Introduction to Bayesian Modeling of Epidemiologic Data

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Outline of Workshop

1. Introduction to Bayesian modeling (*David Dunson*)
2. Bayesian modeling in SAS (*Amy Herring*)
3. Hierarchical models (*Rich MacLehose*)

Background on Perchlorate

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- Concern about effects of perchlorate on the thyroid (*known to inhibit thyroid's ability to absorb iodine from the blood*)
- EPA conducted extensive risk assessment → NAS review of health effects (*recommended new reference dose*)

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- F1 generation treated similarly, with additional exposure during gestation & lactation
- At 19 weeks for F1 rats, thyroid tissues examined histologically
- 2/30 male rats in 30 mg/kg/day dose group had thyroid follicular cell adenomas, with one of these rats having two adenomas.

Analyzing the Perchlorate data

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- The National Toxicology Program (NTP) routinely collects tumor incidence data for control rats in two year studies.
- Would our conclusion change if we included information from the NTP data base?

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- Question: How do we incorporate this information in analysis?

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- Obtained in updating one's *prior distribution* with the likelihood for the data.

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- The posterior, $\pi(\theta \mid \mathbf{y})$, represents the state of knowledge about θ after *updating* the prior, $\pi(\theta)$, with the information in the data, $\mathbf{y}$.

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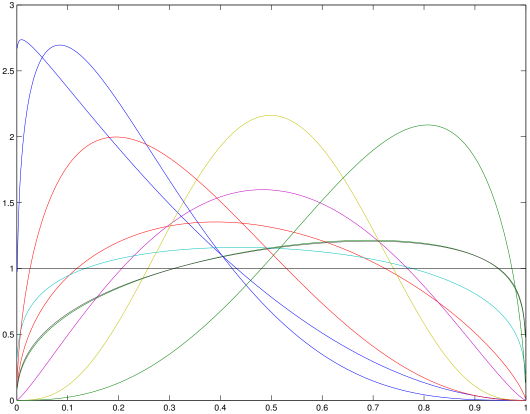
- beta$(1, 1)$ corresponds to uniform distribution $\rightarrow$ has as much information as two subjects (*one with PTB & one without*)

Beta prior distributions for different hyperparameters



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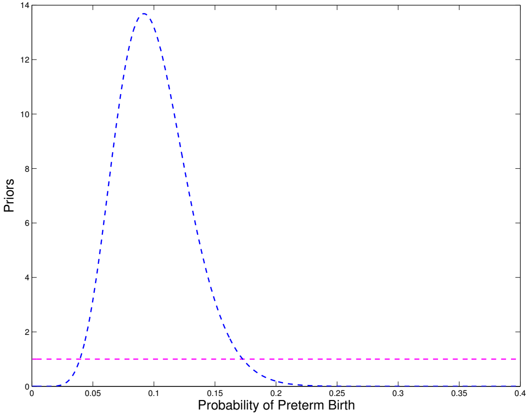
- We collect data for 100 women & observe 7/100 preterm births.

Different Priors



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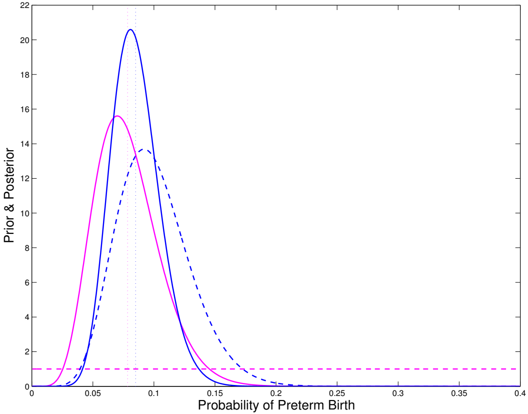
- The posterior distribution of θ is then

$$\pi(\theta \mid \mathbf{y}) = \text{beta}\left(a + \sum_i y_i, b + \sum_i (1 - y_i)\right).$$

Prior and Posteriors



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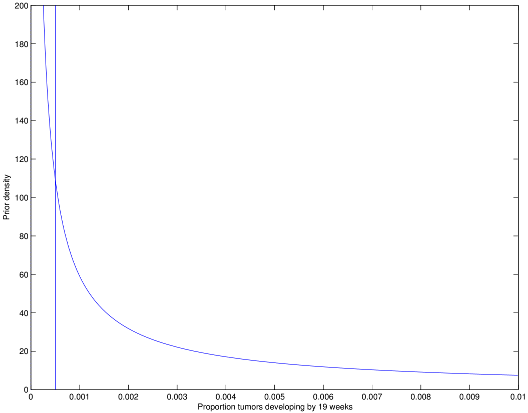
- We choose beta$(38, 3381)$ prior for probability of developing thyroid FCA for a control male rat in a two-year study (γ)
- Based on the $38/(38 + 3381)$ rats observed with these tumors in NTP studies
- We choose beta$(0.11, 2.6)$ prior for ratio:

$$\rho = \frac{\text{probability of developing tumor by 19 weeks}}{\text{probability of developing tumor in two year study}}.$$

Centered on 0.0005 with 95% probability of falling within [0.0000,0.379]

Prior for proportion of thyroid FCA by 19 weeks (ρ)



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- The posterior mean of θ is $1/100,000$
- How likely it is to observe 2 or more rats out of 30 with tumors under the null hypothesis of no effect of perchlorate?
- This probability is $< 1/100,000 \rightarrow$ data support causal effect of perchlorate on increased thyroid tumor incidence

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- Posterior calculation for preterm birth example relied on conjugate prior
- Posterior calculation for perchlorate example relied on numeric integration - easy for two parameters
- For epidemiologic analyses (*e.g.*, *logistic regression*, *survival analysis*), conjugate priors not available & dimension high
- In such settings, there are multiple parameters in θ and one needs to compute the joint posterior:

$$\pi(\theta \,|\, \mathbf{y}) = \frac{\pi(\theta)\, L(\mathbf{y} \,|\theta)}{\int \pi(\theta)\, L(\mathbf{y} \,|\, \theta) d\theta}.$$

Example: Bayesian Logistic Regression

- Logistic regression model:

$$\operatorname{logit} \Pr(y_i = 1 \mid \mathbf{x}_i, \boldsymbol{\beta}) = \mathbf{x}_i' \boldsymbol{\beta},$$

with $\mathbf{x}_i = (1, x_{i2}, \ldots, x_{ip})'$ a vector of predictors & $\boldsymbol{\beta} = (\beta_1, \ldots, \beta_p)'$ coefficients for these predictors

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- $\boldsymbol{\Sigma}$=covariance matrix quantifying uncertainty in this guess

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- Prior variance chosen so that a 90 or 95% prior interval contains a wide range of plausible values
- Useful to choose informative priors for intercept and confounding coefficients, as there is typically substantial information about these coefficients

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- When little information is available about a parameter, results in *shrinkage* towards zero
- Avoids unstable estimates - particularly problematic in high dimensions & for correlated predictors.
- As more information becomes available that the parameter (*e.g., the exposure odds ratio*) is non-zero, the likelihood will dominate.

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- Often yields similar results to maximum likelihood - what's the point?
- No prior is truly non-informative - flat or high variance priors assign most of their probability outside a plausible range for the parameter values.
- Can lead to poor results when insufficient information available about a given parameter in the current data set - typically, the case when many predictors are collected.

Bayes Logistic Regression (continued)

- Posterior distribution:

$$\pi(\boldsymbol{\beta} \mid \mathbf{y}) = \frac{\mathrm{N}_p(\boldsymbol{\beta}; \boldsymbol{\beta}_0, \boldsymbol{\Sigma}) \prod_{l=1}^{n} L(y_i; \mathbf{x}_i, \boldsymbol{\beta})}{\int \mathrm{N}_p(\boldsymbol{\beta}; \boldsymbol{\beta}_0, \boldsymbol{\Sigma}) \prod_{l=1}^{n} L(y_i; \mathbf{x}_i, \boldsymbol{\beta}) d\boldsymbol{\beta}},$$

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  where $L(y_i; \mathbf{x}_i, \boldsymbol{\beta})$ is the likelihood contribution for individual i
- Note that we can write the numerator in this expression in closed form
- However, the denominator involves a nasty high-dimensional integral that has no analytic solution.

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- However, even for moderate to large samples, asymptotic normal approximation may be inaccurate
- In logistic regression for rare outcomes or rare exposure categories, posterior can be highly skewed

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- However, from these samples we can obtain summaries of the posterior distribution for θ
- Summaries of exact posterior distributions of $g(\theta)$, for any functional $g(\cdot)$, can also be obtained.
- For example, if θ is the log-odds ratio, then we could choose $g(\theta) = \exp(\theta)$ to obtain the odds ratio

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  3. Similarly, sample $\theta_3^t, \dots, \theta_p^t$ from the conditional posterior distributions given current values of other parameters.

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- In simple models such as logistic regression, convergence typically occurs quickly & burn-in of 100 iterations should be sufficient (*to be conservative SAS uses 2,000 as default*)

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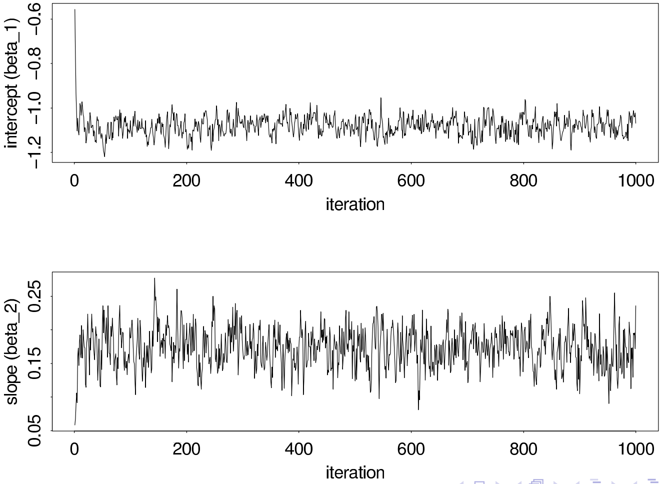
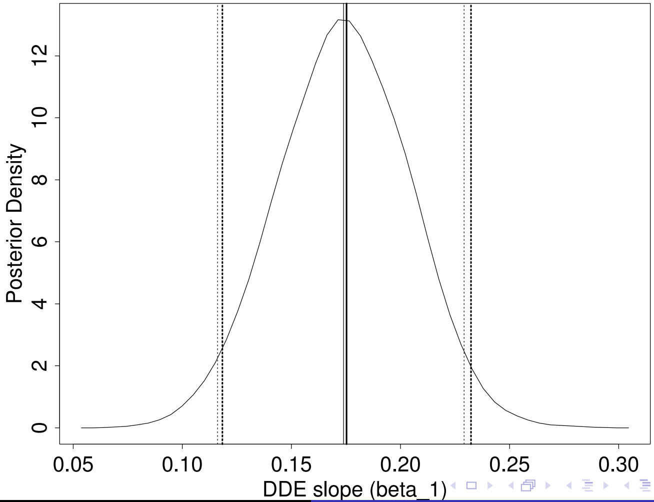
- Probit model is similar to logistic regression, but with different link

Gibbs Sampling output for preterm birth example



Estimated Posterior Density



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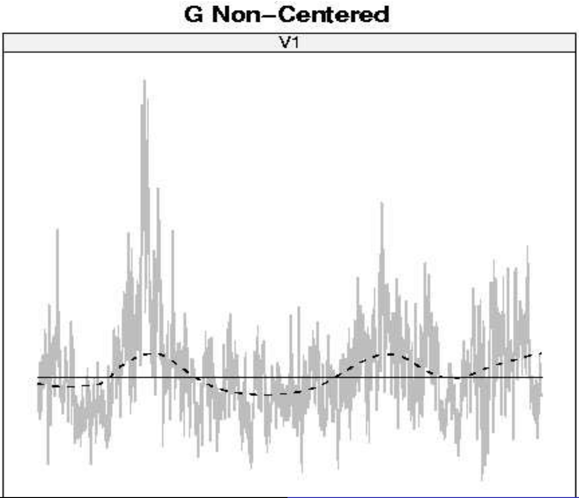
- Trace plot: plot of sampled values of a parameter vs iteration #

Example - trace plot with poor mixing



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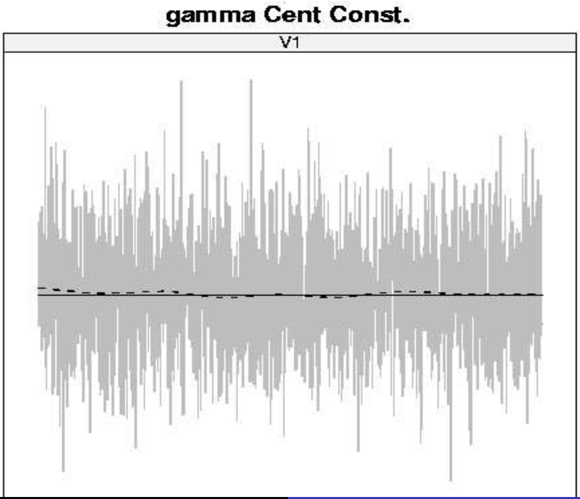
- Routinely examine trace plots!

Example - trace plot with good mixing



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- Credible intervals can be calculated for functionals (e.g., odds ratios) by first applying the function to each MCMC sample

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- A high value (e.g., greater than 0.95) suggests strong evidence in favor of H_1

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- This can be done using a kernel-smoothed density estimation procedure applied to the samples

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- SAS also has several new Bayes Procs available (*Amy will illustrate*)