DBH      0.9786     1.0219    0.9683    0.9890
Pred     1.0842     0.9223    1.0194    1.1532
MT       0.8299     1.2050    0.7329    0.9397
JR       0.9968     1.0032    0.9941    0.9994
NAge     0.9804     1.0199    0.9547    1.0069
```

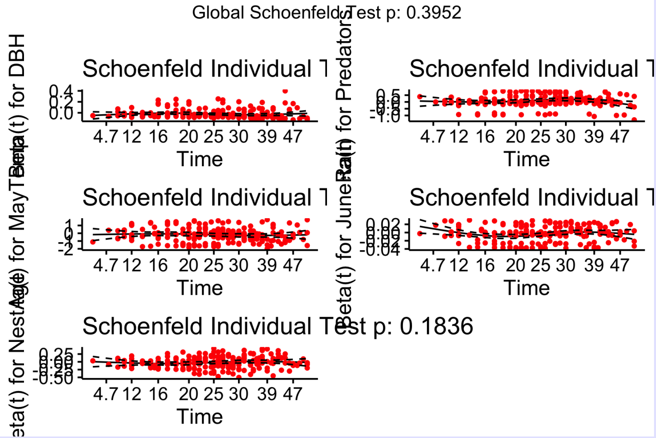
Baseline hazard



Appears to be general increase in hazard over time.

Test for proportioNAgel hazard assumption of best model

	rho	chisq	p
DBH	-0.0604	0.876	0.349
Pred	0.0291	0.164	0.686
MT	-0.0764	1.099	0.294
JR	0.0657	0.841	0.359
NAge	0.0968	1.768	0.184
GLOBAL		5.173	0.395



Look for flatness of curves.

Curves appear to be relatively flat except for June rain fall early in season but CI are very wide.

Summary - Cox PH models I

- Allows for unspecified base hazard function and proportional effects by covariates
- Do not have to model the baseline hazard; slight loss of efficiency in estimating covariate effects.
- Focus on hazard ratios; DSR is of limited interest and difficult to compute.
- Need more experience with *R* and understanding of basic *R* functions.
- Goodness-of-fit for proportionality assumption; if fails try an interaction of covariate and time (the start variable);
- Random effects can be (easily) implemented for Cox PH models

Overall Summary I

- Apparent nest success is positively biased because of failure to account for exposure.
- Mayfield method is an approximate method that assumes constant DSR but is unable to account for covariates.
- Modern modelling uses maximum likelihood estimation
  - Available in n *MARK*, *RMark*, and logistic exposure models.
  - Tradeoff between flexibility and ease of use
  - Goodness-of-fit is underdeveloped for nest success models, but see `http://www.montana.edu/rotella/nestsurv/`
  - Random effects can be implemented in *MARK* and logistic exposure models.
  - Use AIC for model selection and model averaging rather than null hypothesis testing.

Overall Summary II

- Survival analysis methods (from medicine) can also be used
  - Parametric survival modelling. Not covered in this course, but constant DSR = exponential/geometric distribution for time to failure.
  - Cox Proportional Hazard model accounts for undefined baseline hazard and then proportionate effects of covariates.
  - Hazard ratio is of prime interest; DSR much more difficult to determine.
- Additional complications
  - Sample sizes needed to detect effects - simulation methods likely best
  - Individual nest effects (frailty models) with random effects for nests to account for heterogeneity in DSR
  - Spatial effects so that nests close together have similar fates
  - Random effects for multi-year and multi-site studies
  - Random effects for designed experiments, e.g. multiple sandbars for each treatment and multiple nests measured on each sandbar.

Nest survival - Final Summary

Where to get help?

- PhiDot forum `http://www.phidot.org/forum/index.php`
- cschwarz.stat.sfu.ca @ gmail.com

DON'T PANIC!