A Meta-Analysis of One-Year Mortality Rates After CABG and PCI

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When a patient presents with severe Coronary Heart Disease (CHD) there are two common treatments, Coronary Artery Bypass Grafting (CABG) and Percutaneous Coronary Intervention (PCI). In this study, we conduct a Bayesian meta-analysis to determine whether there is a difference between the one-year mortality rates for patients that undergo CABG versus PCI. We use our model to estimate the mean one-year death rate for CABG patients and PCI patients. Our data consist of results from 11 studies comparing PCI and CABG in different populations.

It was difficult to find studies comparing the one-year mortality rates in CABG and PCI patients that were independent of the studies used for data. As such, prior information was elicited from two separate studies focusing on individual procedures. The CABG study followed 3376 patients operated on between January 2004 and July 2008 at the Cardiac Surgery Department of the Ludwig Maximilians University Munich and found a 4.9% one-year mortality rate.[1] Emergency patients, redos, and patients with valvular disease were excluded. The PCI study followed 1313 patients who underwent treatment at The Canberra Hospital in the Australian Capital Territory between January 2006 and December 2013 and found a 7.3% one-year mortality rate.[2] There were no exclusions in this study. Comparisons between the studies will be biased but some bias is acceptable as we are primarily interested in the general scale of the one-year mortality rates.

The quantity μ_i is associated with the logit of a probability, so a normal prior with range $(-\infty,\infty)$ is appropriate for μ_0. We estimate that an overall average of 6% of patients die by one year so the median or mean for the prior distribution of μ_0 is -2.752. 4% seems to be a reasonable lower bound on the average one-year mortality rate. We designate logit(0.04) as the 10^{th} percentile of the distribution of μ_0 and solve for a precision of 9.028. It appears the PCI group has a higher one-year mortality rate than the CABG group but we are not sure of this, so a normal prior with range $(-\infty,\infty)$

is appropriate for δ_0. To specify the mean, we will think of δ_0 as the log odds ratio of death in the PCI group compared to CABG group. If we say 7% of patients die in the PCI group and 5% die in the CABG group, this gives us a prior mean of 0.358. It is possible the CABG group has a higher one-year mortality rate, so we will specify 0 as the 30^{th} percentile of the logit-scale distribution to allow the prior for δ_0 to be negative some of the time. This gives us a precision of 2.149.

Both τ^2 and σ^2 are precision terms with range of $(0, \infty)$ and gamma priors. σ^2 dictates how much μ_i varies across different populations. The most extreme one-year mortality rate observed for subgroups (which can be viewed as different populations) in our prior studies was 1.7%[1]. We want the variance of the variance of μ_i to be high enough to be able to capture 1.7% with reasonable probability. If we consider the overall mean of μ_i, and let the difference between logit(0.06) and logit(0.017) represent one standard deviation of μ_i, then a prior distribution with mean 0.875 and precision 0.25 seems appropriate for σ^2. It is more difficult to estimate the precision of δ_i because comparisons between the prior studies are biased. We expect δ_i to vary a little more than μ_i so a mean of 0.5 and a variance of 0.01 will be used for τ^2.

After the prior distributions were determined, a model was run for 5,000 iterations with 3 chains and convergence was assessed. Autocorrelation appeared to reach zero at about the 70^{th} lag for δ_i values and the 50^{th} lag for μ_i values (Figure 1). For all other values examined the autocorrelation reached zero before lag 70 so the model was run for 70,000 iterations. Time series plots were examined for all parameters and no abnormalities were observed (Figure 2).

Based on our model there does not appear to be a significant difference between the mortality rates in the treatment groups. δ_0 represents the mean log odds ratio of mortality in the PCI group compared to the CABG group. The posterior distribution of δ_0 was centered at 0.09 and had a confidence interval of (-0.23,0.44). This confidence interval contains zero, suggesting that 1 is a plausible value for the odds ratio. The logit-scale mean one-year mortality rates were -2.57 for the

PCI group and -2.66 for the CABG group, translating to 7.11% and 6.54%. The corresponding confidence intervals corresponded to (5.95%,8.47%) for PCI and (5.22%,8.17%) for CABG when transformed to the percentile scale.

A sensitivity analysis was conducted to determine how much one's choice of prior parameters affects the posterior distribution of δ_0. The arguments governing the distribution of μ_0, δ_0, τ^2 and σ^2 were adjusted one at a time. For each argument, two new models were run. One used a value higher the original value and the other used a lower value. The mean of μ_0 was specified as -4.60 then -1.73, corresponding to a 1% then 15% death rate. The variance of μ_0 was specified as 1 then 20. The mean of δ_i was specified as -2.504 then 2.504, corresponding to a 10% increase or decrease between groups, specifically with a 1% death rate in one group and 11% in the other. The parameters governing the distribution of and σ^2 were each changed from their original values of 0.191 and 0.219 to 0.01 then 3.The parameters governing the distribution of τ^2 were each changed from their original values of 0.0025 and 0.005 to 0.0001then 0.1.

Each 95% confidence interval produced in the sensitivity analysis contained 0, so none of the parameter variations affected the overall conclusion of this study (Table 2). Unsurprisingly, varying the mean of δ_0 produced the largest change in the confidence interval for δ_0. Varying the variance of δ_0 produced the second largest difference change in distribution of δ_0, but when densities from the sensitivity analysis were plotted together they looked very similar (Figure 3). Extreme values were used for the mean of δ_0 in the original sensitivity analysis, so changes in the distribution of δ_0 were noticeable. When less extreme values were used for the prior mean of δ_0, there posterior distributions of δ_0 looked more similar (Figure 4). Overall, we conclude that the posterior distribution of δ_0 and our conclusion that there is not difference in the one-year mortality rates between procedures are not overly sensitive to the choice of prior parameters.

References

(1) Eifert S, Kilian E, Beiras-Fernandez A, Juchem G, Reichart B, Lamm P. Early and mid term mortality after coronary artery bypass grafting in women depends on the surgical protocol: retrospective analysis of 3441 on- and off-pump coronary artery bypass grafting procedures. Journal of Cardiothoracic Surgery. 2010;5:90. doi:10.1186/1749-8090-5-90.

(2) Hosseiny AD, Moloi S, Chandrasekhar J, Farshid A. Mortality pattern and cause of death in a long-term follow-up of patients with STEMI treated with primary PCI. Open Heart. 2016; 3(1): e000405.

Appendix 1: Bayesian Model

$$y_{ij} \mid \pi_{ij} \sim \text{Binomial}(n_{ij}, \pi_{ij})$$

$$\text{logit}(\pi_{i1}) = \mu_i - 0.5*\delta_i$$
$$\text{logit}(\pi_{i2}) = \mu_i + 0.5*\delta_i$$

$$\mu_i \mid \mu_0, \sigma^2 \sim \text{No}(\mu_0, \sigma^2)$$
$$\delta_i \mid \delta_0, \tau^2 \sim \text{No}(\delta_0, \tau^2)$$

$\mu_0 \sim$ No(a, b) where a = -2.752 and b = 9.028
$\delta_0 \sim$ No(c, d) where c = 0.368 and d = 2.149
$\sigma^2 \sim$ Gamma(e, f) where e = 0.1914 and f = 0.2188
$\tau^2 \sim$ Gamma(g, h) where g = 0.0025 and h = 0.0050

i = 1, … , 11 studies
j = 1, 2 treatments

y_{ij} is the number of deaths in study i for treatment j
π_{i1} is the probability of death in study i for the CABG group
π_{i2} is the probability of death in study i for the PCI group
n_{ij} is the number of patients in study i for treatment j

μ_i is the mean log odds of death in study i
δ_i is the difference between the two log odds of death in study i

μ_0 is the mean log odds of death across all studies
σ^2 allows the log odds of death to vary across different studies
δ_0 is the mean difference between the log odds of death across all studies
τ^2 allows the difference between the log odds of death to vary across different studies

Appendix 2: Figures and Tables

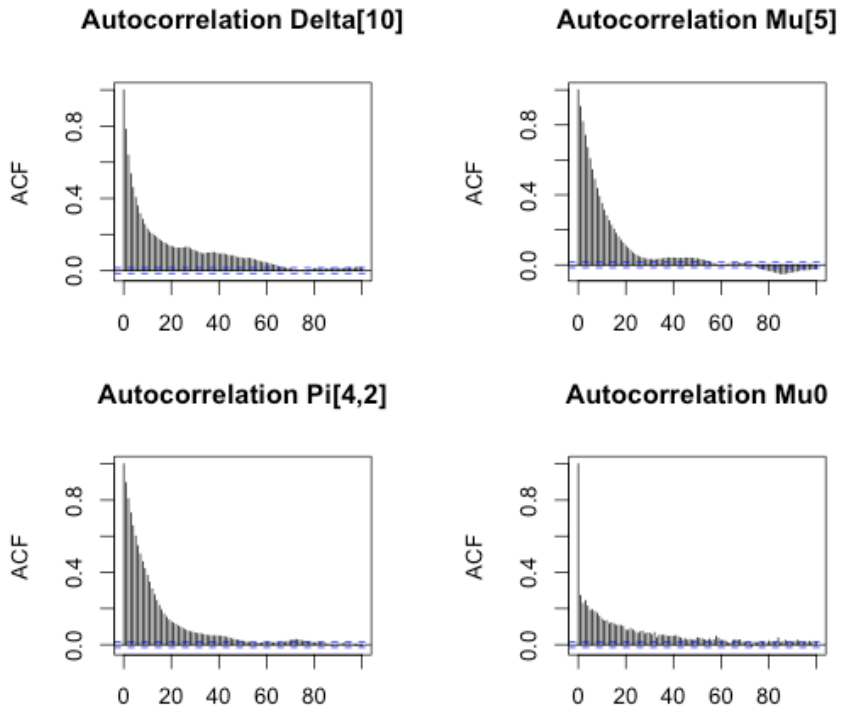

Figure 1. Representative Autocorrelation Plots (5,000 iterations)

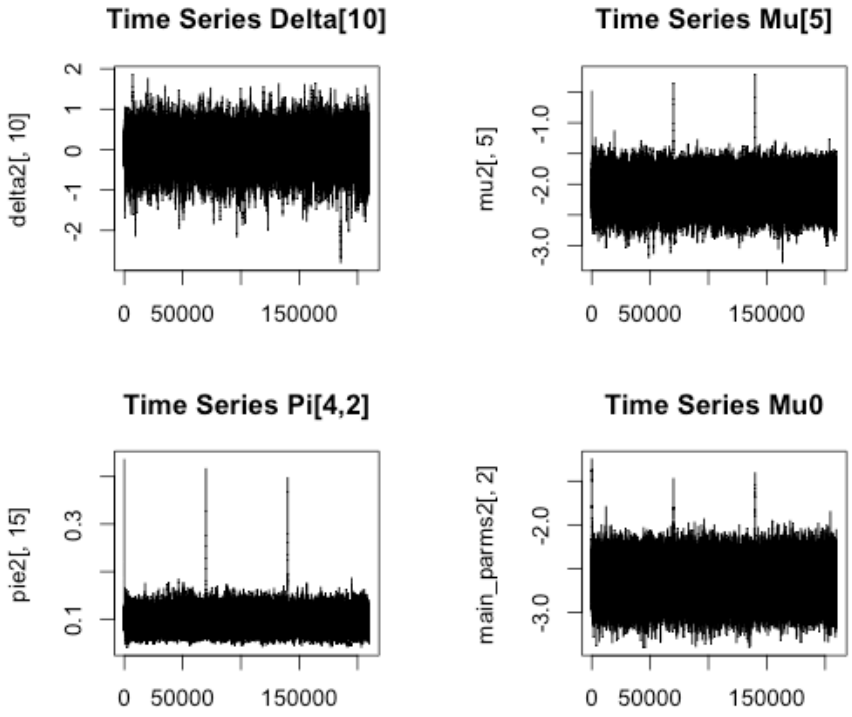

Figure 2. Representative Time Series Plots (70,000 iterations)

	Mean	SD	95% CI Low	95% CI High	Proportion Negative	Proportion Zero	Proportion Positive
δ_0	0.09	0.17	-0.23	0.44	0.30	0.00	0.70
μ_0	-2.64	0.16	-2.96	-2.33	1.00	0.00	0.00
τ^{-2}	0.09	0.15	0.00	0.49	0.00	0.00	1.00
σ^{-2}	0.29	0.18	0.10	0.75	0.00	0.00	1.00
δ_i mean	0.09	0.15	-0.20	0.38	0.28	0.00	0.72
μ_i mean	-2.61	0.08	-2.77	-2.46	1.00	0.00	0.00
CABG mean	-2.66	0.12	-2.90	-2.42	1.00	0.00	0.00
PCI mean	-2.57	0.10	-2.76	-2.38	1.00	0.00	0.00

Table 1. Summary statistics for main parameters of interest

	Mean	SD	95% CI Low	95% CI High
Mean $\mu_0 = -4.75$	0.11	0.18	-0.23	0.47
Mean $\mu_0 = -2.753$	0.09	0.17	-0.24	0.43
Mean $\mu_0 = -1.75$	0.07	0.16	-0.24	0.40
Var $\mu_0 = 1$	0.09	0.17	-0.23	0.43
Var $\mu_0 = 9.028$	0.09	0.17	-0.24	0.43
Var $\mu_0 = 20$	0.09	0.17	-0.24	0.43
mean $\delta_0 = -2.504$	-0.09	0.19	-0.49	0.24
mean $\delta_0 = 0.358$	0.09	0.17	-0.24	0.43
mean $\delta_0 = 2.504$	0.25	0.21	-0.10	0.73
var $\delta_0 = 0.1$	0.07	0.17	-0.26	0.42
var $\delta_0 = 2.149$	0.09	0.17	-0.24	0.43
var $\delta_0 = 10$	0.14	0.15	-0.16	0.45
σ^{-2} a = 0.01	0.09	0.17	-0.23	0.43
σ^{-2} a = 0.191	0.09	0.17	-0.24	0.43
σ^{-2} a = 3	0.10	0.17	-0.23	0.43
σ^{-2} b = 0.01	0.09	0.17	-0.23	0.43
σ^{-2} b = 0.219	0.09	0.17	-0.24	0.43
σ^{-2} b = 3	0.09	0.17	-0.23	0.43
τ^{-2} a = 0.0001	0.09	0.17	-0.23	0.43
τ^{-2} a = 0.0025	0.09	0.17	-0.24	0.43
τ^{-2} a = 0.1	0.09	0.16	-0.22	0.42
τ^{-2} b = 0.0001	0.08	0.15	-0.21	0.39
τ^{-2} b = 0.005	0.09	0.17	-0.24	0.43
τ^{-2} b = 0.1	0.11	0.21	-0.28	0.53

Table 2. Summary statistics for the posterior distribution of δ_0 in the sensitivity analysis

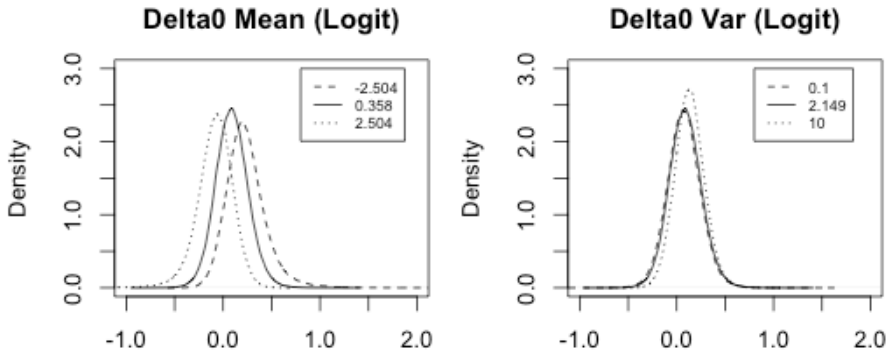

Figure 3. Variations in distribution of δ_0 for different prior specification of the mean and variance

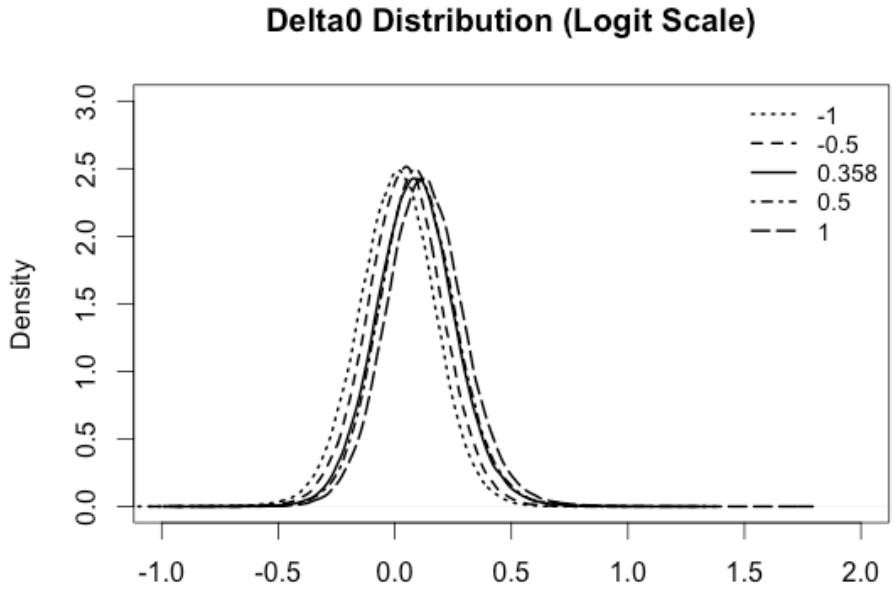

Figure 4. Variations in distribution of δ_0 for different prior specification of the mean of δ_0

Appendix 3: JAGS Code for Original Model

```
model
{

   for (i in 1:N){

      for (j in 1:2){
          y[i,j] ~ dbinom(pie[i,j],n[i,j])
       }

       pie[i,1] <- ilogit(mu[i]-delta[i]/2)
       pie[i,2] <- ilogit(mu[i]+delta[i]/2)
       mu[i] ~ dnorm(mu0,sigma2)
       delta[i] ~ dnorm(delta0,tau2)
       x1[i] <- mu[i] - delta[i]/2 # individual group mean
       x2[i] <- mu[i] + delta[i]/2
      }

   mu0 ~ dnorm(mu.a,mu.b)
   sigma2 ~ dgamma(sigma2.a,sigma2.b)
   delta0 ~ dnorm(delta.a,delta.b)
   tau2 ~ dgamma(tau2.a,tau2.b)

   var_mu <- 1/sigma2
   var_delta <- 1/tau2
   x1_mean <- mean(x1)
   x2_mean <- mean(x2)
}

data1 <- list(mu.a = -2.752, mu.b = 9.028, sigma2.a = 0.1914062, sigma2.b = 0.21875, delta.a =
0.358, delta.b = 2.149, tau2.a = .0025, tau2.b = .005, N = 11,
n=cbind(c(71,52,107,49,86,49,357,516,186,36,70),c(174,53,142,238,103,241,348,512,218,41,80)),
y=cbind(c(4,1,3,2,12,3,15,19,18,5,11),c(10,4,9,25,11,20,15,17,25,4,5)))

params1 <-
c("mu","pie","delta","var_mu","var_delta","mu0","delta0","x1_mean","x2_mean",tau2,sigma2)

inits1 <- rep((list(list(mu=rep(0,N), delta=rep(0,N)))),3)

model2 <- jags (data1, inits1, params1, "DAP1.txt", n.chains=3, n.iter=70000, n.burnin=0, n.thin=1,
DIC=FALSE)
```