Coursework 5: STAT 570

Philip Pham

November 2, 2018

1. Consider the data given in Table 1, which are a simplified version of those reported in Breslow and Day (1980). These data arose from a case-control study that was carried out to investigate the relationship between esophageal cancer and various risk factors. Disease status is denoted Y with $Y = 0$ and $Y = 1$ corresponding to without/with disease and alcohol consumption is represented by X with $X = 0$ and $X = 1$ denoting less than 80g and greater than or equal to 80g on average per day. Let the probabilities of high alcohol consumption in the cases and controls be denoted

$$p_1 = \mathbb{P}(X = 1 \mid Y = 1) \text{ and } p_2 = \mathbb{P}(X = 1 \mid Y = 0), \tag{1}$$

respectively. Further, let X_1 be the number exposed from n_1 cases and X_2 be the number exposed from n_2 controls. Suppose $X_i \mid p_i \sim \text{Binomial}(n_i, p_i)$ in the case $(i = 1)$ and control $(i = 2)$ groups.

(a) Of particular interest in studies such as this is the odds ratio defined by

$$\theta = \frac{\mathbb{P}(Y = 1 \mid X = 1)/\mathbb{P}(Y = 0 \mid X = 1)}{\mathbb{P}(Y = 1 \mid X = 0)/\mathbb{P}(Y = 0 \mid X = 0)}. \tag{2}$$

Show that the odds ratio is equal to

$$\theta = \frac{\mathbb{P}(X = 1 \mid Y = 1)/\mathbb{P}(X = 0 \mid Y = 1)}{\mathbb{P}(X = 1 \mid Y = 0)/\mathbb{P}(X = 0 \mid Y = 0)} = \frac{p_1/(1-p_1)}{p_2/(1-p_2)}. \tag{3}$$

Solution: We have that

$$\mathbb{P}(Y = y \mid X = x) = \frac{\mathbb{P}(X = x \mid Y = y)\,\mathbb{P}(Y = y)}{\mathbb{P}(X = x)} \tag{4}$$

by Bayes' rule. Applying Equation 4 to Equation 2, we get

$$\theta = \frac{[\mathbb{P}(X = 1 \mid Y = 1)\,\mathbb{P}(Y = 1)] / [\mathbb{P}(X = 0 \mid Y = 1)\,\mathbb{P}(Y = 0)]}{[\mathbb{P}(X = 0 \mid Y = 1)\,\mathbb{P}(Y = 1)] / [\mathbb{P}(X = 0 \mid Y = 0)\,\mathbb{P}(Y = 0)]}. \tag{5}$$

The $\mathbb{P}(Y = y)$ factors cancel and we obtain the first part of Equation 3. Using Equation 1, we substitute to obtain the second part of Equation 3.

	$X = 0$	$X = 1$	
$Y = 1$	104	96	200
$Y = 0$	666	109	775

Table 1: Case-control data: $Y = 1$ corresponds to the event of esophageal cancer, and $X = 1$ exposure to greater than 80g of alcohol per day. There are 200 cases and 775 controls.

(b) Obtain the MLE and a 90% confidence interval for θ, for the data of Table 1.

Solution: The likelihood and log-likelihood functions are

$$
\begin{aligned}
L(p_1, p_2) &= \binom{n_1}{x_1} p_1^{x_1} (1-p_1)^{n_1 - x_1} + \binom{n_2}{x_2} p_2^{x_2} (1-p_2)^{n_2 - x_2} \qquad (6) \\
l(p_1, p_2) &= \log L(p_1, p_2) \\
&= \sum_{i=1}^{2} \left[\log \binom{n_i}{x_i} + x_i \log p_i + (n_i - x_i) \log (1 - p_i) \right],
\end{aligned}
$$

so the score function is

$$
S(p_1, p_2) = \nabla \log L(p_1, p_2) = \begin{pmatrix} \frac{x_1 - n_1 p_1}{p_1(1-p_1)} \\ \frac{x_2 - n_2 p_2}{p_2(1-p_2)}. \end{pmatrix} \tag{7}
$$

Thus, the Fisher information is

$$
I(p_1, p_2) = \mathbb{E}\left[S(p_1, p_2) S(p_1, p_2)^\intercal\right] = \begin{pmatrix} \frac{n_1}{p_1(1-p_1)} & 0 \\ 0 & \frac{n_2}{p_2(1-p_2)} \end{pmatrix}. \tag{8}
$$

From Equation 7, we can solve $S(\hat{p}_1, \hat{p}_2) = \mathbf{0}$ to get the MLEs $\hat{p}_1 = x_1/n_1$ and $\hat{p}_2 = x_2/n_2$. Since the MLE is invariant to reparameterization, we have the MLE for θ:

$$
\boxed{\hat{\theta} = \frac{\hat{p}_1/(1-\hat{p}_1)}{\hat{p}_2/(1-\hat{p}_2)} = \frac{1992}{1417} \approx 5.640.} \tag{9}
$$

We estimate the confidence interval for $\log \hat{\theta}$ which works since log is a monotonic transform. Using the delta method and Equation 8, we have that

$$
\begin{aligned}
\operatorname{Var}\left(\log \hat{\theta}\right) &\approx \left(\nabla \log \hat{\theta}\right)^\intercal \left(I(\hat{p}_1, \hat{p}_2)\right)^{-1} \left(\nabla \log \hat{\theta}\right) \\
&= \begin{pmatrix} \frac{1}{\hat{p}_1(1-\hat{p}_1)} & \frac{1}{\hat{p}_2(1-\hat{p}_2)} \end{pmatrix} \begin{pmatrix} \frac{\hat{p}_1(1-\hat{p}_1)}{n_1} & 0 \\ 0 & \frac{\hat{p}_2(1-\hat{p}_2)}{n_2} \end{pmatrix} \begin{pmatrix} \frac{1}{\hat{p}_1(1-\hat{p}_1)} \\ \frac{1}{\hat{p}_2(1-\hat{p}_2)} \end{pmatrix} \\
&= \frac{1}{n_1 \hat{p}_1 (1-\hat{p}_1)} + \frac{1}{n_2 \hat{p}_2 (1-\hat{p}_2)} \\
&= \frac{1}{n_1 \hat{p}_1} + \frac{1}{n_1(1-\hat{p}_1)} + \frac{1}{n_2 \hat{p}_2} + \frac{1}{n_2(1-\hat{p}_2)}. \qquad (10)
\end{aligned}
$$

Numerically, this is $\operatorname{Var}\left(\log \hat{\theta}\right) \approx 0.0307$.

The 90% confidence interval for $\log \hat{\theta}$ is approximately

$$
\left(\log \hat{\theta} - \Phi^{-1}(0.95) \sqrt{\operatorname{Var}\left(\log \hat{\theta}\right)}, \log \hat{\theta} + \Phi^{-1}(0.95) \sqrt{\operatorname{Var}\left(\log \hat{\theta}\right)}\right), \tag{11}
$$

which is about $(1.441, 2.018)$. Taking the exponent of both sides, we have a 90% confidence interval for $\hat{\theta}$ of $\boxed{(4.228, 7.524).}$

(c) We now consider a Bayesian analysis. Assume that the prior distribution for p_i is the beta distribution $\operatorname{Beta}(a, b)$ for $i = 1, 2$. Show that the posterior distribution $p_i \mid x_i$ is given by the beta distribution $\operatorname{Beta}(a + x_i, b + n_i - x_i)$, $i = 1, 2$.

Solution: From Equation 6, we have that the posterior:

$$\begin{aligned} p\left(p_i \mid X_i = x_i\right) &\propto \mathbb{P}\left(X_i = x_i \mid p_i\right) p\left(p_i\right) \\ &\propto p_i^{x_i + a - 1}\left(1 - p_i\right)^{n_i - x_i + b - 1}. \end{aligned}$$

Integration from 0 to 1, we have the beta fnction, so

$$p\left(p_i \mid X_i = x_i\right) = \frac{\Gamma\left(a + x_i + b + n_i - x_i\right)}{\Gamma\left(a + x_i\right)\Gamma\left(b + n_i - x_i\right)} p_i^{a + x_i - 1}\left(1 - p_i\right)^{b + n_i - x_i - 1}, \quad (12)$$

which is the $\operatorname{Beta}\left(a + x_i, b + n_i - x_i\right)$ distribution.

(d) Consider the case $a = b = 1$. Obtain expressions for the posterior mean, mode, and standard deviation. Evaluate these posterior summaries for the data of Table 1. Report 90% posterior credible intervals for p_1 and p_2.

Solution: For $a = b = 1$, we have that $p_1 \mid x_1 \sim \operatorname{Beta}\left(97, 105\right)$ and $p_2 \mid x_2 \sim \operatorname{Beta}\left(110, 667\right)$.

For the posterior means, we have that $\mathbb{E}\left[p_1 \mid x_1\right] = 97/202$ and $\mathbb{E}\left[p_2 \mid x_2\right] = 110/777$.

The mode of a $\operatorname{Beta}\left(\alpha, \beta\right)$ distributed random variable is $\frac{\alpha - 1}{\alpha + \beta - 2}$. So, for the posterior modes, we have that $\operatorname{mode}\left(p_1 \mid x_1\right) = 12/25$ and $\operatorname{mode}\left(p_2 \mid x_2\right) = 109/775$.

The variance of a $\operatorname{Beta}\left(\alpha, \beta\right)$ distributed random variable is $\frac{\alpha\beta}{(\alpha + \beta)^2(\alpha + \beta + 1)}$. For $p_1 \mid x_1$ and $p_2 \mid x_2$, we have standard errors:

$$\begin{aligned} \sigma_{p_1 \mid x_1} &= \frac{1}{202}\sqrt{\frac{10185}{203}} \approx 0.0351 \\ \sigma_{p_2 \mid x_2} &= \frac{1}{777}\sqrt{\frac{36685}{389}} \approx 0.0125. \end{aligned}$$

For the 90% credible interval, I choose l and u such that $\mathbb{P}\left([l, u]\right) = 0.9$, $\mathbb{P}\left((-\infty, l)\right) = 0.05$ and $\mathbb{P}\left((u, \infty)\right) = 0.05$. This is called the *equal-tailed interval*.

For $p_1 \mid x_1$, the interval is $[0.4226, 0.5380]$. For $p_2 \mid x_2$, the inverval is $[0.1215, 0.1626]$ This is computed numerically with `scipy.stats.beta.interval` in `case_control.ipynb`.

(e) Obtain the asymptotic form of the posterior distribution and obtain 90% credible intervals for p_1 and p_2. Compare this interval with the exact calculation of the previous part.

Solution: We can reparameterize the beta distribution in terms of two gamma random variables. Let $r_a \sim \operatorname{Gamma}\left(a, 1\right)$ and $r_b \sim \operatorname{Gamma}\left(b, 1\right)$. Let $x = r_a / \left(r_a + r_b\right)$ and $s = r_a + r_b$, so we can invert and get $r_a = xs$ and $r_b = \left(1 - x\right)s$.

Taking the Jacobina and hanging variables, we'll have the density function

$$\begin{aligned} p\left(x, s\right) &= \left(\frac{1}{\Gamma\left(a\right)}\left(xs\right)^{a-1}\exp\left(-xs\right)\right)\left(\frac{1}{\Gamma\left(b\right)}\left(\left(1 - x\right)s\right)^{b-1}\exp\left(-\left(1 - x\right)s\right)\right)s \\ &= \frac{1}{\Gamma\left(a\right)\Gamma\left(b\right)} x^{a-1}\left(1 - x\right)^{b-1}\left(s^{a+b-1}\exp\left(-s\right)\right). \end{aligned}$$

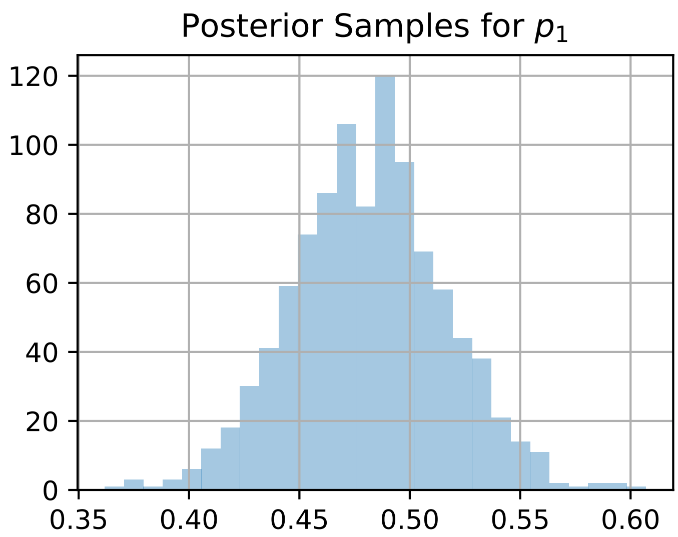


Figure 1: 1,000 samples from the posterior $p_1 \mid x_1$.

We recognize the gamma function and marginalize over s to obtain that $x \sim \text{Beta}\,(a, b)$.
Now, sums of gamma random variables are also gamma random variables, so as $a \to \infty$ and $b \to \infty$ r_a and r_b converge in distribution to the normal distribution.
Thus, we can apply the delta method to get an asymptotic distribution for the beta distribution. Let $h\,(z_1, z_2) = z_1/\,(z_1 + z_2)$. Then, $x = h\,(z_1, z_2)$, and

$$\mathbb{E}\,[x] = h\,(\mathbb{E}\,[z_1]\,, \mathbb{E}\,[z_2]) = \frac{a}{a+b} \tag{13}$$

$$\begin{aligned}\operatorname{Var}(x) &\approx \begin{pmatrix} \frac{b}{(a+b)^2} & -\frac{a}{(a+b)^2} \end{pmatrix}^{\intercal} \begin{pmatrix} a & 0 \\ 0 & b \end{pmatrix} \begin{pmatrix} \frac{b}{(a+b)^2} \\ -\frac{a}{(a+b)^2} \end{pmatrix} \\ &= \left(\frac{1}{a+b}\right)\left(\frac{a}{a+b}\right)\left(\frac{b}{a+b}\right). \end{aligned} \tag{14}$$

which results in the same mean, and the variance is asymptotically equivalent to the variance in the previous part.
Applying Equations 13 and 14, we obtain the 90% intervals $(0.4224, 0.5380)$ for p_1 and $(0.1210, 0.1621)$ for p_2, which are virtually identically to the exact calculation in the previous part, which is unsurprising since n_1 and n_2 are quite large.

(f) Simulate samples $p_1(t)$, $p_2(t)$, $t = 1, \ldots, T = 1000$ from the posterior distributions $p_1 \mid x_1$ and $p_2 \mid x_2$. Form histogram representations of the posterior distributions using these samples and obtain sample-based 90% credible intervals.

Solution: The histogram of samples from $p_1 \mid x_1$ and $p_2 \mid x_2$ and be found in Figures 1 and 2, respectively.
The sample 90% interval for p_1 was $(0.4255, 0.5393)$. The sampled 90% intervals for p_2 were $(0.1209, 0.1634)$, which agree with the previous interval calculations.

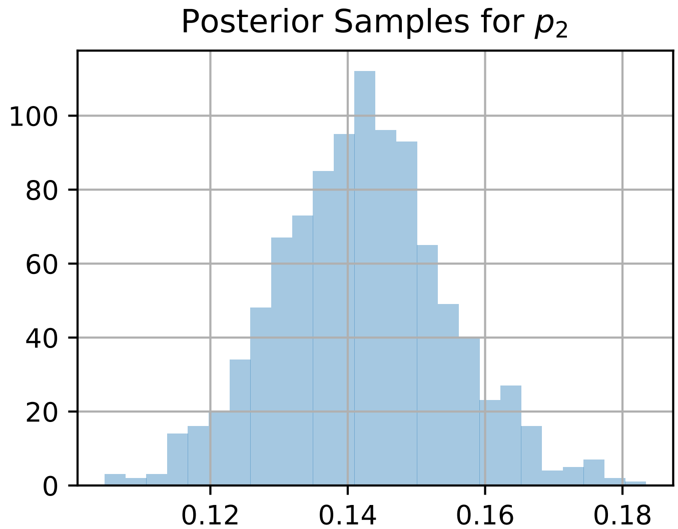


Figure 2: 1,000 samples from the posterior $p_2 \mid x_2$.

(g) Obtain samples from the posterior distribution of $\theta | x_1, x_2$ and form the histogram representation of the posterior. Obtain the posterior median and 90% credible interval for $\theta \mid x_1, x_2$ and compare with the likelihood analysis.

Solution: To get a posterior sample for θ, we draw samples from $p_1 \mid x_1$ and $p_2 \mid x_2$ and calculate θ. The samples can be seen in Figure 3.
The samples 90% credible interval was $(6.3137, 6.4755)$, and the sampled posterior median was 5.6486. The median is very close to the MLE in Equation 9. The 90% credible interval is much smaller however since we make the prior beta assumption for p_1 and p_2.
The computations for the analysis can be found in `case_control.ipynb`.

(h) Suppose the rate of esophageal cancer is 18 in 100,000. Describe how this information may be used to evaluate $q_1 = \mathbb{P}(Y = 1 \mid X = 1)$ and $q_0 = \mathbb{P}(Y = 1 \mid X = 0)$.

Solution: We can apply Bayes' rule since we know $\mathbb{P}(Y = 1) = 9/50,000 = 0.00018$ and $\mathbb{P}(Y = 0) = 49,991/50,000 = 0.99982$.
Thus, we have that

$$\begin{aligned}
\mathbb{P}(Y = 1 \mid X = 1) &= \frac{\mathbb{P}(X = 1 \mid Y = 1)\,\mathbb{P}(Y = 1)}{\mathbb{P}(X = 1 \mid Y = 0)\,\mathbb{P}(Y = 0) + \mathbb{P}(X = 1 \mid Y = 1)\,\mathbb{P}(Y = 1)} \\
&= \frac{p_1 \mathbb{P}(Y = 1)}{p_2 \mathbb{P}(Y = 0) + p_1 \mathbb{P}(Y = 1)} \\
\mathbb{P}(Y = 1 \mid X = 0) &= \frac{\mathbb{P}(X = 0 \mid Y = 1)\,\mathbb{P}(Y = 1)}{\mathbb{P}(X = 0 \mid Y = 0)\,\mathbb{P}(Y = 0) + \mathbb{P}(X = 0 \mid Y = 1)\,\mathbb{P}(Y = 1)} \\
&= \frac{(1 - p_1)\,\mathbb{P}(Y = 1)}{(1 - p_2)\,\mathbb{P}(Y = 0) + (1 - p_1)\,\mathbb{P}(Y = 1)}.
\end{aligned}$$

We can either substitute the the MLE $\hat{p}_i$ for p_i or integrate over the posteriors $p_1 \mid x_1$ and $p_2 \mid x_2$.
For example, the MLE estimates are $\hat{q}_1 \approx 0.0006140$ and $\hat{q}_2 \approx 0.0001089$.

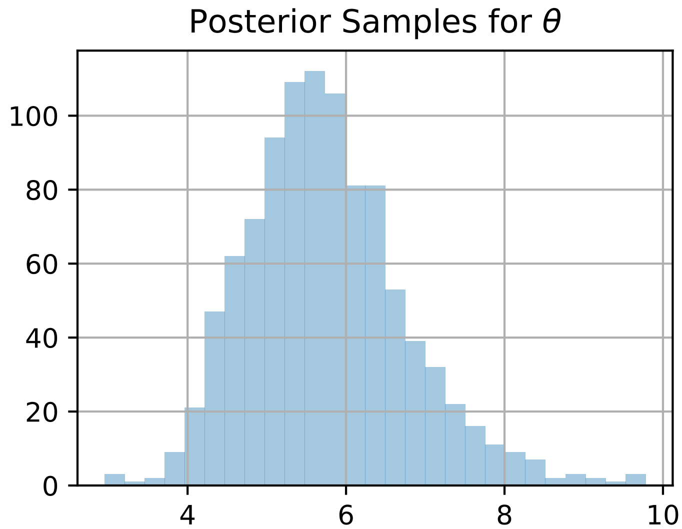


Figure 3: 1,000 samples from the posterior $\theta \mid x_2$.

2. (a) Consider the likelihood, $\hat{\theta} \mid \theta \sim \mathcal{N}(\theta, V)$ and the prior $\theta \sim \mathcal{N}(0, W)$ with V and W known. Show that $\theta \mid \hat{\theta} \sim \mathcal{N}\left(r\hat{\theta}, rV\right)$, where $r = W/(V+W)$.

   Solution: This result follows from the conjugacy of the normal distribution with itself:

$$
\begin{aligned}
p\left(\theta \mid \hat{\theta}\right) &\propto p\left(\hat{\theta} \mid \theta\right) p(\theta) \\
&\propto \exp\left(-\frac{1}{2V}\left(\hat{\theta}-\theta\right)^2 - \frac{1}{2W}\theta^2\right) \\
&\propto \exp\left(-\frac{V+W}{2(VW)}\left(\frac{W}{V+W}\hat{\theta}^2 - 2\frac{W}{V+W}\hat{\theta}\theta + \theta^2\right)\right) \\
&\propto \exp\left(-\frac{V+W}{2(VW)}\left(\theta - \frac{W}{V+W}\hat{\theta}\right)^2\right) = \exp\left(-\frac{1}{2(rV)}\left(\theta - r\hat{\theta}\right)^2\right)
\end{aligned}
$$

   after completing the square. We recognize this distribution as being part of the normal family, which gives us the result.

   (b) Suppose we wish to compare the models M_0: $\theta = 0$ versus M_1: $\theta \neq 0$. Show that the Bayes factor is given by

$$
\frac{p\left(\hat{\theta} \mid M_0\right)}{p\left(\hat{\theta} \mid M_1\right)} = \frac{1}{\sqrt{1-r}} \exp\left(-\frac{Z^2}{2} r\right), \tag{15}
$$

   where $Z = \hat{\theta}/\sqrt{V}$.

Solution: We have that

$$\begin{aligned} p\left(\hat{\theta} \mid M_0\right) &= p\left(\hat{\theta} \mid \theta = 0\right) = \frac{1}{\sqrt{2\pi V}} \exp\left(-\frac{1}{2V}\hat{\theta}^2\right) \\ p\left(\hat{\theta} \mid M_1\right) &= \int_{-\infty}^{\infty} p\left(\hat{\theta} \mid \theta\right) p(\theta)\, \mathrm{d}\theta \\ &= \frac{1}{\sqrt{2\pi (V+W)}} \exp\left(-\frac{1}{2(V+W)}\hat{\theta}^2\right) \end{aligned}$$

after completing the square. Substituting into the left-hand side of Equation 15, we obtain

$$\frac{p\left(\hat{\theta} \mid M_0\right)}{p\left(\hat{\theta} \mid M_1\right)} = \sqrt{\frac{V+W}{V}} \exp\left(-\frac{1}{2} \cdot \frac{W}{V+W} \cdot \frac{\hat{\theta}^2}{V}\right) = \frac{1}{\sqrt{1-r}} \exp\left(-\frac{Z^2}{2} r\right)$$

as desired.

(c) Suppose we have a prior probability $\pi_1 = \mathbb{P}(M_1)$ of model M_1 being true. Write down an expression for the posterior probability $\mathbb{P}\left(M_1 \mid \hat{\theta}\right)$ in terms of the Bayes factor.

Solution: Let K be the Bayes factor. By applying Bayes' rule, we have that

$$\begin{aligned} \mathbb{P}\left(M_1 \mid \hat{\theta}\right) &= \frac{\mathbb{P}\left(\hat{\theta} \mid M_1\right) \mathbb{P}(M_1)}{\mathbb{P}\left(\hat{\theta} \mid M_0\right) \mathbb{P}(M_0) + \mathbb{P}\left(\hat{\theta} \mid M_1\right) \mathbb{P}(M_1)} \\ &= \frac{K^{-1} \mathbb{P}\left(\hat{\theta} \mid M_0\right) \pi_1}{\mathbb{P}\left(\hat{\theta} \mid M_0\right)(1-\pi_1) + K^{-1}\mathbb{P}\left(\hat{\theta} \mid M_0\right)\pi_1} \\ &= \frac{K^{-1}\pi_1}{(1-\pi_1) + K^{-1}\pi_1} = \frac{\pi_1}{K(1-\pi_1)+\pi_1}. \end{aligned}$$

(d) Now suppose we have summaries from two studies, θ_j, V_j, $j = 1, 2$. Assuming, $\theta_j \mid \theta \sim \mathcal{N}(\theta, V_j)$ and the prior $\theta \sim \mathcal{N}(0, W)$, derive the posterior $p(\theta \mid \theta_1, \theta_2)$.

Solution: We have

$$\begin{aligned} p(\theta \mid \theta_1, \theta_2) &\propto p(\theta_2 \mid \theta_1, \theta)\, p(\theta_1 \mid \theta)\, p(\theta) = p(\theta_2 \mid \theta)\, p(\theta_1 \mid \theta)\, p(\theta) \\ &\propto \exp\left(-\frac{1}{2V_2}(\theta_2 - \theta)^2\right) \exp\left(-\frac{V_1 + W}{2(V_1 W)}\left(\theta - \frac{W}{V_1 + W}\theta_1\right)^2\right) \\ &\propto \exp\left(-\frac{V_1V_2 + V_1W + V_2W}{2(V_1V_2W)}\left(\theta - \frac{V_2W\theta_1 + V_1W\theta_2}{V_1V_2 + V_1W + V_2W}\right)^2\right), \end{aligned}$$

after repeatedly completing the square and dropping factors that don't depend on θ.

Thus, we have that

$$\theta \mid \theta_1, \theta_2 \sim \mathcal{N}\left(\frac{V_2W\theta_1 + V_1W\theta_2}{V_1V_2 + V_1W + V_2W}, \frac{V_1V_2W}{V_1V_2 + V_1W + V_2W}\right). \tag{16}$$

(e) Derive the Bayes factor

$$\frac{p(\theta_1, \theta_2 \mid M_0)}{p(\theta_1, \theta_2 \mid M_1)}, \tag{17}$$

again comparing the models M_0: $\theta = 0$ versus M_1: $\theta \neq 0$.

Solution: (θ_1, θ_2) have a bivariate normal distribution. Under M_0, we have that

$$\begin{aligned} p(\theta_1, \theta_2 \mid M_0) &= p(\theta_1, \theta_2 \mid \theta = 0) \\ &= \frac{1}{2\pi\sqrt{V_1 V_2}} \exp\left(-\frac{1}{2}\begin{pmatrix}\theta_1 & \theta_2\end{pmatrix}\begin{pmatrix}\frac{1}{V_1} & 0 \\ 0 & \frac{1}{V_2}\end{pmatrix}\begin{pmatrix}\theta_1 \\ \theta_2\end{pmatrix}\right). \end{aligned} \tag{18}$$

Under M_1, we have that

$$p(\theta_1, \theta_2 \mid M_1) = \int_{-\infty}^{\infty} p(\theta_1, \theta_2 \mid \theta)\, p(\theta)\, \mathrm{d}\theta. \tag{19}$$

We can consider θ as having the improper prior $\mathcal{N}\left(\mathbf{0}, \begin{pmatrix} W & W \\ W & W \end{pmatrix}\right)$, which results in

$$\theta_1, \theta_2 \mid M_1 \sim \mathcal{N}\left(\mathbf{0}, \begin{pmatrix} V_1 + W & W \\ W & V_2 + W \end{pmatrix}\right) \tag{20}$$

by conjugacy of the multivariate normal distribution.

The Bayes factor can then be computed:

$$\sqrt{\frac{V_1 V_2 + V_1 W + V_2 W}{V_1 V_2}} \exp\left(-\frac{1}{2}\begin{pmatrix}\theta_1 & \theta_2\end{pmatrix} \Lambda \begin{pmatrix}\theta_1 \\ \theta_2\end{pmatrix}\right), \tag{21}$$

where

$$\Lambda = \begin{pmatrix}\frac{1}{V_1} & 0 \\ 0 & \frac{1}{V_2}\end{pmatrix} + \frac{1}{V_1 V_2 + V_1 W + V_2 W}\begin{pmatrix} V_2 + W & -W \\ -W & V_1 + W \end{pmatrix}. \tag{22}$$

(f) We will show these results can be used in the context of a genome-wide association study on Type II diabetes, reported by Frayling et al. (2007, Science). Two sets of data were independently collected, resulting in two log odds ratios $\hat{\theta}_j$, $j = 1, 2$, for each SNP.

For SNP rs9939609 point estimates (95% confidence intervals) were 1.27 (1.16, 1.37) and 1.15 (1.09,1.23). Suppose we have a normal prior for the odds ratio that has a 95% range (0.67, 1.50).

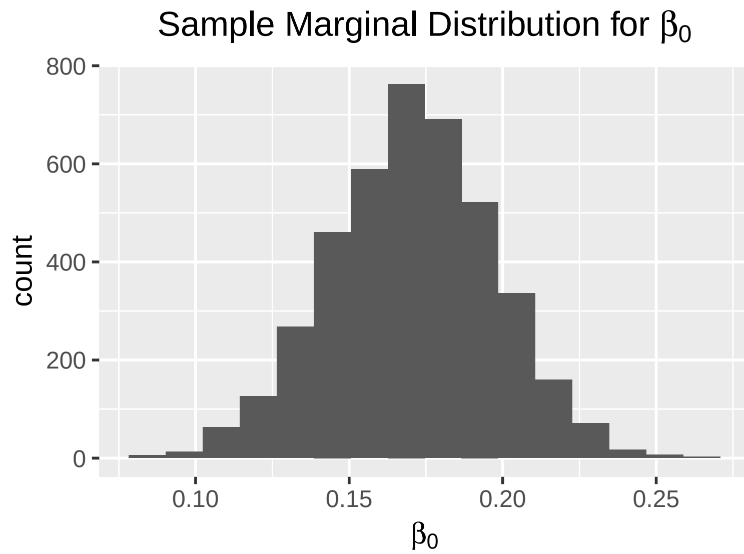
i. Find W from this interval, and then calculate the posterior median and 95% intervals for θ based on (i) the first dataset only, (ii) both of the populations.

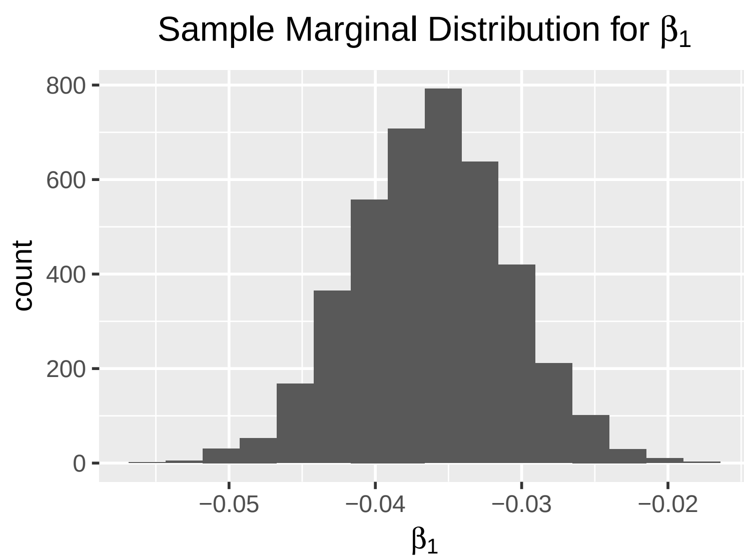
Solution: The analysis can be found at `genome_association.ipynb`.

ii.

iii.

3. We will carry out a Bayesian analysis of the lung cancer and radon data, that were examined in lectures, using INLA. These data are available on the class website. The likelihood is $Y_i \mid \beta \sim \text{Poisson}\left(E_i \exp\left(\beta_0 + \beta_1 x_i\right)\right)$ independently distributed, where $\beta = \begin{pmatrix}\beta_0 & \beta_1\end{pmatrix}^\mathsf{T}$, Y_i and E_i are observed and expected counts of lung cancer incidence in Minnesota in 1998–2002, and x_i is a measure of residential radon in county i, $i = 1, \ldots, n$.





(a) Analyze these data using the default prior specifications in INLA. Produce figures of the INLA approximations to the marginal distributions of β_0 and β_1, along with the posterior means, posterior standard deviations, and 2.5%, 50%, 97.5% quantiles.

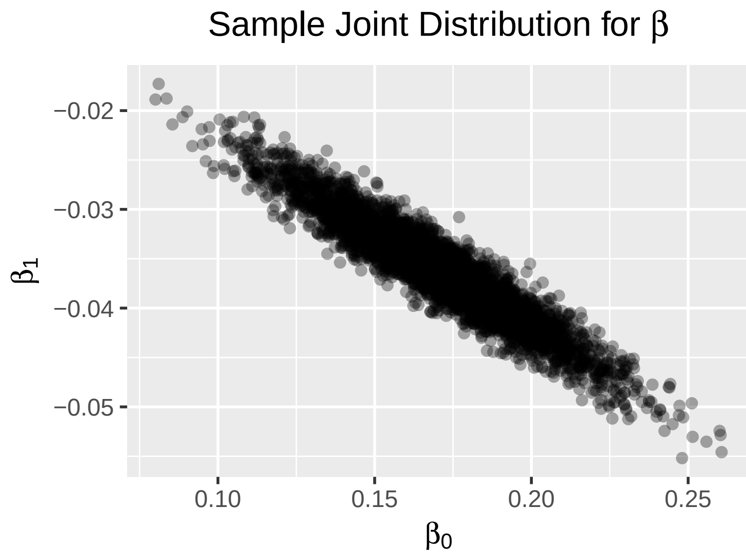
Solution: Details of the analysis can be found in `lung_cancer_radon.ipynb`.

(b) For a more informative prior specification we may reparameterize the model as independently distributed

$$Y_i \mid \theta \sim \text{Poisson}\left(E_i \theta_0 \theta_1^{x_i - \bar{x}_i}\right), \tag{23}$$

where $\theta = \begin{pmatrix}\theta_0 & \theta_1\end{pmatrix}^\intercal$ and

$$\theta_0 = \mathbb{E}\left[\frac{Y}{E} \mid x = \bar{x}\right] = \exp\left(\beta_0 + \beta_1 \bar{x}\right) \tag{24}$$



where is the expected standardized mortality ratio in an area with average radon. The parameter $\theta_1 = \exp(\beta_1)$ is the relative risk associated with a one-unit increase in radon. For θ_0 we assume a lognormal prior with 2.5% and 97.5% quantiles of 0.67 and 1.5 to give $\mu = 0$ and $\sigma = 0.21$. For θ_1 we again take a lognormal prior and assume the relative risk associated with a one-unit increase in radon is between 0.8 and 1.2 with probability 0.95, to give $\mu = -0.02$ and $\sigma = 0.10$. By converting these into normal priors in INLA, rerun your analysis, and report the same summaries.

Solution: For the priors, we have two independent normals

$$\log\theta_0 \sim \mathcal{N}\left(0, 0.21^2\right)$$
$$\log\theta_1 \sim \mathcal{N}\left(-0.02, 0.1^2\right).$$

We can rewrite

$$E_i\theta_0\theta_1^{x_i-\bar{x}_i} = E_i\exp\left(\log\theta_0 + (x_i - \bar{x})\log\theta_1\right), \tag{25}$$

so after centering the x_i, we can specify priors on the intercept and coefficients as usual.

4. Consider the simple linear regression model $Y_i = \beta_0 + \beta_1 x_i + \epsilon_i$, with $\epsilon_i \mid \sigma^2 \sim_{\text{iid}} \mathcal{N}(0, \sigma^2)$, $i = 1, \ldots, n$. Suppose the prior distribution is of the form

$$\pi\left(\beta_0, \beta_1, \sigma^2\right) = \pi(\beta_0, \beta_1)\,\pi\left(\sigma^{-2}\right). \tag{26}$$

The prior for $\begin{pmatrix}\beta_0 & \beta_1\end{pmatrix}^\intercal$ is

$$\begin{pmatrix}\beta_0\\ \beta_1\end{pmatrix} \sim \mathcal{N}\left(\begin{pmatrix}m_0\\ m_1\end{pmatrix}, \begin{pmatrix}v_{00} & v_{01}\\ v_{01} & v_{11}\end{pmatrix}\right) \tag{27}$$

and the prior for σ^{-2} is $\text{Gamma}(a, b)$. In this exercise the conditional distribution required for Gibbs sampling will be derived.

(a) Write down the form of the posterior distribution (up to proportionality) and derive the conditional distributions $p\left(\beta_0 \mid \beta_1, \sigma^2, \mathbf{y}\right)$, $p\left(\beta_1 \mid \beta_0, \sigma^2, \mathbf{y}\right)$ and $p\left(\sigma^2 \mid \beta_0, \beta_1, \mathbf{y}\right)$. Hence, give details of the Gibbs sampling algorithm.

Solution: Using the normal likelihood and prior, we have the posterior

$$\begin{aligned} p\left(\beta_0, \beta_1, \sigma^2 \mid \mathbf{y}\right) &\propto p\left(\mathbf{y} \mid \beta_0, \beta_1, \sigma^2\right) \pi\left(\beta_0, \beta_1, \sigma^2\right) \\ &\propto \pi\left(\beta_0, \beta_1\right) \pi\left(\sigma^{-2}\right)\left(\frac{\sigma^{-2}}{2\pi}\right)^{n/2} \prod_{i=1}^{n} \exp\left(-\frac{1}{2\sigma^2}\left(y_i - \beta_0 + \beta_1 x_i\right)^2\right), \end{aligned}$$

where

$$\begin{aligned} \pi\left(\beta_0, \beta_1\right) &\propto \exp\left(-\frac{1}{2}(\beta - m)^{\intercal} V^{-1}(\beta - m)\right), \text{ where } V = \begin{pmatrix} v_{00} & v_{01} \\ v_{01} & v_{11} \end{pmatrix} \\ \pi\left(\sigma^{-2}\right) &\propto \left(\sigma^{-2}\right)^{a-1} \exp\left(-b\sigma^{-2}\right). \end{aligned}$$

For $p\left(\sigma^2 \mid \beta_0, \beta_1, \mathbf{y}\right)$, we can drop all the factors without σ^2, so we have

$$\begin{aligned} p\left(\sigma^2 \mid \beta_0, \beta_1, \mathbf{y}\right) &\propto \left(\sigma^{-2}\right)^{a+n/2-1} \exp\left(-b\sigma^{-2}\right) \prod_{i=1}^{n} \exp\left(-\frac{1}{2\sigma^2}\left(y_i - \beta_0 + \beta_1 x_i\right)^2\right) \\ &\propto \left(\sigma^{-2}\right)^{a+n/2-1} \exp\left(-\sigma^{-2}\left(b + \frac{1}{2}\sum_{i=1}^{n}\left(y_i - \beta_0 - \beta_1 x_i\right)^2\right)\right), \end{aligned}$$

so $\boxed{\left(\sigma^{-2} \mid \beta_0, \beta_1, \mathbf{y}\right) \sim \text{Gamma}\left(a + \frac{n}{2}, b + \frac{1}{2}\sum_{i=1}^{n}\left(y_i - \beta_0 - \beta_1 x_i\right)^2\right).}$

The conditional posteriors for β_0 and β_1 can be obtained from marginalizing $p\left(\beta \mid \sigma^2, \mathbf{y}\right)$ from the next part. We'll get

$$\begin{aligned} \left(\beta_0 \mid \beta_1, \sigma^2, \mathbf{y}\right) &\sim \mathcal{N}\left(m_1^*, V_{11}^*\right) \\ \left(\beta_1 \mid \beta_0, \sigma^2, \mathbf{y}\right) &\sim \mathcal{N}\left(m_2^*, V_{22}^*\right). \end{aligned}$$

(b) Another blocked Gibbs sampling algorithm would simulate from the distributions $p\left(\beta \mid \sigma^2, \mathbf{y}\right)$ and $p\left(\text{ÏČ}^{-2} \mid \beta, \mathbf{y}\right)$. Derive the distributions

$$\left(\beta \mid \sigma^2, \mathbf{y}\right) \sim \mathcal{N}\left(m^*, V^*\right) \tag{28}$$

$$\left(\sigma^2 \mid \beta, \mathbf{y}\right) \sim \text{Gamma}\left(a + \frac{n}{2}, b + \frac{1}{2}(\mathbf{y} - X\beta)^{\intercal}(\mathbf{y} - X\beta)\right), \tag{29}$$

where

$$\begin{aligned} m^* &= W\hat{\beta} + \left(I_2 - W\right) m \\ V^* &= W \,\text{Var}\left(\hat{\beta}\right) \end{aligned}$$

and $W = \left(X^{\intercal}X + V^{-1}\sigma^2\right)^{-1} X^{\intercal}X$ and $\hat{\beta}$ is the MLE of β.

Solution: Let X be the a $n \times 2$ matrix with all 1s in the first column and $\left(x_1 \cdots x_n\right)^\intercal$ as the second column.

Then, Equation 29 follows from the previous part after rewriting the term

$$\frac{1}{2}\sum_{i=1}^{n}\left(y_i - \beta_0 - \beta_1 x_i\right)^2 = \frac{1}{2}\left(\mathbf{y} - X\beta\right)^\intercal \left(\mathbf{y} - X\beta\right). \tag{30}$$

As before, we complete the square to derive the posterior for β:

$$\begin{aligned}
&\left(\mathbf{y} - X\beta\right)^\intercal \sigma^{-2} I_n \left(\mathbf{y} - X\beta\right) + \left(\beta - m\right)^\intercal V^{-1}\left(\beta - m\right)\\
&= \beta^\intercal \sigma^{-2} X^\intercal X\beta + \beta^\intercal V^{-1}\beta - 2\beta^\intercal \left(\sigma^{-2}X^\intercal y + V^{-1}m\right) + \sigma^{-2}y^\intercal y - m^\intercal V^{-1} m\\
&= \beta^\intercal \left(\sigma^{-2}X^\intercal X + V^{-1}\right)\beta\\
&\quad - 2\beta^\intercal \left(\sigma^{-2}X^\intercal X + V^{-1}\right)\left(\sigma^{-2}X^\intercal X + V^{-1}\right)^{-1}\left(\sigma^{-2}X^\intercal y + V^{-1}m\right) + C,
\end{aligned}$$

where we have collapsed the terms that don't depend on β into C.

Recall that $\mathrm{Var}\left(\hat{\beta}\right) = \sigma^2\left(X^\intercal X\right)^{-1}$, so we have that

$$\left(\sigma^{-2}X^\intercal X + V^{-1}\right)^{-1} = \left(X^\intercal X + \sigma^2 V^{-1}\right)^{-1}\left(X^\intercal X\right)\sigma^2\left(X^\intercal X\right)^{-1} = V^*,$$

so continuing the process of completing the square:

$$\begin{aligned}
&\beta^\intercal \left(V^*\right)^{-1}\beta - 2\beta^\intercal\left(V^*\right)^{-1} W\left(X^\intercal X\right)^{-1}\left(X^\intercal y + \sigma^2 V^{-1}m\right) + C\\
&= \beta^\intercal \left(V^*\right)^{-1}\beta - 2\beta^\intercal\left(V^*\right)^{-1}\left(W\hat{\beta} + W\sigma^2\left(X^\intercal X\right)^{-1}V^{-1}m\right) + C\\
&= \beta^\intercal \left(V^*\right)^{-1}\beta - 2\beta^\intercal\left(V^*\right)^{-1}\left(W\hat{\beta} + \sigma^2\left(V\left(X^\intercal X + \sigma^2 V^{-1}\right)\right)^{-1} m\right) + C\\
&= \beta^\intercal \left(V^*\right)^{-1}\beta - 2\beta^\intercal\left(V^*\right)^{-1}\left(W\hat{\beta} + \sigma^2\left(VX^\intercal X + \sigma^2 I\right)^{-1} m\right) + C\\
&= \beta^\intercal \left(V^*\right)^{-1}\beta - 2\beta^\intercal\left(V^*\right)^{-1}\left(W\hat{\beta} + \left(I_2 - W\right)m\right) + C\\
&= \left(\beta - m^*\right)^\intercal\left(V^*\right)^{-1}\left(\beta - m^*\right) + C',
\end{aligned}$$

where we have applied the Woodbury matrix identity.

Thus, all the factors that contain β can be written as a quadratic form which gives us the result in Equation 28.