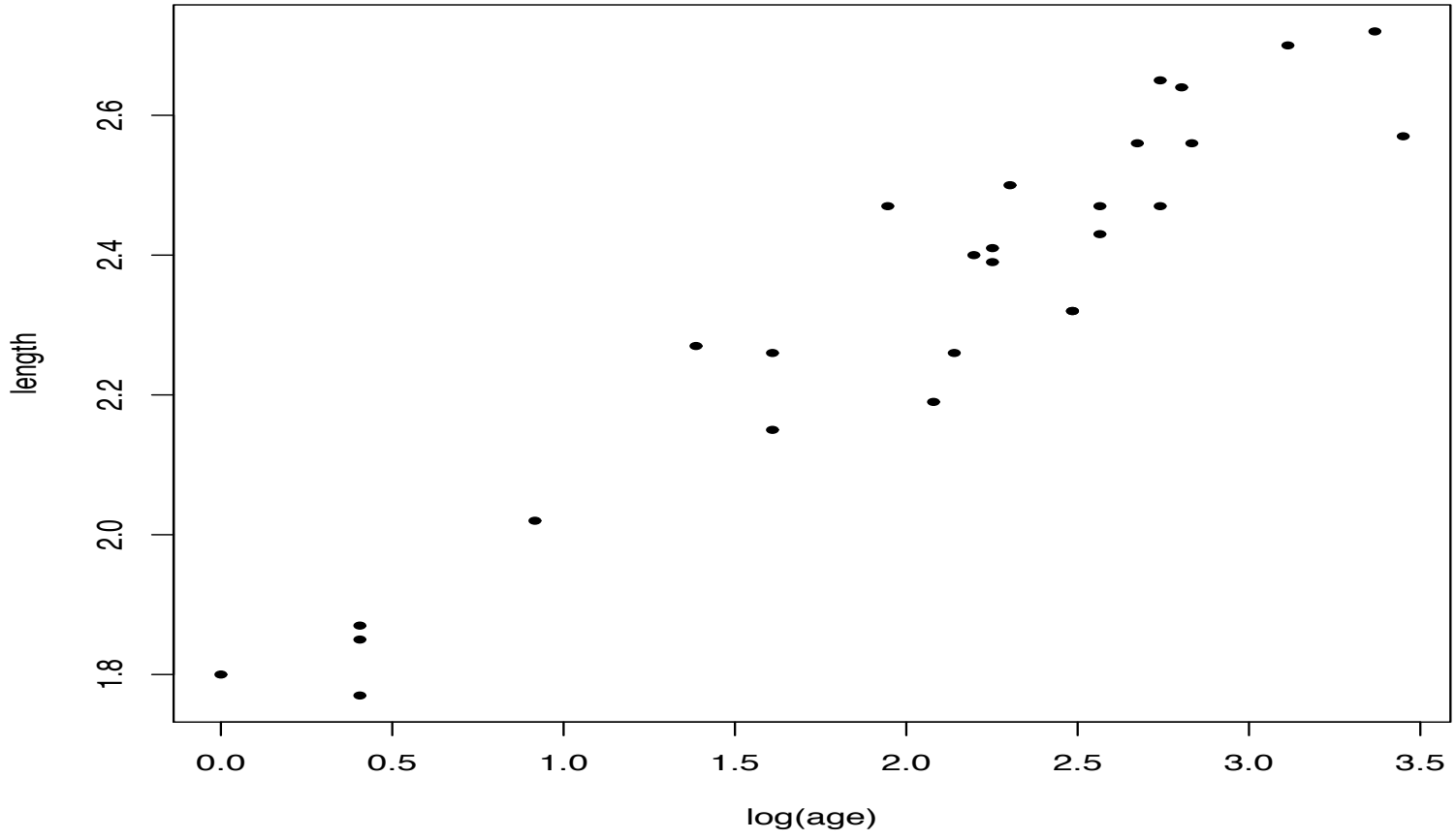
BUGS Example 1: Linear Regression



- For $n = 27$ captured samples of the sirenian species *dugong* (sea cow), relate an animal's length in meters, Y_i, to its age in years, x_i.

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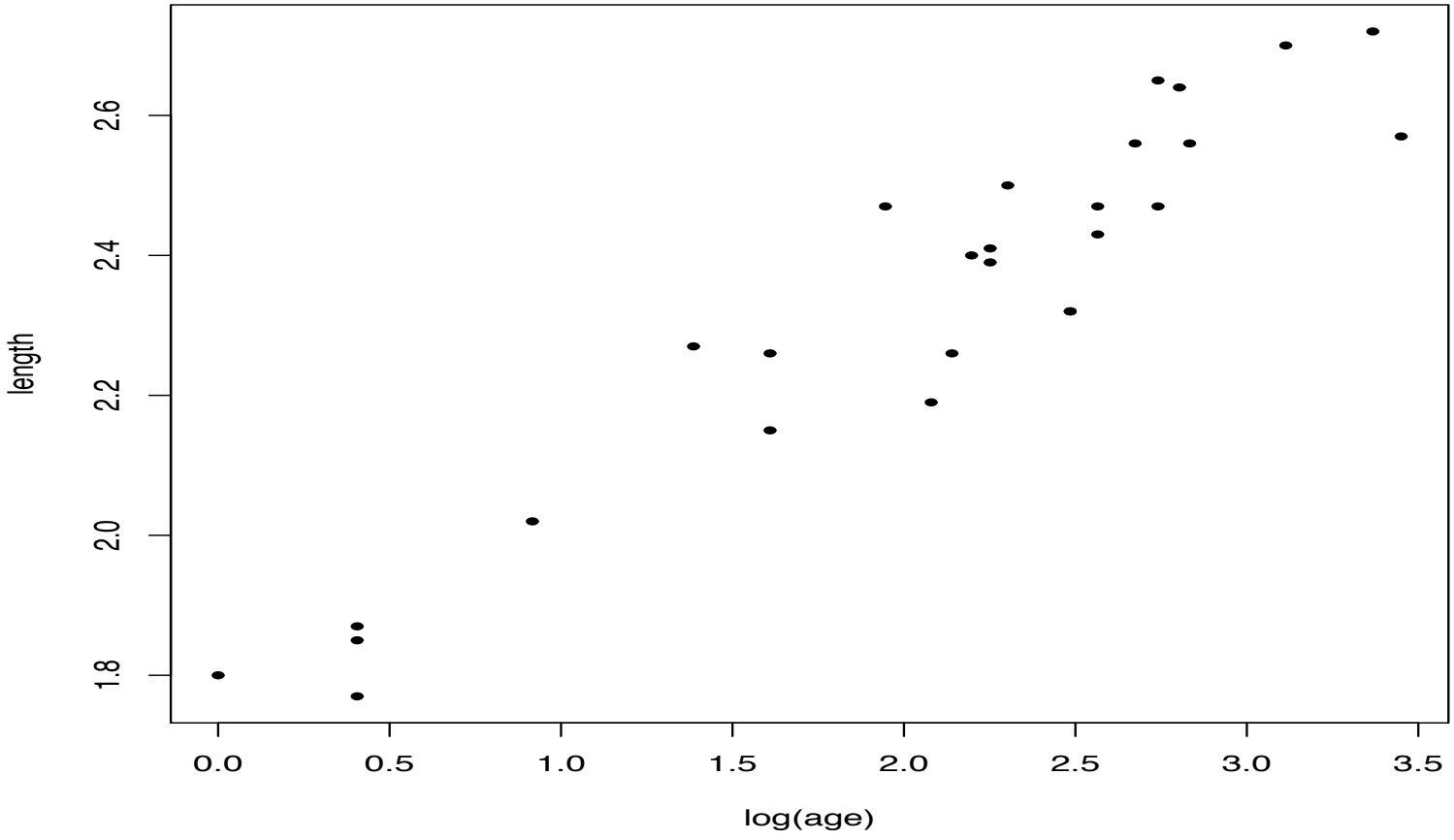

- For $n = 27$ captured samples of the sirenian species *dugong* (sea cow), relate an animal's length in meters, Y_i, to its age in years, x_i.
- To avoid a nonlinear model for now, transform x_i to the log scale; plot of Y versus $\log(x)$ looks fairly linear!

Simple linear regression in WinBUGS

$$Y_i = \beta_0 + \beta_1 \log(x_i) + \epsilon_i, \ i = 1, \ldots, n$$

where $\epsilon_i \overset{iid}{\sim} N(0, \tau)$ and $\tau = 1/\sigma^2$, the precision in the data.

- Prior distributions:
  - flat for β_0, β_1
  - vague gamma on τ (say, Gamma(0.1, 0.1), which has mean 1 and variance 10) is traditional

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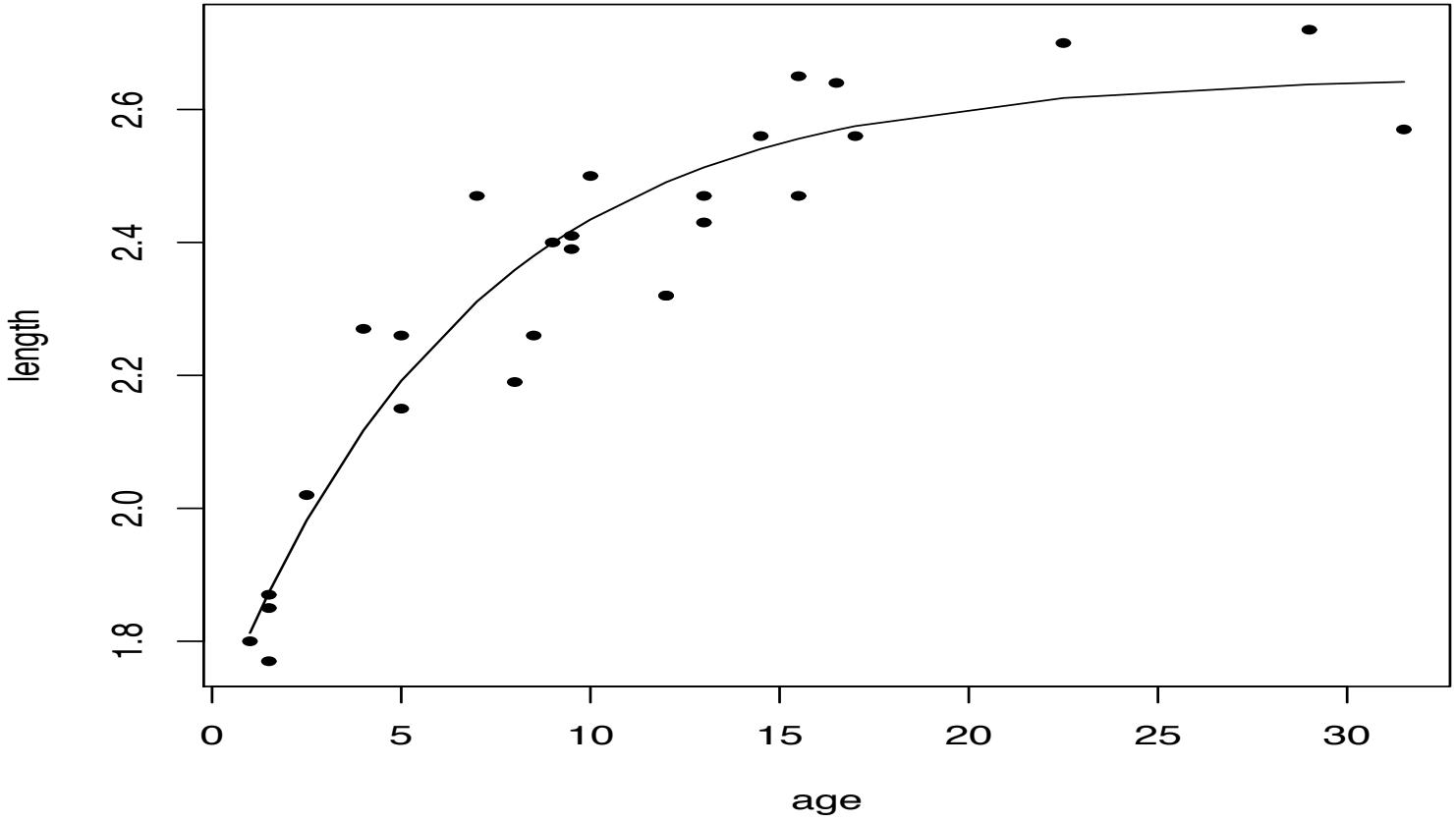
- Code: www.biostat.umn.edu/∼brad/data/dugongs_BUGS.txt

BUGS Example 2: Nonlinear Regression



- Model the untransformed dugong data as

$$Y_i = \alpha - \beta\gamma^{x_i} + \epsilon_i,\ i = 1, \ldots, n\ ,$$

where $\alpha > 0$, $\beta > 0$, $0 \leq \gamma \leq 1$, and as usual $\epsilon_i \overset{iid}{\sim} N(0, \tau)$ for $\tau \equiv 1/\sigma^2 > 0$.

Nonlinear regression in WinBUGS

- In this model,
  - α corresponds to the average length of a fully grown dugong ($x \to \infty$)
  - $(\alpha - \beta)$ is the length of a dugong at birth ($x = 0$)
  - γ determines the growth rate: lower values produce an initially steep growth curve while higher values lead to gradual, almost linear growth.

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- Code: www.biostat.umn.edu/∼brad/data/dugongsNL_BUGS.txt
- Obtain posterior density estimates and autocorrelation plots for α, β, γ, and σ, and investigate the bivariate posterior of (α, γ) using the Correlation tool on the Inference menu!

BUGS Example 3: Logistic Regression

- Consider a binary version of the dugong data,

$$Z_i = \begin{cases} 1 & \text{if } Y_i > 2.4 \text{ (i.e., the dugong is “full-grown”)} \\ 0 & \text{otherwise} \end{cases}$$

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- A logistic model for $p_i = P(Z_i = 1)$ is then

$$logit(p_i) = \log[p_i/(1-p_i)] = \beta_0 + \beta_1 log(x_i) \ .$$

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- Two other commonly used link functions are the probit,

$$probit(p_i) = \Phi^{-1}(p_i) = \beta_0 + \beta_1 log(x_i) \ ,$$

and the complementary log-log (cloglog),

$$cloglog(p_i) = \log[-\log(1-p_i)] = \beta_0 + \beta_1 log(x_i) \ .$$

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- DIC scores for the three models:

model	$\overline{D}$	p_D	DIC
logit	19.62	1.85	21.47
probit	19.30	1.87	21.17
cloglog	18.77	1.84	20.61

In fact, these scores can be obtained from a single run; see the "trick version" at the bottom of the BUGS file!

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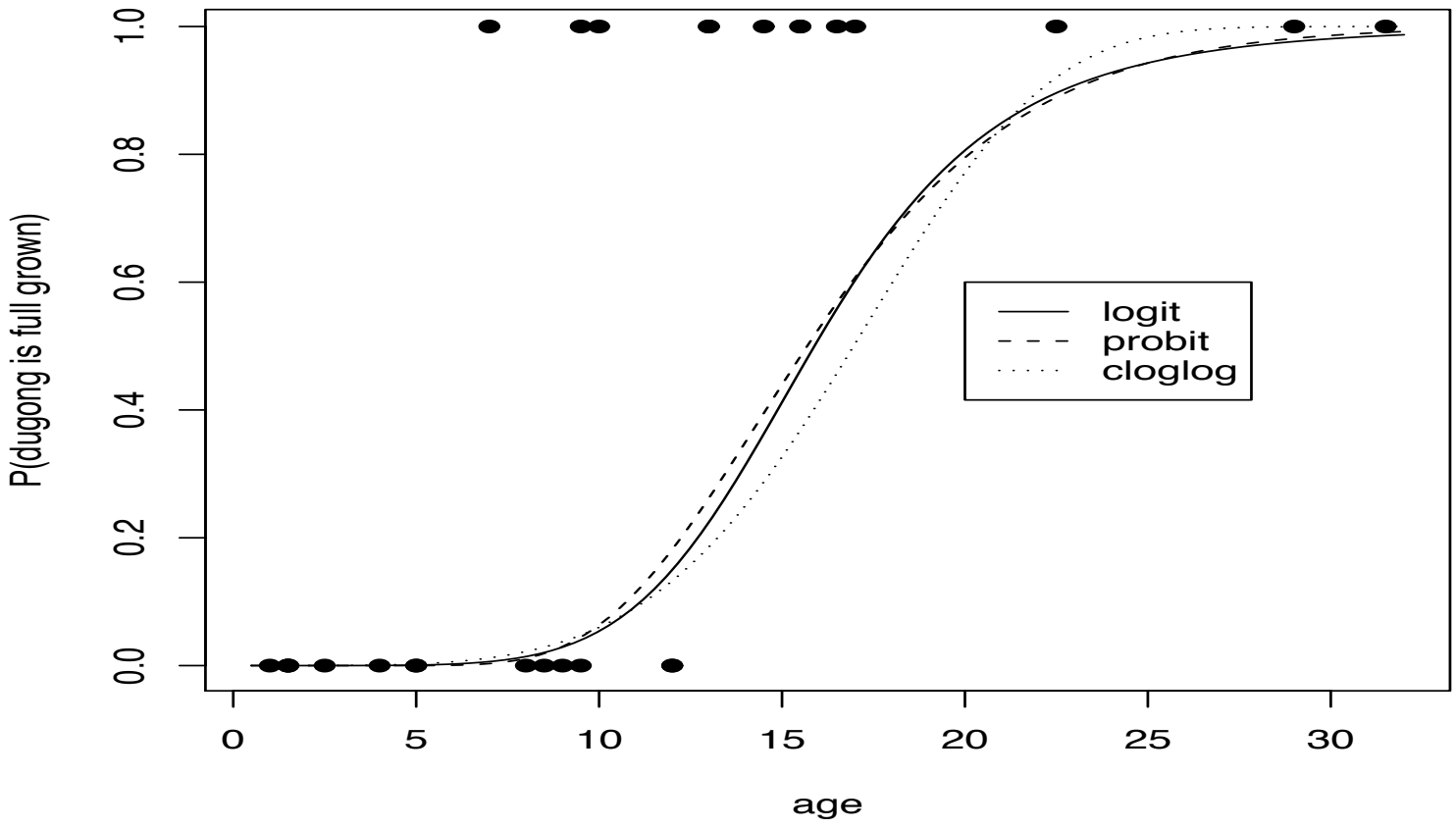
- Use the Comparison tool to compare the posteriors of β_1 across models, and the Correlation tool to check the bivariate posteriors of (β_0, β_1) across models.

Fitted binary regression models



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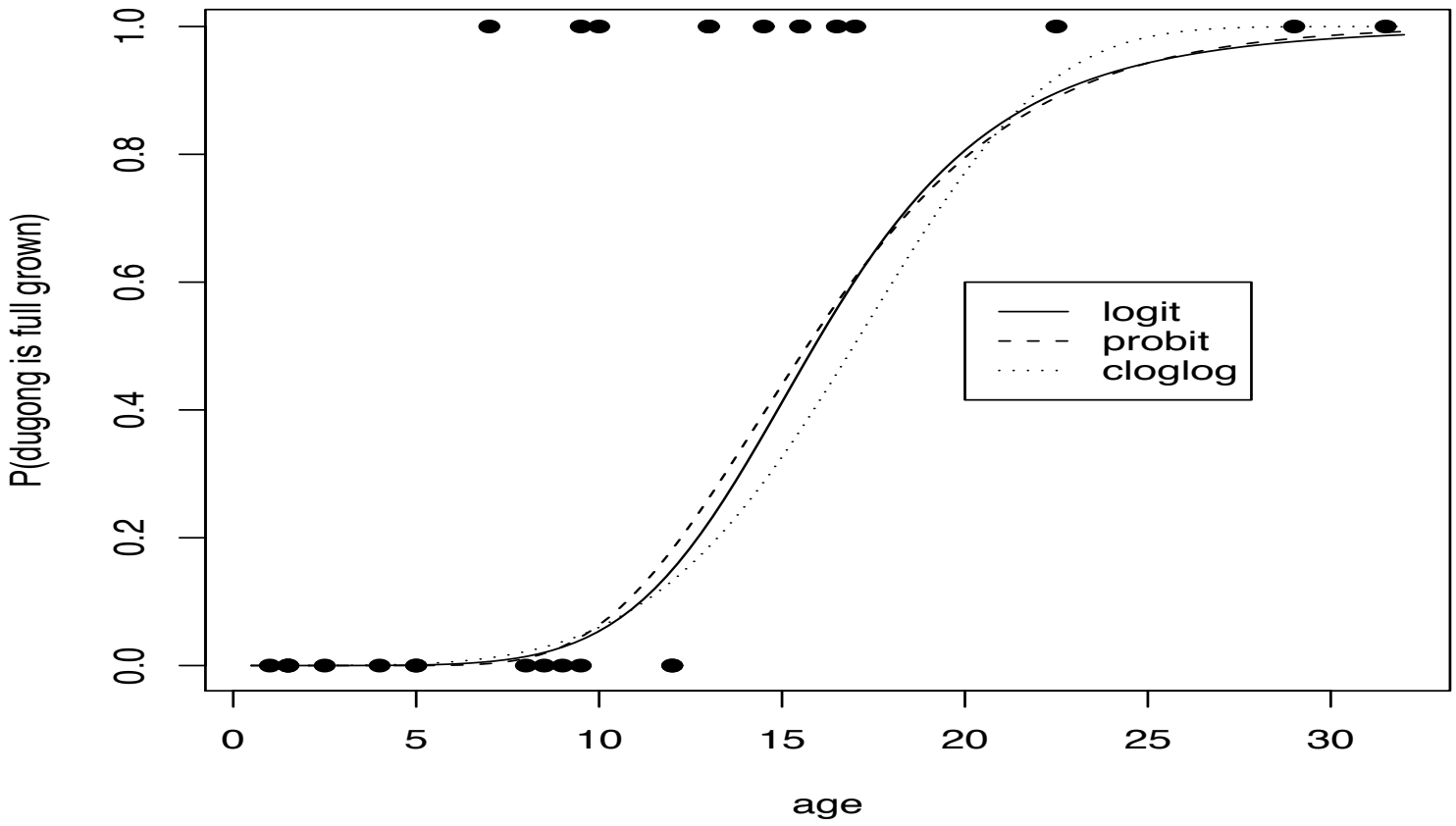

- The logit and probit fits appear very similar, but the cloglog fitted curve is slightly different
- You can also compare p_i posterior boxplots (induced by the link function and the β_0 and β_1 posteriors) using the Comparison tool.

BUGS Example 4: Hierarchical Models

- Extend the usual two-stage (likelihood plus prior) Bayesian structure to a hierarchy of L levels, where the joint distribution of the data and the parameters is

$$f(\mathbf{y}|\boldsymbol{\theta}_1)\pi_1(\boldsymbol{\theta}_1|\boldsymbol{\theta}_2)\pi_2(\boldsymbol{\theta}_2|\boldsymbol{\theta}_3)\cdots\pi_L(\boldsymbol{\theta}_L|\boldsymbol{\lambda}).$$

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- L is often determined by the number of subscripts on the data. For example, suppose Y_{ijk} is the test score of child k in classroom j in school i in a certain city. Model:

$$\begin{aligned}
Y_{ijk}|\theta_{ij} &\overset{ind}{\sim} N(\theta_{ij}, \tau_\theta) && (\theta_{ij} \text{ is the classroom effect}) \\
\theta_{ij}|\eta_i &\overset{ind}{\sim} N(\eta_i, \tau_\eta) && (\eta_i \text{ is the school effect}) \\
\eta_i|\lambda &\overset{iid}{\sim} N(\lambda, \tau_\lambda) && (\lambda \text{ is the grand mean})
\end{aligned}$$

Priors for λ and the τ's now complete the specification!

Cross-Study (Meta-analysis) Data

- Data: estimated log relative hazards $Y_{ij} = \hat{\beta}_{ij}$ obtained by fitting separate Cox proportional hazards regressions to the data from each of $J = 18$ clinical units participating in $I = 6$ different AIDS studies.

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- Data: estimated log relative hazards $Y_{ij} = \hat{\beta}_{ij}$ obtained by fitting separate Cox proportional hazards regressions to the data from each of $J = 18$ clinical units participating in $I = 6$ different AIDS studies.
- To these data we wish to fit the cross-study model,

$$Y_{ij} = a_i + b_j + s_{ij} + \epsilon_{ij},\ i = 1, \ldots, I,\ j = 1, \ldots, J,$$

where a_i = study main effect

b_j = unit main effect

s_{ij} = study-unit interaction term, and

$\epsilon_{ij} \overset{iid}{\sim} N(0, \sigma_{ij}^2)$

and the estimated standard errors from the Cox regressions are used as (known) values of the σ_{ij}.

Cross-Study (Meta-analysis) Data

Estimated Unit-Specific Log Relative Hazards						
Unit	Toxo	ddI/ddC	NuCombo ZDV+ddI	NuCombo ZDV+ddC	Fungal	CMV
A	0.814	NA	-0.406	0.298	0.094	NA
B	-0.203	NA	NA	NA	NA	NA
C	-0.133	NA	0.218	-2.206	0.435	0.145
D	NA	NA	NA	NA	NA	NA
E	-0.715	-0.242	-0.544	-0.731	0.600	0.041
F	0.739	0.009	NA	NA	NA	0.222
G	0.118	0.807	-0.047	0.913	-0.091	0.099
H	NA	-0.511	0.233	0.131	NA	0.017
I	NA	1.939	0.218	-0.066	NA	0.355
J	0.271	1.079	-0.277	-0.232	0.752	0.203
K	NA	NA	0.792	1.264	-0.357	0.807
⋮	⋮	⋮	⋮	⋮	⋮	⋮
R	1.217	0.165	0.385	0.172	-0.022	0.203

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- Next slide shows a plot of the Y_{ij} values and associated approximate 95% CIs...

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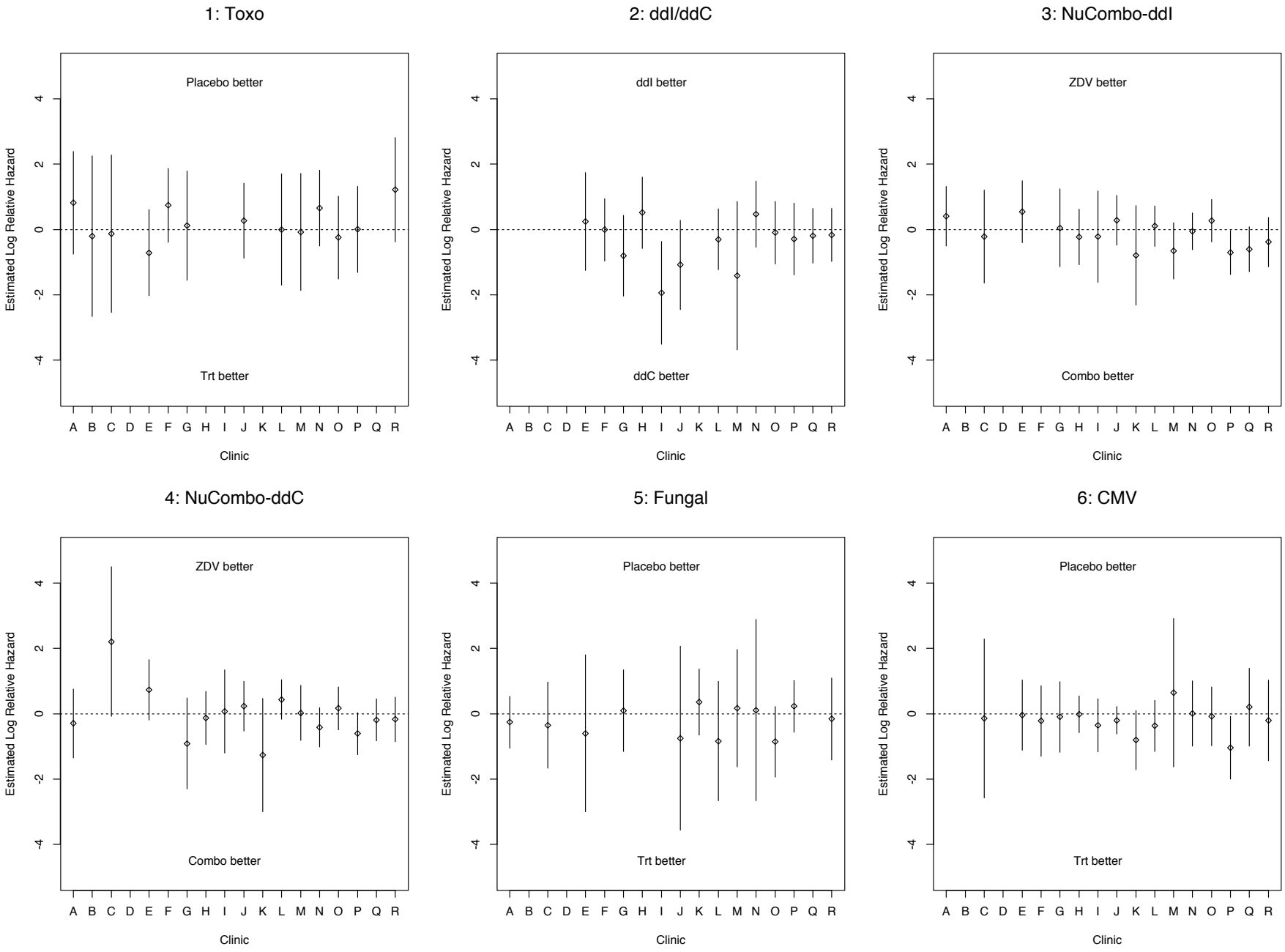

Cross-Study (Meta-analysis) Data

- Second stage of our model:

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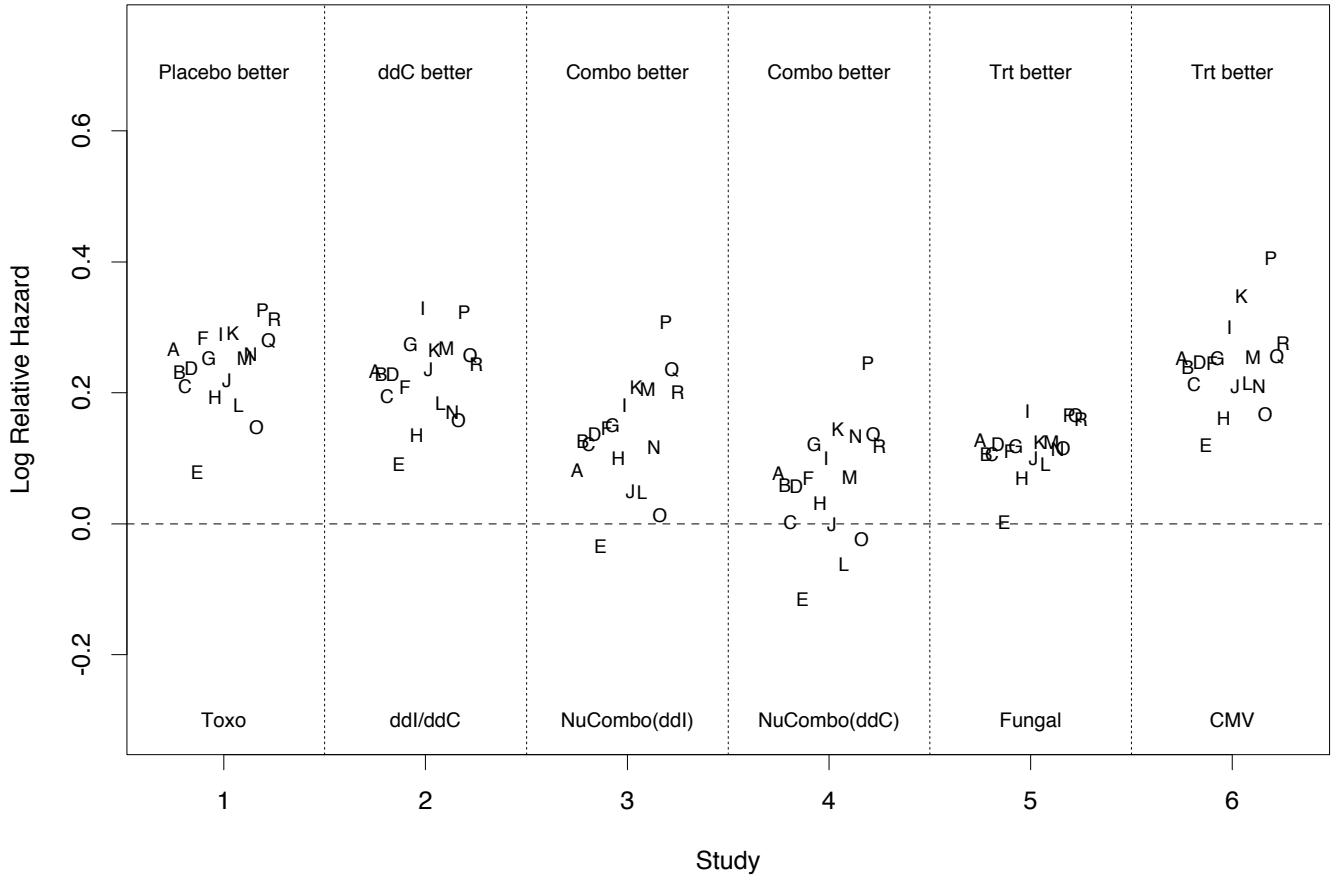
- With $I + J + IJ$ parameters but fewer than IJ data points, some effects must be treated as random!
- Code: www.biostat.umn.edu/∼brad/data/crprot_BUGS.txt

Plot of θ_{ij} posterior means



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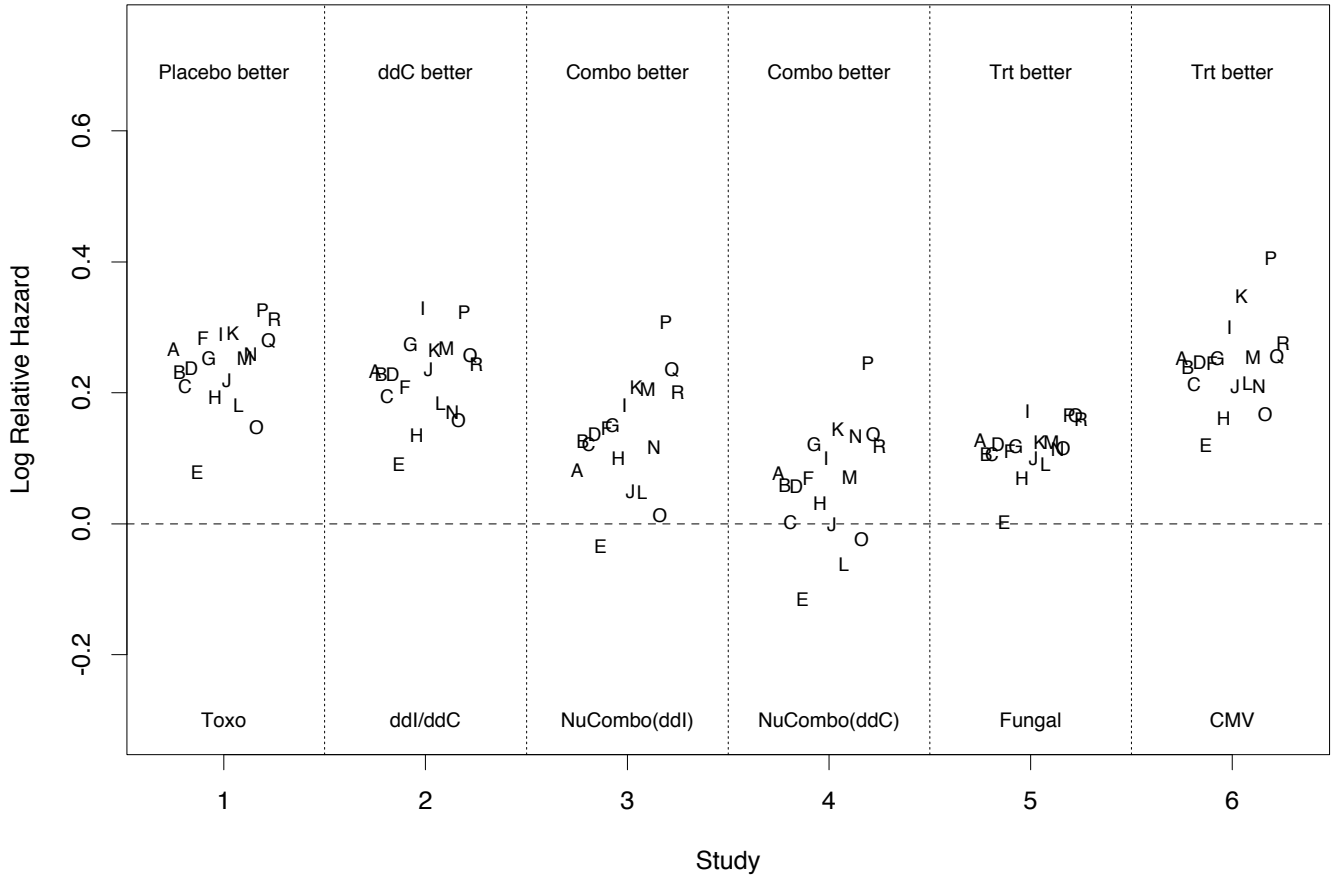

- Unit P is an opinion leader; Unit E is a dissenter
- Substantial shrinkage towards 0 has occurred: mostly positive values; no estimated θ_{ij} greater than 0.6

Model Comparision via DIC

Since we lack replications for each study-unit (i-j) combination, the interactions s_{ij} in this model were only weakly identified, and the model might well be better off without them (or even without the unit effects b_j).

As such, compare a variety of reduced models:

```
  Y[i,j] ~ dnorm(theta[i,j],P[i,j])
#    theta[i,j] <- a[i]+b[j]+s[i,j]  # full model
#    theta[i,j] <- a[i] + b[j]       # drop interactions
#    theta[i,j] <- a[i] + s[i,j]     # no unit effect
#    theta[i,j] <- b[j] + s[i,j]     # no study effect
#    theta[i,j] <- a[1] + b[j]       # unit + intercept
#    theta[i,j] <- b[j]              # unit effect only
    theta[i,j] <- a[i]              # study effect only
```

Investigate p_D values for these models; are they consistent with posterior boxplots of the b_i and s_{ij}?

DIC results for Cross-Study Data:

model	$\overline{D}$	p_D	DIC
full model	122.0	12.8	134.8
drop interactions	123.4	9.7	133.1
no unit effect	123.8	10.0	133.8
no study effect	121.4	9.7	131.1
unit + intercept	120.3	4.6	124.9
unit effect only	122.9	6.2	129.1
study effect only	126.0	6.0	132.0

The DIC-best model is the one with only an intercept (a role played here by a_1) and the unit effects b_j.

These DIC differences are not much larger than their possible Monte Carlo errors, so almost any of these models could be justified here.

BUGS Example 5: Survival Modeling

- Our data arises from a clinical trial comparing two treatments for *Mycobacterium avium* complex (MAC), a disease common in late stage HIV-infected persons. Eleven clinical centers ("units") have enrolled a total of 69 patients in the trial, of which 18 have died.

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- For $j = 1, \ldots, n_i$ and $i = 1, \ldots, k$, let

$$t_{ij} = \text{time to death or censoring}$$

$$x_{ij} = \text{treatment indicator for subject j in stratum i}$$

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- Next page gives survival times (in half-days) from the MAC treatment trial, where "+" indicates a censored observation...

MAC Survival Data

unit	drug	time	unit	drug	time	unit	drug	time
A	1	74+	E	1	214	H	1	74+
A	2	248	E	2	228+	H	1	88+
A	1	272+	E	2	262	H	1	148+
A	2	344				H	2	162
			F	1	6			
B	2	4+	F	2	16+	I	2	8
B	1	156+	F	1	76	I	2	16+
			F	2	80	I	2	40
C	2	100+	F	2	202	I	1	120+
			F	1	258+	I	1	168+
D	2	20+	F	1	268+	I	2	174+
D	2	64	F	2	368+	I	1	268+
D	2	88	F	1	380+	I	2	276
D	2	148+	F	1	424+	I	1	286+
...	...	...	...	...	...	...	...	...
						K	2	106+

MAC Survival Data

- With proportional hazards and a Weibull baseline hazard, stratum i's hazard is

$$\begin{aligned} h(t_{ij}; x_{ij}) &= h_0(t_{ij})\omega_i \exp(\beta_0 + \beta_1 x_{ij}) \\ &= \rho_i t_{ij}^{\rho_i - 1} \exp(\beta_0 + \beta_1 x_{ij} + W_i) \ , \end{aligned}$$

where $\rho_i > 0$, $\boldsymbol{\beta} = (\beta_0, \beta_1)' \in \Re^2$, and $W_i = \log \omega_i$ is a clinic-specific frailty term.

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  where $\rho_i > 0$, $\boldsymbol{\beta} = (\beta_0, \beta_1)' \in \Re^2$, and $W_i = \log \omega_i$ is a clinic-specific frailty term.

- The W_i capture overall differences among the clinics, while the ρ_i allow differing baseline hazards which either increase ($\rho_i > 1$) or decrease ($\rho_i < 1$) over time. We assume i.i.d. specifications for these random effects,

$$W_i \overset{iid}{\sim} N(0, 1/\tau) \quad \text{and} \quad \rho_i \overset{iid}{\sim} G(\alpha, \alpha) \ .$$

MAC Survival Data

- As in the `mice` example (`WinBUGS` Examples Vol 1),

$$\mu_{ij} = \exp(\beta_0 + \beta_1 x_{ij} + W_i) \ ,$$

so that

$$t_{ij} \sim Weibull(\rho_i, \mu_{ij}) \ .$$

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- We recode the drug covariate from (1,2) to (–1,1) (i.e., set $x_{ij} = 2drug_{ij} - 3$) to ease collinearity between the slope β_1 and the intercept β_0.

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- We recode the drug covariate from (1,2) to (–1,1) (i.e., set $x_{ij} = 2drug_{ij} - 3$) to ease collinearity between the slope β_1 and the intercept β_0.
- We place vague priors on β_0 and β_1, a moderately informative $G(1, 1)$ prior on τ, and set $\alpha = 10$.

MAC Survival Data

- As in the `mice` example (`WinBUGS` Examples Vol 1),

$$\mu_{ij} = \exp(\beta_0 + \beta_1 x_{ij} + W_i) \ ,$$

so that

$$t_{ij} \sim Weibull(\rho_i, \mu_{ij}) \ .$$

- We recode the drug covariate from (1,2) to (–1,1) (i.e., set $x_{ij} = 2drug_{ij} - 3$) to ease collinearity between the slope β_1 and the intercept β_0.
- We place vague priors on β_0 and β_1, a moderately informative $G(1, 1)$ prior on τ, and set $\alpha = 10$.
- Data: www.biostat.umn.edu/∼brad/data/MAC.dat
  Code:
  www.biostat.umn.edu/∼brad/data/MACfrailty_BUGS.txt

MAC Survival Results

node (unit)	mean	sd	MC error	2.5%	median	97.5%
W_1 (A)	–0.04912	0.835	0.02103	–1.775	–0.04596	1.639
W_3 (C)	–0.1829	0.9173	0.01782	–2.2	–0.1358	1.52
W_5 (E)	–0.03198	0.8107	0.03193	–1.682	–0.02653	1.572
W_6 (F)	0.4173	0.8277	0.04065	–1.066	0.3593	2.227
W_9 (I)	0.2546	0.7969	0.03694	–1.241	0.2164	1.968
W_{11} (K)	–0.1945	0.9093	0.02093	–2.139	–0.1638	1.502
ρ_1 (A)	1.086	0.1922	0.007168	0.7044	1.083	1.474
ρ_3 (C)	0.9008	0.2487	0.006311	0.4663	0.8824	1.431
ρ_5 (E)	1.143	0.1887	0.00958	0.7904	1.139	1.521
ρ_6 (F)	0.935	0.1597	0.008364	0.6321	0.931	1.265
ρ_9 (I)	0.9788	0.1683	0.008735	0.6652	0.9705	1.339
ρ_{11} (K)	0.8807	0.2392	0.01034	0.4558	0.8612	1.394
τ	1.733	1.181	0.03723	0.3042	1.468	4.819
β_0	–7.111	0.689	0.04474	–8.552	–7.073	–5.874
β_1	0.596	0.2964	0.01048	0.06099	0.5783	1.245
RR	3.98	2.951	0.1122	1.13	3.179	12.05

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- Note: This has all been for two sets of random effects (W_i and ρ_i), called "Model 2" in the BUGS code. You will also see models having three (adding β_{1i}), one (deleting ρ_i), or zero sets of random effects!

BRugs Example 1: Model assessment

- Basic tool here is the cross-validation residual

$$r_i = y_i - E(y_i|\mathbf{y}_{(i)}) \ ,$$

where $\mathbf{y}_{(i)}$ denotes the vector of all the data except the i^{th} value, i.e.

$$\mathbf{y}_{(i)} = (y_1, \ldots, y_{i-1}, y_{i+1}, \ldots, y_n)'.$$

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- Also of interest is the conditional predictive ordinate, $p(y_i|\mathbf{y}_{(i)}) = \int p(y_i|\boldsymbol{\theta}, \mathbf{y}_{(i)}) p(\boldsymbol{\theta}|\mathbf{y}_{(i)}) d\boldsymbol{\theta}$, the height of the conditional density at the observed value of y_i
$\Longrightarrow$ large values indicate good prediction of y_i.

Residuals: Approximate method

- Using MC draws $\boldsymbol{\theta}^{(g)} \sim p(\boldsymbol{\theta}|\mathbf{y})$, we have

$$\begin{aligned} E(y_i|\mathbf{y}_{(i)}) &= \int\int y_i f(y_i|\boldsymbol{\theta}) p(\boldsymbol{\theta}|\mathbf{y}_{(i)}) dy_i d\boldsymbol{\theta} \\ &= \int E(y_i|\boldsymbol{\theta}) p(\boldsymbol{\theta}|\mathbf{y}_{(i)}) d\boldsymbol{\theta} \\ &\approx \int E(y_i|\boldsymbol{\theta}) p(\boldsymbol{\theta}|\mathbf{y}) d\boldsymbol{\theta} \\ &\approx \frac{1}{G} \sum_{g=1}^{G} E(y_i|\boldsymbol{\theta}^{(g)}) \ . \end{aligned}$$

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  - Same $\boldsymbol{\theta}^{(g)}$'s may be used for each $i = 1, \ldots, n$.

Approximate methods in WinBUGS

- The ratio to compute the standardized residuals d_i must be done outside of `WinBUGS`. Might instead define

$$d_i^* = \frac{y_i - E(y_i|\boldsymbol{\theta})}{\sqrt{Var(y_i|\boldsymbol{\theta})}} \ .$$

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- For the exact method, we must evaluate $E(y_i|\mathbf{y}_{(i)})$ and $Var(y_i|\mathbf{y}_{(i)})$ separately. For the latter, use the facts that $Var(y_i|\mathbf{y}_{(i)}) = E(y_i^2|\mathbf{y}_{(i)}) - [E(y_i|\mathbf{y}_{(i)})]^2$, and

$$\begin{aligned} E(y_i^2|\mathbf{y}_{(i)}) &= \int E(y_i^2|\boldsymbol{\theta}) p(\boldsymbol{\theta}|\mathbf{y}_{(i)}) d\boldsymbol{\theta} \\ &= \int \{Var(y_i|\boldsymbol{\theta}) + [E(y_i|\boldsymbol{\theta})]^2\} p(\boldsymbol{\theta}|\mathbf{y}_{(i)}) d\boldsymbol{\theta} \ . \end{aligned}$$

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- All necessary programs and instructions can be downloaded from www.biostat.umn.edu/∼brad/software/BRugs
- Note that we will now have both:
  - an `R` program that organizes the dataset, contains all the `BRugs` commands, and summarizes the output
  - a piece of `BUGS` code that is sent by `R` to `OpenBUGS`

Numerical illustration: Stack Loss data

- An oft-analyzed dataset, featuring the stack loss Y (ammonia escaping), and three covariates X_1 (air flow), X_2 (temperature), and X_3 (acid concentration).

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- See also "stacks" in `WinBUGS` Examples Volume I!

Approximate vs. Exact Results

	sresid		CPO	
obs	approx	exact	approx	exact
1	0.948	1.098	0.178	0.124
2	–0.566	–0.628	0.224	0.188
3	1.337	1.461	0.122	0.084
4	1.672	1.851	0.078	0.047
5	–0.504	–0.477	0.251	0.244
⋮	⋮	⋮	⋮	⋮
21	–2.126	–3.012	0.046	0.005

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- Approximate residuals are too small, especially for the most outlying observations!
- Approximate CPOs also tend to understate lack of fit

BRugs Example 2: Clinical Trial Design

- Following our MAC survival model, let t_i be the time until death for subject i, with corresponding treatment indicator x_i (= 0 or 1 for control and treatment, respectively). Suppose

$$t_i \sim \text{Weibull}(r, \mu_i), \quad \text{where } \mu_i = e^{-(\beta_0 + \beta_1 x_i)} \ .$$

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- The value of β_1 corresponding to a 15% increase in median survival in the treatment group satisfies

$$e^{\beta_1 / r} = 1.15 \iff \beta_1 = r \log(1.15) \ .$$

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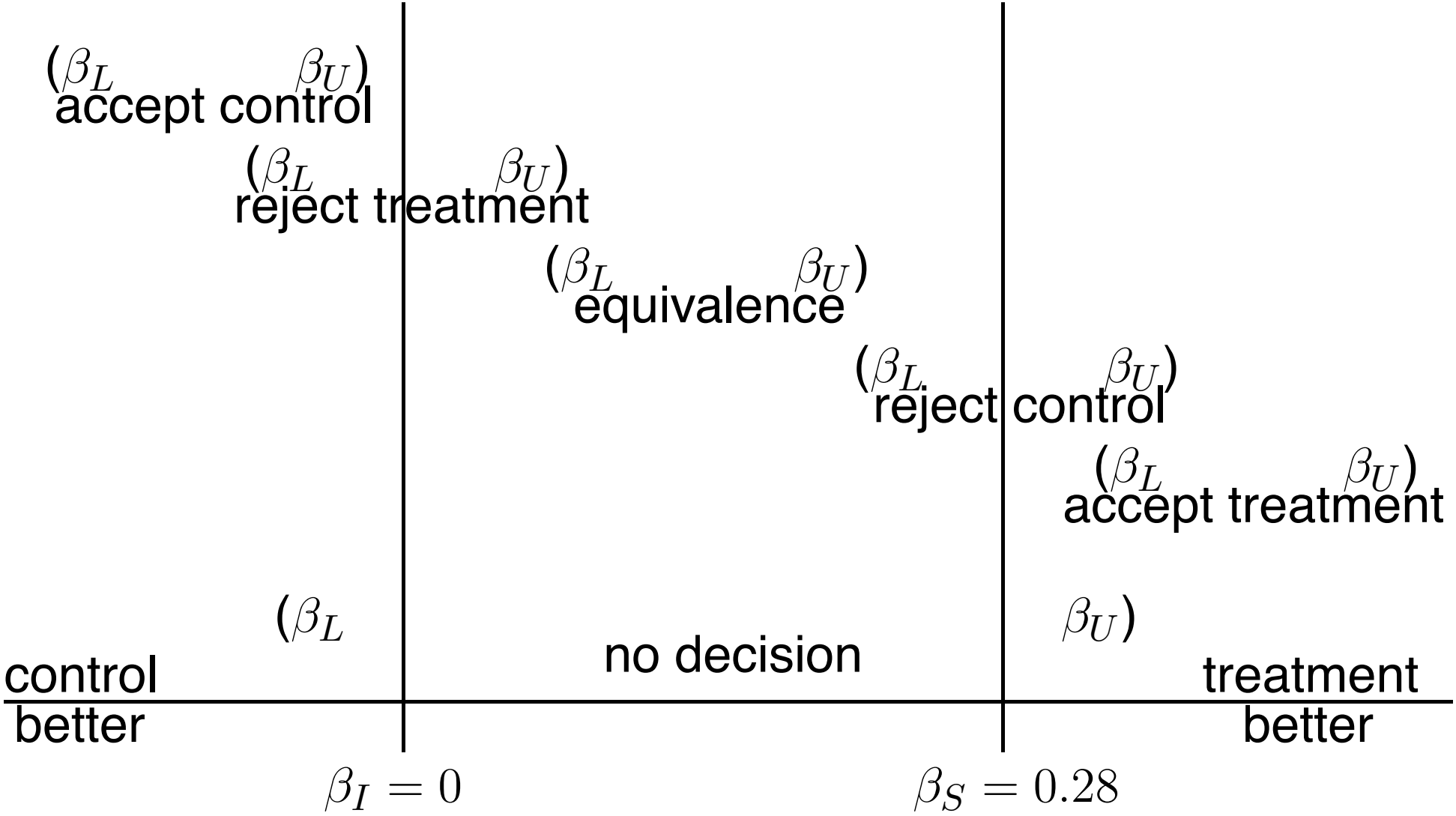
  - Example: If $r = 2$, then $\beta_S = 2\log(1.15) \approx 0.28$ corresponds to 15% improvement in median survival
- The outcome of the trial can then be based on the location of the 95% posterior confidence interval for β_1, say (β_L, β_U), relative to the indifference zone!....

The six possible outcomes and decisions



- Note both "acceptance" and "rejection" are possible!

Community of priors

Spiegelhalter et al. (1994) recommend considering several priors, in order to represent the broadest possible audience:

- Skeptical Prior
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- Reference (or Noninformative) Prior
  - One that expresses no particular opinion about the treatment's merit
  - Often a improper uniform ("flat") prior is permissible

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- Compute (β_L, β_U) by calling `OpenBUGS` from `R`
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- Repeat this process $Nrep$ times; report empirical frequencies of the six possible outcomes

Results from Power.BRugs

- Assuming:
  - Weibull shape $r = 2$, and $N = 50$ in each group
  - median survival of 36 days with 50% improvement in the treatment group
  - a $N(80, 20)$ censoring distribution
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  We obtain the following output from $Nrep = 100$ reps:
- Here are simulated outcome frequencies for N= 50
  accept control: 0
  reject treatment: 0.07
  equivalence: 0
  reject control: 0.87
  accept treatment: 0.06
  no decision: 0
  End of BRugs power simulation

Homework Problems

- WinBUGS
  - PK hierarchical linear model: www.biostat.umn.edu/∼brad/data/PK_BUGS.txt
  - PK hierarchical nonlinear model: www.biostat.umn.edu/∼brad/data/PKNL_BUGS.txt
  - Interstim multivariate model: www.biostat.umn.edu/∼brad/data/InterStim.odc
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- *Thanks for your attention!*