Is birth weight on the causal pathway to infant mortality: Maternal age?

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Abstract

It is a common theoretical view that (low) birth weight is a correlate of adverse birth outcomes but is not on the, causal pathway to infant mortality. On the other hand, the United States' national policy for reducing infant mortality is to reduce low birth weight. If the theoretical view is correct, lowering the low birth weight rate may have little effect on infant mortality. The development of covariate density defined mixtures of logistic regression, a non-linear structural equation like model, allows a formal test of the casual relationship between birth weight and infant mortality. This paper determines if maternal age influences birth outcomes directly, and/or indirectly through birth weight in four populations. The results indicate that a) the majority of maternal age effects on infant mortality are direct and do not operate through birth weight, b) maternal age does influence the birth weight distribution, but c) the effect of maternal age on the birth weight distribution has little or no effect on infant mortality, because the birth weight specific mortality curve shifts to compensate for changes in the birth weight distribution. This is consistent with the theoretical view that birth weight may not be causal.

Introduction

Several theoritions have argued that birth weight is not on the causal pathway to infant mortality. For example, Mosley and Chen (Mosely and Chen 1984) in their influential paper concerning the proximate determinants of childhood mortality argued that birth weight might be an indicator of adverse conditions, but was not a cause *per se*. Wilcox (Wilcox and Russell 1990) and Wise (Wise 2003) also question whether birth

weight is on the causal pathway to infant mortality or simply correlated with infant mortality. Wilcox (Wilcox and Russell 1990; Wilcox and Russell 1983a, 1983b) and http://eb.niehs.gov/bwt/subcwhy.htm in particular has provided a detailed theory of "causality" with respect to birth weight and infant mortality and argues that for fetus's undergoing "normal" development, birth weight is not causally related to infant mortality. These views differ dramatically from current national policy, which is to reduce infant mortality by reducing the low birth weight rate as stated in Healthy People 2010. Underlying this is a large literature demonstrating a high correlation between birth weight and infant mortality. However, if birth weight is not on the "causal" pathway to infant mortality prevention strategies that target birth weight might not have the intended effect of lowering infant mortality.

Wilcox's (Wilcox and Russell 1990; Wilcox and Russell 1983a, 1983b) and http://eb.niehs.gov/bwt/subcwhy.htm definition of causality with respect to birth weight and infant mortality is sufficiently detailed to be explicitly testable. The basis of his argument is that while the birth weight distribution does shift in response to external covariates, the birth weight specific mortality curve also shifts horizontally by a similar amount in the same direction, so that there is no indirect effect due to the covariate on infant mortality. In addition he argues that the same external covariates may have direct effects on infant mortality by increasing or decreasing the birth weight specific mortality curve vertically at all birth weights. A graphical depiction of this argument is presented in Figure 1. Finally Wilcox argues that this applies only to "normal" (versus "residual") births identified by his semi-parametric mixture model of birth weight(Wilcox and Russell 1983b). Essentially, this mixture model consists of a Gaussian distribution fitted to the central part of the birth weight distribution with "residual" distributions accounting for the heavy lower (Wilcox and Russell 1983b) and upper (Umbach and Wilcox 1996) tails of the birth weight distribution. Thus the "residual" distribution accounts for many, but not necessarily all, low birth weight and macrosomic births, who are considered to be undergoing "compromised" fetal development. For example, Wilcox has argued graphically that the birth weight

distribution shifts to the left with increasing altitude (Figure 1a) but that the birth weight specific infant mortality shifts along with it so that there is no resultant change in infant mortality. The same phenomenon occurs comparing non-smoking with smoking mothers accept that the birth weight specific infant mortality curve also increases at every birth weight as a direct effect of smoking. A direct effect without a shift in the birth weight distribution is shown in Figure 1b. On the other hand, an indirect effect would occur if the shift in the birth weight specific infant mortality curve did not correspond precisely with the shift in the birth weight distribution. However, these graphical arguments have not been rigorously tested, primarily because there is no statistical technique that can control for both horizontal and vertical shifts in infant mortality and simultaneously account for "normal" versus "residual" births.

The primary aim of this paper is to present a statistical method for rigorously testing Wilcox's argument. In particular, we propose a model that statistically distinguishes horizontal and vertical shifts in the birth weight specific infant mortality curve separately for both "normal" and "compromised" births and can test the hypothesis that the shifts in birth weight and birth weight specific mortality curve are identical. We will examine the impact of maternal age on infant mortality, stratified by sex, parity and African versus European American ancestry. As such, the results also represent a statistical examination of the "weathering" hypothesis (Geronimus 1992; Geronimus and Bound 1990).

Data and Methods:

The data for this analysis consists of all African and European American singleton live births in New York State, 1985-88. Births with missing sex, parity and ethnic designations, maternal ages, and birth weights are omitted from the analysis. Third and higher order parity births are also omitted to reduce heterogeneity in the multiparous strata, and since only a small proportion of women have more than three births. Analyses are carried out stratified by ethnicity, sex, and parity (primiparous

(parity =0) versus multiparous (parity = 1, 2). The characteristics of the samples are presented in Table 1.

Table 1 about here

Gage et al. (Gage 2002);(Gage et al. 2004) defined CDDmlr (covariate density defined mixture of logistic regressions) in their application to birth outcomes as the joint density of birth weight (x) and the occurrence of death (y):

$$f((x,y);\beta,\theta) = f(y \mid x;\beta,\theta) f(x;\theta) \qquad \text{Eq. 1}$$

that is, the product of the conditional mortality submodel $f(y \mid x;\beta,\theta)$ and the birth weight density submodel $f(x;\theta)$.

For the mixture of two Gaussian subpopulation case,

$$\begin{aligned} & f(x;\theta = (\pi_p, \theta_p, \theta_s)) \\ & = \pi_p \times N_0(x;\theta_p = (\mu_p, \sigma_p^2)) + (1-\pi_p) \times N_0(x;\theta_s = (\mu_s, \sigma_s^2)) \end{aligned} \qquad \text{Eq. 2}$$

with π_p defined as the proportion of births belonging to the subpopulation labeled p, (the mixing proportions). For i = p and s, $N_0(x;\theta_i)$ represents the Gaussian density, truncated at 0, with mean μ_i and variance σ_i^2.

The probability of death conditioned on variable x is given by:

$$\begin{aligned} & f(y=1 \mid x;\beta = (\beta_p, \beta_s), \theta) \\ & \quad = q(w;\theta) \times P(x;\beta_p) + (1 - q(w;\theta)) \times P(x;\beta_s) \end{aligned} \qquad \text{Eq. 3}$$

where $P(x;\beta_i)$ is the probability of death for an infant of birth weight x in the i subpopulation, given by a quadratic logistic form:

$$P(x;\beta_i = (a_i, b_i, c_i)) = \frac{e^{a_i + b_i x + c_i x^2}}{1 + e^{a_i + b_i x + c_i x^2}} \qquad \text{Eq. 4}$$

and $q(x;\theta)$ is the conditional probability of that infant belonging to subpopulation p. The mixture submodel (Eq. 2) determines that:

$$q(x;\theta) = \frac{\pi_p \times N_0(x;\theta_p)}{\pi_p \times N_0(x;\theta_p) + (1-\pi_p) \times N_0(x;\theta_s)} \qquad \text{Eq. 5}$$

The mixing proportion is specified as $\eta = logit(\pi_p)$, which transforms the 0.0 and 1.0 bounds on π_p to minus and plus infinity respectively. Birth weight specific infant mortality is generally considered to be U-shaped, hence the quadratic assumption in Eq. 4.

Here we extend the original model in two different ways. The first extension includes the effects of an exogenous covariate z. It is incorporated into the mixture submodel by defining the mixture submodel parameters as functions of z, i.e. assuming nonlinear (2nd degree polynomial) effects for the i subpopulation:

$$logit(\pi_p(z)) = \eta(z) = \alpha_0 + \alpha_1 z + \alpha_2 z^2 \quad \text{Eq. 6}$$

$$\mu_i(z) = \gamma_{i,0} + \gamma_{i,1} z + \gamma_{i,2} z^2 \quad \text{Eq. 7}$$

$$\sigma_i(z) = \lambda_{i,0} + \lambda_{i,1} z + \lambda_{i,2} z^2 \quad \text{Eq. 8}$$

The covariate z is also employed in the mortality submodel by adding it to the logistic probabilities (Eq. 4), that is:

$$P(x,z;\beta_i = (a_i, b_{ix}, c_{ix}, b_{iz}, c_{iz}, d_i)) = \frac{e^{a_i + b_{ix}x + c_{ix}x^2 + b_{iz}z + c_{iz}z^2 + d_i xz}}{1 + e^{a_i + b_{ix}x + c_{ix}x^2 + b_{iz}z + c_{iz}z^2 + d_i xz}} \quad \text{Eq. 9}$$

Second, birth weight (x) is standardized based on the mean and variance of the respective subpopulation and then the resulting Z-score (x^*) is used in Eq. 8 for the corresponding subpopulation, that is:

$$P(x,z;\beta_i) = P(x_i^*, z; \theta_i, \beta_i^* = (a_i^*, b_{ix}^*, c_{ix}^*, b_{iz}^*, c_{iz}^*, d_i^*))$$

$$= \frac{e^{a_i^* + b_{ix}^*(x^*) + c_{ix}^*(x^*)^2 + b_{iz}^* z + c_{iz}^* z^2 + d_i^*(x^*)z}}{1 + e^{a_i^* + b_{ix}^*(x^*) + c_{ix}^*(x^*)^2 + b_{iz}^* z + c_{iz}^* z^2 + d_i^*(x^*)z}} \quad \text{Eq. 10}$$

Overall, there are 27 parameters, 15 for the mixture submodel and 12 for the mortality submodel. Their definitions are summarized in Table 2.

Table 2 about here

Defining the mixture submodel parameters as functions of z (Eq. 6-8) represents the effects of covariate z on the birth weight distribution and the potential indirect effects of z on infant mortality through birth weight. Adding covariates z to the mortality submodel (Eq. 9-10) represents the direct effects of that covariate (i.e. vertical

shifts) on infant mortality. By redefining birth weight as the Z-score of birth weight in the mortality submodel (Eq. 9), horizontal shifts (of a magnitude equal to the shift in the birth weight distribution) are automatically accounted for and all other effects of birth weight on infant mortality are encompassed in the interaction of x (birth weight) and z (maternal age). Thus a significant interaction term indicates the presence of an indirect effect of z through the birth weight distribution on infant mortality, i.e., that birth weight is on the causal pathway to infant mortality, at least as defined by Wilcox (Wilcox and Russell 1990; Wilcox and Russell 1983a, 1983b) and http://eb.niehs.gov/bwt/subcwhy.htm.

Results

Maternal age has a strong effect on the mean birth weight of the primary subpopulation and the variance of the secondary subpopulation (Table 3). In particular both linear and second-degree parameters of the polynomial of maternal age on primary subpopulation mean birth weight are significant at all parities in all populations examined. Multiparous births are significantly larger than primiparous births particularly at maternal ages greater than 25 years (Figure 2). On the other hand, maternal age effects on the secondary subpopulation mean birth weight are significant in only one of sixteen parameters tested (Table 3). There are no significant differences in secondary mean birth weight by parity at any maternal age (Figure 2). Maternal age influences the variance in birth weight of the secondary subpopulation in all eight populations examined (15 of 16 parameters), but only effects the variance in birth weight of the primary subpopulation in two of the eight populations examined. Thus the most consistent effects concern the mean of birth weight in the primary subpopulation, and the variance in birth weight in the secondary subpopulation. In general, mean primary birth weight is n-shaped with maximum mean birth weight between 25 and 35 years of age, while the variance of the secondary distribution increases with maternal age (Figure 2).

Figure 2

Table 3

Maternal age has significant effects on the mixing proportion of all four European American cohorts, but none of the African American birth cohorts (Table 3). Among European American births the proportion of secondary births is significantly U-shaped with maternal age (Figure 2c). Multiparous European American birth cohorts have a significantly lower proportion of secondary births, particularly during the period 25 to 35 years of age. These differences with maternal age are not significant for African Americans, although the trends are similar. African Americans have generally higher proportions of secondary births particularly during the peak childbearing years.

The direct effects of maternal age on infant mortality occur in four of the eight primary subpopulations, and three of the eight secondary subpopulations (Table 3). In general, infant mortality tends to decline with maternal age to a minimum before increasing again, although this pattern is not always significant (Figure 3 and Table 3).

Figure 3 about here.

Finally, maternal age has little or no statistically detectable indirect effect on infant mortality. The birth weight by maternal age interaction terms are all insignificant with the exception of multiparous European American male secondary births (Table 3). Thus there are significant shifts in birth weight distributions, primarily though the primary subpopulation mean, but in all cases, birth weight specific infant mortality shifts along with the shifts in the birth weight distribution, as Wilcox argues, so that there is no change in overall mortality due to the shifts in the birth weight distribution, particularly in the primary subpopulation. Among multiparous European American male secondary births, the interaction term is significant, but in this case there are no significant maternal age effects on the mean of the secondary subpopulation. Thus there is a shift in the birth weight specific mortality curve relative to mean birth weight, but no shift in mean birth weight.

Characteristic patterns of birth weight specific infant mortality at several maternal ages are presented in Figure 4. Of particular interest is the "pediatric paradox" with respect to maternal age in Figure 4c. Infants of women in their prime

childbearing years have higher infant mortality at low birth weights, but lower mortality at "normal" birth weights compared to infants of older women and younger women. Whether younger and/or older women display this effect varies by parity and race with the effect being stronger for primiparous births to young women and births to older African American women.

Figure 4 about here

Finally, a decomposition of maternal age effects on mortality based on the full model is presented in Table 4. This includes the impact of "trends" as well as, the statistically significant aspects of the model. Nevertheless, they are in close agreement with the significant aspects of the model. Typically, more than 70% of the impact of maternal age on infant mortality is due to direct effects. The exception is primiparous African American males where the direct effect accounts for only about 34% of the total. Comparison of primiparous versus multiparous results suggests that secondary direct effects might be more important in primiparious births, and primary direct effects might be more important in multiparous births. On the other hand, the indirect effects, that is the impact of maternal age on infant mortality mediated through birth weight, are small. The primary indirect effects are all very small, less then 2%. The trends in the secondary indirect effects are usually less then 30%, but reach, as high as, 64% in the case of African American primiparous males. There is some suggestion that secondary indirect effects may be larger in primiparous then multiparous births. However, with the exception of multiparous European American males, none of the indirect effects are statistically significant. Interestingly, there is little effect of the mixing proportion on total mortality, generally less then 0.5%. despite significant effects of maternal age on the mixing proportion and significant differences in mortality between primary and secondary births. The various effects of the mixing proportion appear to cancel out at the level of total infant mortality.

Table 4 about here

Discussion

The primary aim of this paper is to present a statistical methodology capable of testing Wilcox's definition of causality in the context of infant mortality and present a preliminary application using maternal age. One possible limitation of our approach is that the parametric mixture model used here is not mathematically identical to Wilcox's semi-parametric model. However, like Wilcox, Fryer et al, (Fryer, Hunt and Simons 1984) and Gage and others (Gage and Therriault 1998) have argued that the primary subpopulation represents births undergoing "normal" fetal development, while the secondary subpopulation represents births "compromised" during fetal development. In both parametric and semi-parametric models, this conclusion is based simply on the fact that the secondary (residual) subpopulation accounts for the majority of births who have traditionally been considered "compromised" on the basis of birth weight, i.e. low birth weight and macrosomic births. On the other hand, Wilcox's models, because they depend upon binned birth weight data (as opposed to individual data) are not easily generalizable to include mortality submodels. Thus despite minor differences, the primary subpopulation, as presented above, is a reasonable and possibly better operational definition of Wilcox's concept of "normal" births. Thus the model is capable of testing Wilcox's definition of causality.

Based on Wilcox's definition of "causal" and our preliminary application to maternal age, it is clear that birth weight is not on the causal pathway to infant mortality. Maternal age does significantly influence the birth weight distribution among "normal" births, but these changes are compensated for by shifts in birth weight specific infant mortality so that "normal" infant mortality is unaffected. Since the null hypothesis of the test is complete compensation, which is easily falsified, this is a strong test of Wilcox's hypothesis.

Wilcox did not include "compromised" births in his discussion of birth weight and causation. The preliminary results presented above, however, suggest that there are few indirect effects of maternal age on infant mortality among "compromised" births, as well as "normal" births. European American male secondary births displayed the only significant result out of 16 total tests. It may be that this is simply a Type 1

error due to multiple tests. Additional analysis will be necessary to understand the true significance of this result, although the maternal age effect reported above is very small. Regardless of whether this is a spurious result, however, it does raise the theoretical possibility of types of causality, which Wilcox has not considered. Here, the birth weight distribution remains fixed but birth weight specific infant mortality shifts with maternal age.

Further Wilcox's theory applies to "normal" births, however, dividing births into "normal" and "compromised" categories implies that there is another way that maternal age could indirectly effect infant mortality, that is, maternal age could influence the proportion of "normal" to "compromised" births. Since these subpopulations of births differ significantly with respect to their birth weight distributions, and birth weight specific infant mortality (Gage 2002; Gage et al. 2004) maternal age could operate "indirectly" on infant mortality through this mechanism. The results above indicate that maternal age effects on the mixing component are significant for European Americans, although not for African Americans (Table 3). The lack of significant results could be due to low statistical power in the case of the African American samples, which are relatively small (Table 1). Analyses with larger samples will be necessary to determine if maternal age influences the proportion of "normal" to "compromised" births differently in African versus European Americans. On the other hand, the decomposition of the preliminary results presented above suggest that in all cases the indirect effects of maternal age operating through the mixing proportion tend to cancel out and are very small (Table 4).

Finally, while we have failed to falsify Wilcox's argument that birth weight is not "causal" with respect to infant mortality, this does not mean that this hypothesis is correct. All that is necessary to falsify the argument is that some covariate have an indirect effect among "normal" births and we have only examined one covariate, maternal age. Other relevant covariates will need to be explored. We expect that some might influence mortality indirectly through birth weight while others like maternal age do not.

These preliminary results fail to support Geronimus' weathering hypothesis. This theory states that maternal stores decline with maternal age and parity increasing the low birth weight rate and resulting in higher infant mortality. The process is hypothesized to occur faster among African American women compared to European American women, thus in part explaining racial disparities in infant mortality(Geronimus 1992; Geronimus and Bound 1990). The theory assumes that birth weight is on the "causal" pathway to infant mortality. However, we do not find strong statistical evidence that birth weight is on the "causal" pathway to infant mortality, even if we consider effects on "normal" and "compromised" births and not just the effects on the "normal" subpopulation as argued by Wilcox. Failure to support Geronimus' hypothesis could result from lack of power due to the smaller African American sample. Conclusive evidence, and rigorous comparisons of African and European American birth cohorts, will need to await the analysis of larger African American samples. However, the decomposition of maternal age effects (Table 4), which is based on the full model and not just the significant trends, indicates that the direct effects of maternal age are larger then all but one of the indirect or mixing proportion effects. Thus our analysis provides little support for the weathering hypothesis *per se*.

The US national policy, which is to lower the low birth weight rate in an effort to lower infant mortality, makes the most sense if birth weight is on the "causal" pathway to infant mortality. For example, a national policy might be devised, which could influence the distribution of maternal ages in order to improve birth weight with the intention of improving infant mortality. The results presented above suggest that such a policy would influence birth weight, particularly among "normal" births, but would have little or no effect on infant mortality. Choosing to influence the birth weight distribution by intervening with respect to maternal age on the basis of the proportion of "normal" versus "compromised" births will influence infant mortality slightly, particularly among European American populations, but may not impact infant mortality among African American birth cohorts. Finally the direct effects of maternal

age on infant mortality account for the vast majority of total maternal age effects. Clearly it would be more effective to devise interventions based on the direct effects of maternal age on infant mortality.

Conclusions

Covariate Density Defined mixtures of logistic regression is an important methodology for examining "causal" hypotheses with respect to birth outcomes. It can test Wilcox's hypothesis, as well as, several additional "causal" hypotheses not discussed by Wilcox. Preliminary examination of the causal impact of maternal age on infant mortality indicates statistically significant direct effects, but few significant indirect effects operating through birth weight. Indirect effects can and do operate through the proportion of "normal" to "compromised" births and hence birth weight, at least in European Americans. However, these do not account for a large proportion of the total maternal age effect on infant mortality. The majority of the impact of maternal age on infant mortality occurs as direct effects and does not operate through birth weight. The most effective interventions should minimize these direct effects regardless of there effect on birth weight.

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Table 1 Descriptive statistics for the sample populations

Birth Cohort	Af. Am. F		Af. Am. M		Eu. Am. F		Eu. Am. M	
Parity	0	1 & 2	0	1 & 2	0	1 & 2	0	1 & 2
# Births	22981	24801	24028	25931	111203	124120	117657	130811
# Deaths	294	263	366	336	547	594	730	776
CDR	12.79	10.60	15.23	12.96	4.92	4.79	6.20	5.93
Birth weight (grams) distribution								
Min	195	140	120	116	78	100	170	113
5%	2041	2155	2146	2250	2500	2608	2552	2693
25%	2807	2835	2920	2977	3033	3118	3147	3232
50%	3120	3175	3260	3317	3345	3402	3459	3550
75%	3450	3515	3572	3640	3657	3720	3799	3884
95%	3941	4026	4082	4167	4139	4206	4309	4394
max	6522	6120	6350	6719	7999	7919	7709	7940
Maternal age distribution								
Min	12	14	12	14	11	15	10	15
5%	17	19	17	19	19	21	19	21
25%	20	24	20	23	23	25	23	26
50%	24	27	24	27	26	29	26	29
75%	28	31	28	31	30	32	30	32
95%	34	37	34	37	35	37	35	36
max	45	47	48	48	47	55	55	58

Af. = African, Eu. = European, Am. = American, F. = Females, M. = Males

CDR = Crude death rate (deaths per 1000 births)

Table 2 Definitions of the model parameters

Symbol	Definition
Mixture Submodel parameters for the i subpopulation (i = s and p)	
--- functions of covariate z (maternal age)	
$\pi_p(z)$	Mixing proportion (% primary subpopulation)
α_0	Constant in the nonlinar function for $\pi_p(z)$
α_1	Linear term in the nonlinar function for $\pi_p(z)$
α_2	Square term in the nonlinar function for $\pi_p(z)$
$\mu_i(z)$	Mean birth weight
$\gamma_{i,0}$	Constant in the nonlinar function for $\mu_i(z)$
$\gamma_{i,1}$	Linear term in the nonlinar function for $\mu_i(z)$
$\gamma_{i,2}$	Square term in the nonlinar function for $\mu_i(z)$
$\sigma_i(z)$	Standard deviation of birth weight
$\lambda_{i,0}$	Constant in the nonlinar function for $\sigma_i(z)$
$\lambda_{i,1}$	Linear term in the nonlinar function for $\sigma_i(z)$
$\lambda_{i,2}$	Square term in the nonlinar function for $\sigma_i(z)$
Mortality submodel parameters for the i subpopulation (i = s and p)	
--- coefficients of a second degree bivariate polynomial	
a^*_{ix}	Constant
b^*_{ix}	Linear term for standardized birth weight (x^*_i)
c^*_{ix}	Square term for standardized birth weight (x^*_i)
b^*_{iz}	Linear term for covariate z (maternal age)
c^*_{iz}	Square term for covariate z (maternal age)
d^*_i	Interaction term for standardized birth weight (x^*_i) and covariate z (maternal age)

Table 3 Significance of the parameters based on bias-adjusted bootstraps

Birth Cohort	Af. Am. F		Af. Am. M		Eu. Am. F		Eu. Am. M	
Parity	0	1 & 2	0	1 & 2	0	1 & 2	0	1 & 2
α_1	0	0	0	0	2	2	1	2
α_2	0	0	0	0	1	1	1	1
$\gamma_{s,1}$	0	1	0	0	0	0	0	0
$\gamma_{s,2}$	0	0	0	0	0	0	0	0
$\lambda_{s,1}$	2	2	1	2	2	1	1	2
$\lambda_{s,2}$	1	1	0	1	1	1	1	1
$\gamma_{p,1}$	1	1	1	1	1	1	1	1
$\gamma_{p,2}$	1	1	1	1	1	1	1	1
$\lambda_{p,1}$	0	0	0	0	1	0	0	1
$\lambda_{p,2}$	0	0	0	0	1	0	0	1
b^*_{sx}	2	0	2	0	2	2	2	2
c^*_{sx}	1	0	1	0	1	1	1	1
b^*_{sz}	0	0	0	0	1	1	0	0
c^*_{sz}	0	0	0	0	0	1	0	0
d^*_s	0	0	0	0	0	0	0	1
b^*_{px}	1	2	2	1	1	2	1	2
c^*_{px}	1	1	1	1	1	1	1	1
b^*_{pz}	0	1	0	0	0	1	1	1
c^*_{pz}	0	1	0	0	0	0	1	1
d^*_p	0	0	0	0	0	0	0	0

0 not significant

1 significant

2 significant (higher order term is significant)

Table 4 Decomposition (%) of Maternal Age Effect on Total Infant Mortality

Birth Cohort	Af. Am. F		Af. Am. M		Eu. Am. F		Eu. Am. M	
Parity	0	1 & 2	0	1 & 2	0	1 & 2	0	1 & 2
mixing proportion (p_p)	0.0	0.0	0.2	0.0	0.0	0.6	0.2	0.1
primary indirect effect	1.9	0.9	1.8	0.3	1.1	1.5	0.0	1.3
secondary indirect effect	31.3	28.6	64.3	13.2	16.0	21.7	28.3	4.6
primary direct effect	3.3	57.4	21.9	6.6	2.7	60.2	28.1	69.5
secondary direct effect	63.3	13.0	11.9	79.8	80.2	15.8	43.4	24.5
Total	100	100	100	100	100	100	100	100

Figure Captions

Figure 1. Characteristic changes in birth weight and mortality based on Wilcox's theory of the relationship of birth weight and infant mortality. Panel a indicates the expected effect of a covariate that influences mean birth weight, resulting in a similar shift in birth weight specific infant mortality. If the shifts are identical there is no change in mortality and birth weight is not on the "causal" pathway, that is there is no indirect effect of the covariate on mortality. Panel B. indicates a direct effect of a covariate on mortality, identical at all birth weights. Of course, a covariate could influence birth weight and have a direct effect. Whether birth weight is "causal" in this case depends upon the lateral shift in birth weight specific mortality compensates or not, as in Panel a. See Wilcox's website for additional details (http://eb.niehs.gov/bwt/subcwhy.htm).

Figure 2. Characteristic changes in the means, variances, and mixing proportions with maternal age of the primary and secondary birth weight density components by parity. Panel a presents the means, panel b presents the square root of the variances, while panel c presents the mixing proportions. The results are for European American males and are similar to the results for all populations examined except as noted in the text. —— primary primiparous; - · - · - primary multiparous; - - - - secondary primiparous; ····· secondary multiparous. Bold lines represent the model-based estimation and lighter lines represent the bias-adjusted 95% confidence intervals.

Figure 3. Characteristic changes in infant mortality by maternal age and by parity. Panel a, b, and c present total, primary, and secondary infant mortality, respectively. The results are for European American males and are similar to results for all populations examined except as noted in the text. ——

primiparous; - - - - - multiparous. Bold lines represent the model-based estimation and lighter lines represent the bias-adjusted 95% confidence intervals.

Figure 4 Characteristic model estimated birth weight specific infant mortality curves by maternal ages for primiparous European American males. Panel a, b, and c present changes in the primary subpopulation, the secondary subpopulation and the total birth cohort, respectively. —— 15 years; **- - - -** 25 years ; ·····35 years; **- · - · -** 45 years. Panel c shows, the pediatric paradox with maternal age, births to 45 year old mother's have lower mortality at low birth weights but higher mortality at normal birth weights compared to 25 and 35 year old mothers.

Figure 1a

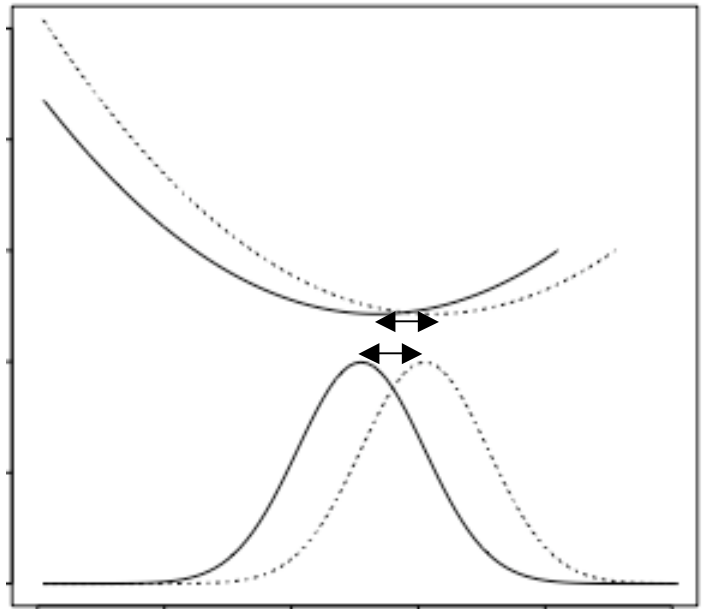

Figure 1b

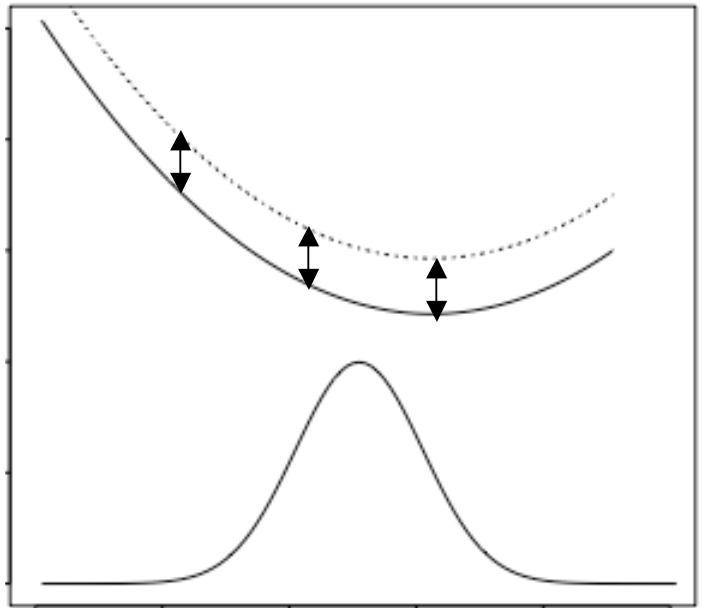

Figure 2a: European American Males Mean Birth Weight

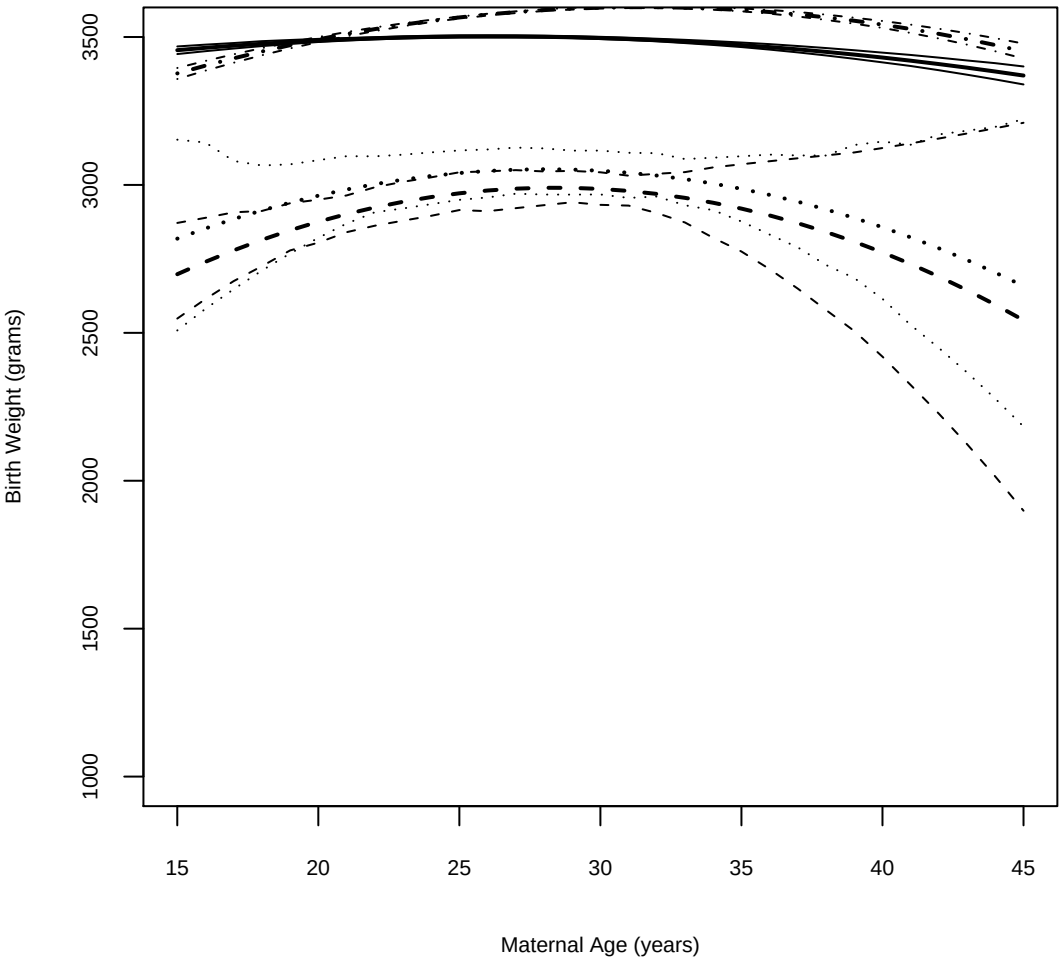

Figure 2b: European American Males Standard Deviation

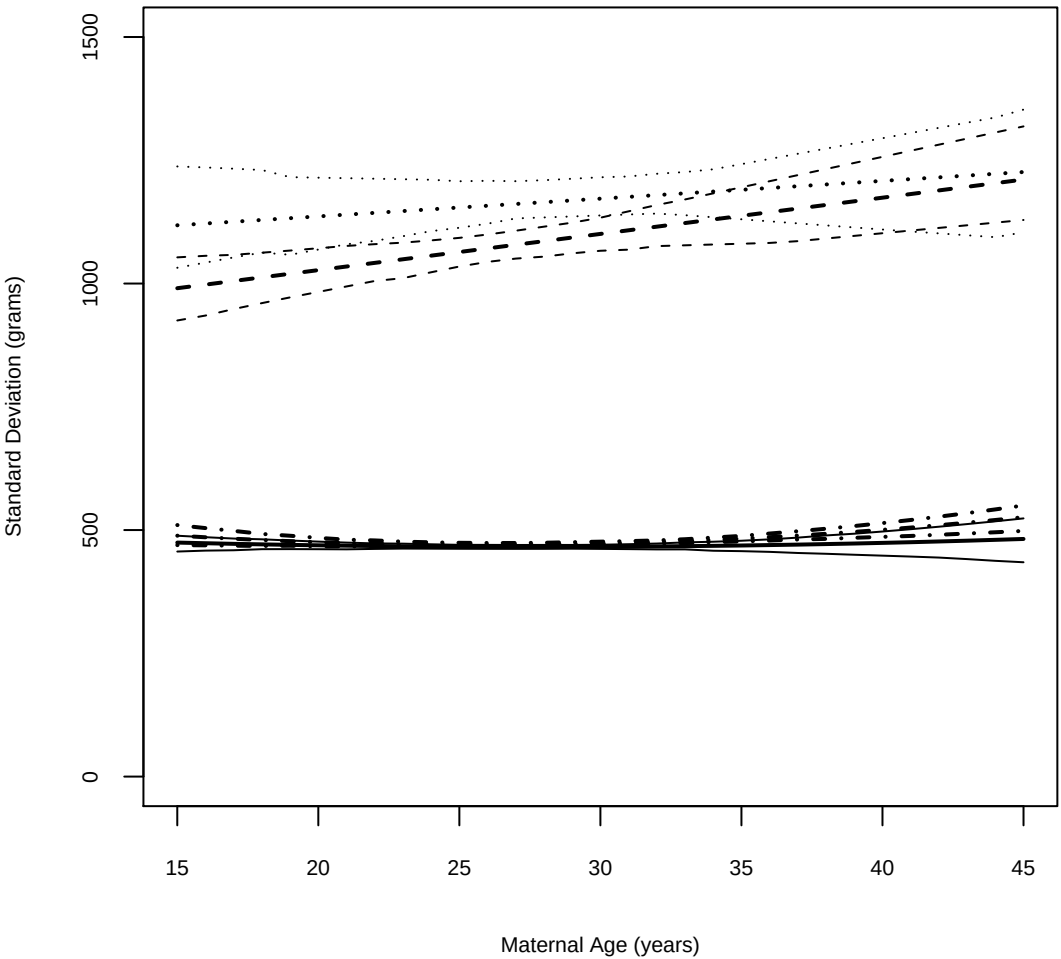

Figure 2c: European American Males Proportion in Secondary Population

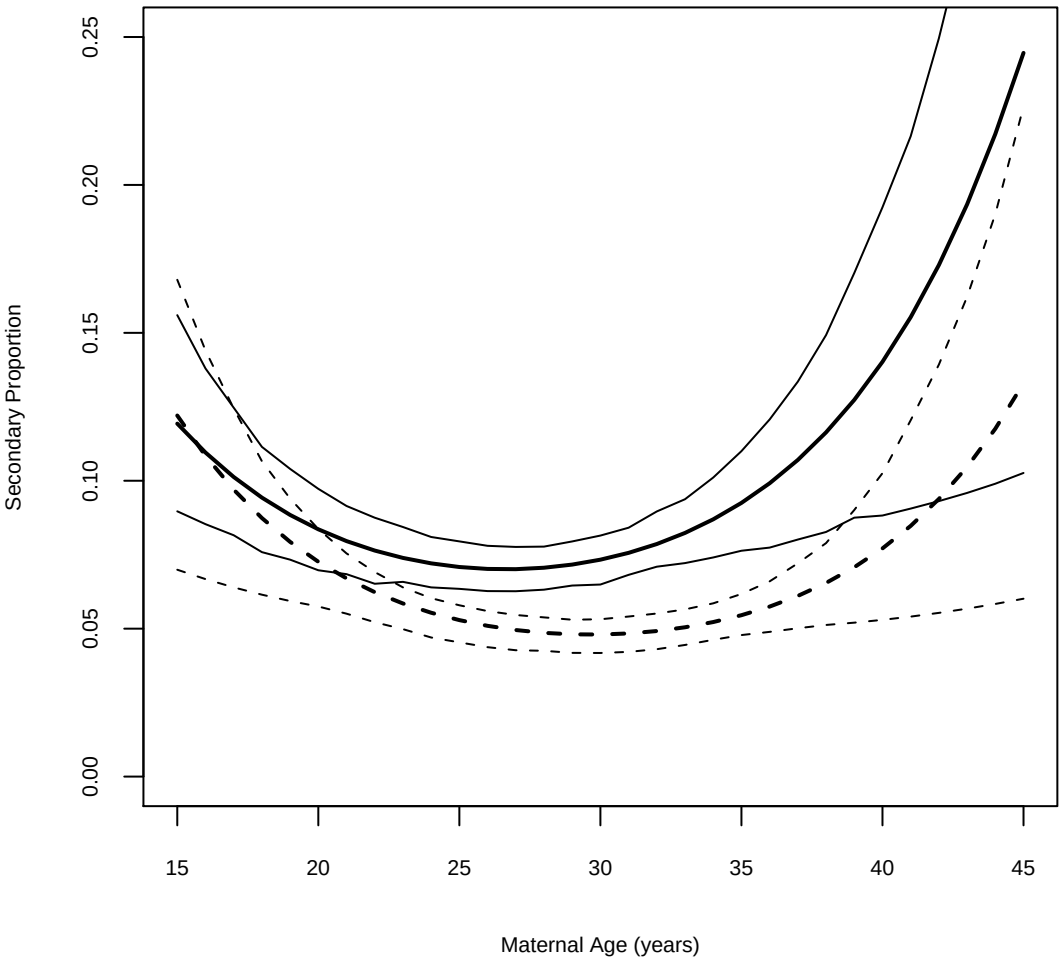

Figure 3a: European American Males Total Mortality

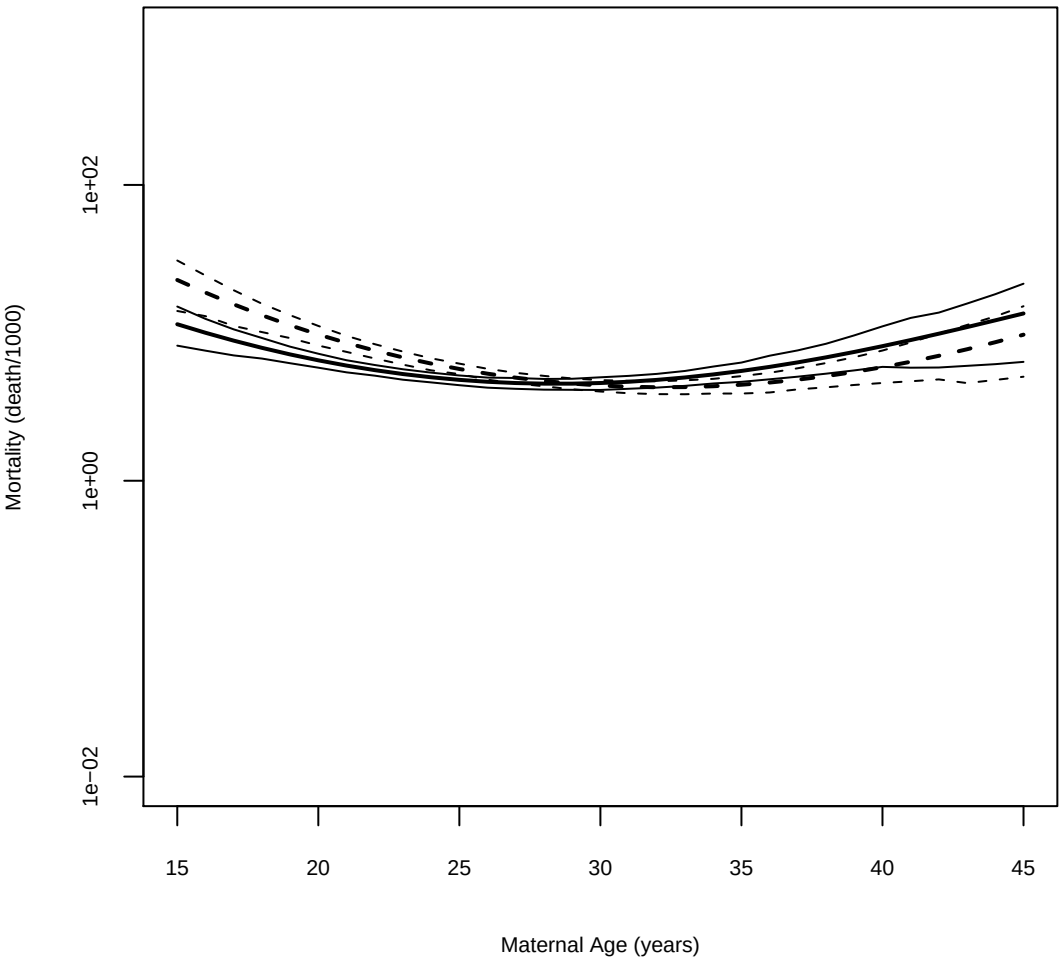

Figure 3b: European American Males Primary Mortality

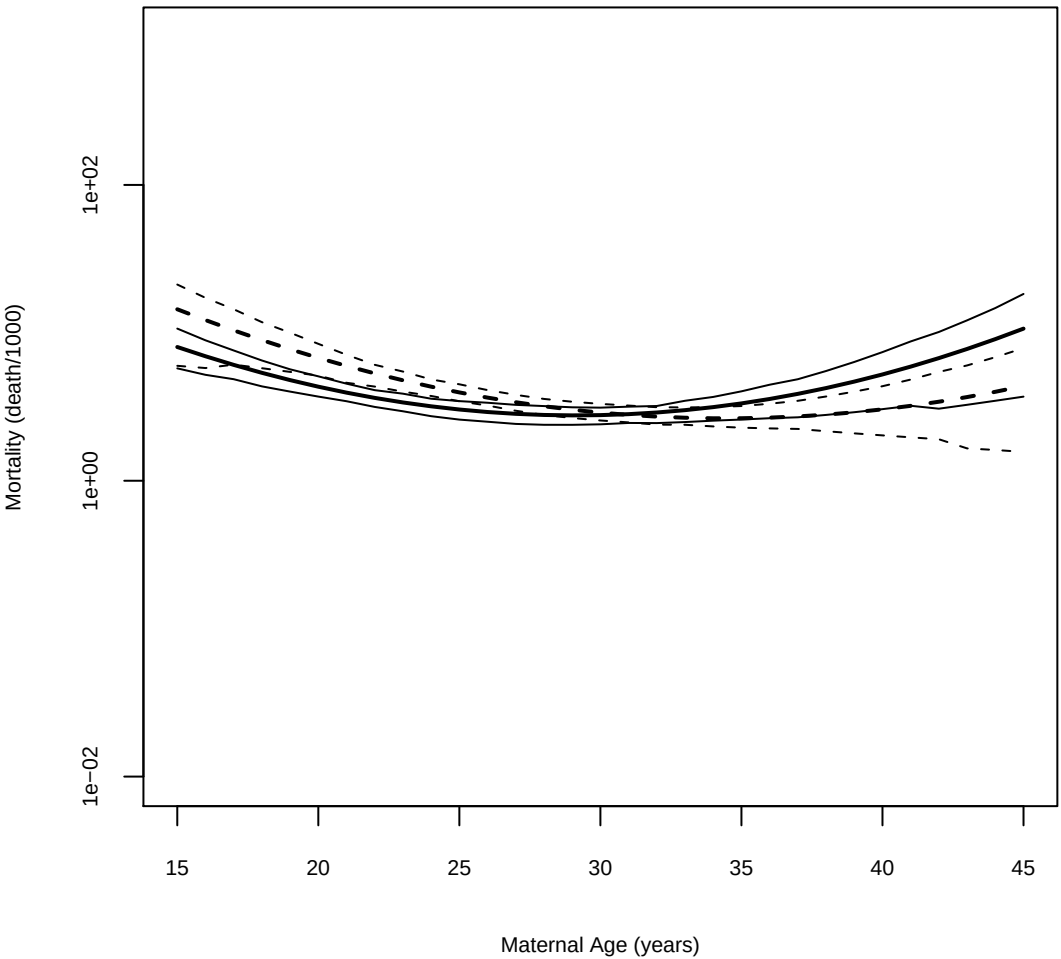

Figure 3c: European American Males Secondary Mortality

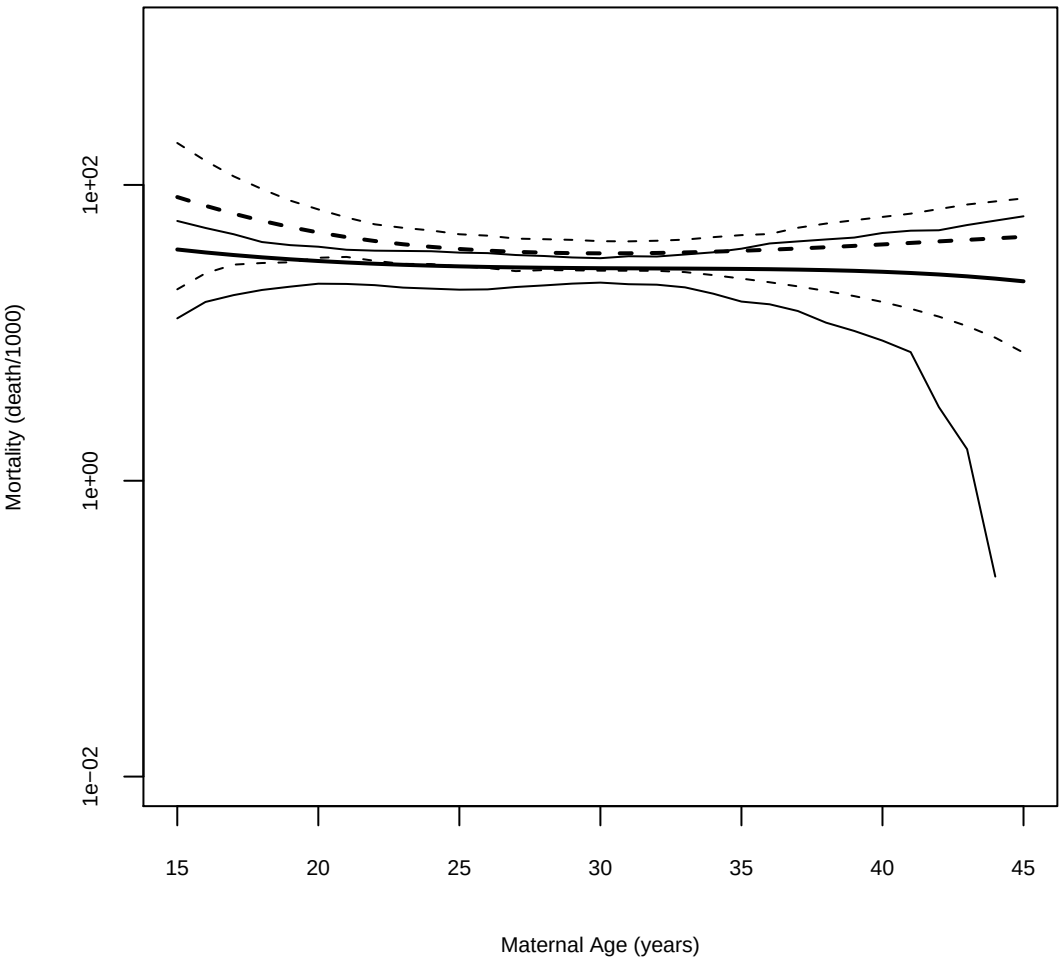

Figure 4a: European American Males Primiparious Primary Mortality

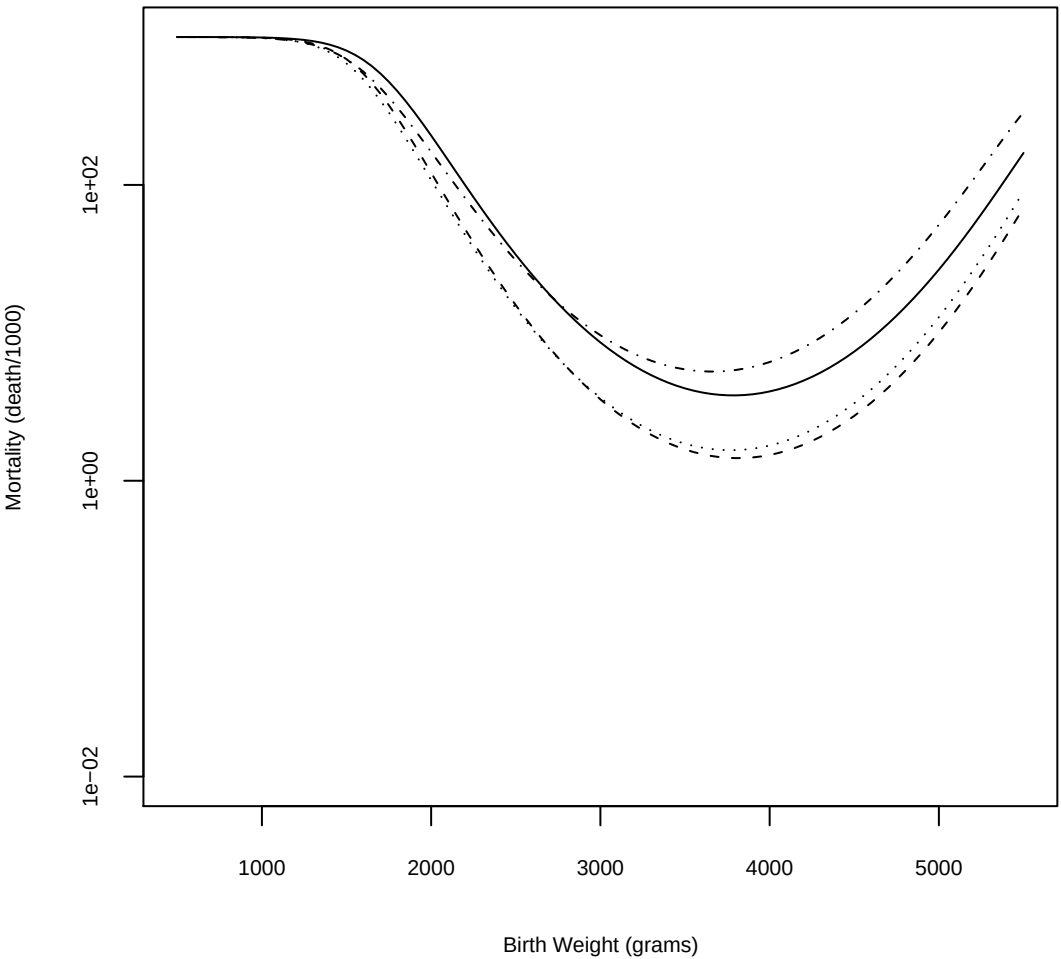

Figure 4b: European American Males Primiparious Secondary Mortality

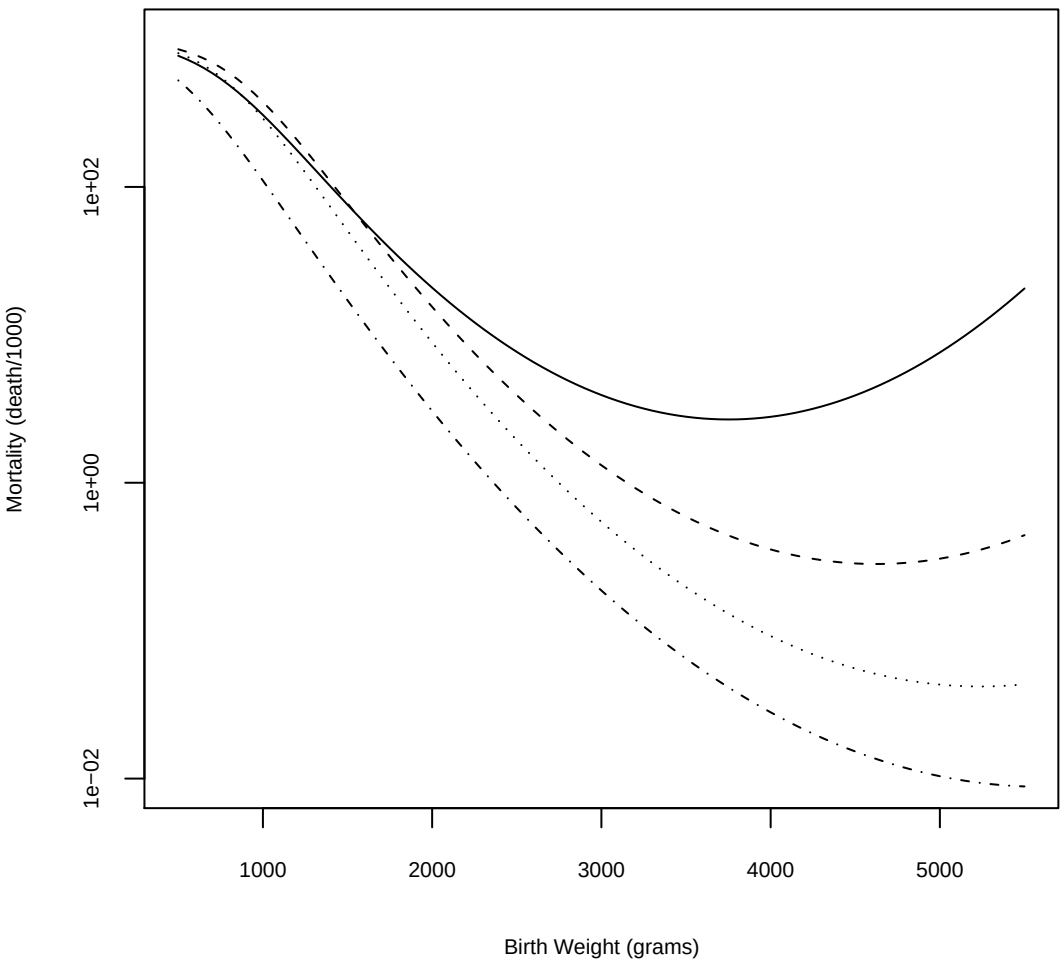

Figure 4c: European American Males Primiparious Total Mortality