Relation between infants’ birth weight and mothers’ mortality: prospective observational study
George Davey Smith, Seeromanie Harding, Michael Rosato

Several studies have shown inverse associations between birth weight and incidence of cardiovascular disease in adulthood, suggesting that development in early life may influence the risk of disease many years later. The existence of intergenerational influences on birth weight, illustrated by correlations between the birth weight of parents and the birth weight of their offspring, suggests that birth weight of offspring should be associated with the risk of mortality from cardiovascular disease among parents. So far only one small study has investigated this possibility. In that study each kilogram decrease in birth weight of the infant was associated with a doubling in the risk of parental cardiovascular mortality associated with offspring. We found a strong inverse relation between infants’ birth weight and mothers’ mortality from all causes and from cardiovascular disease. The relative risk of maternal cardiovascular mortality associated with a 1 kg lower birth weight in offspring was closely similar to that seen in the previous study of this issue (2.00 (1.18 to 3.35)); the corresponding associated risks for the other two major causes of death (153 deaths from cancer (1.33; 1.03 to 1.72) and 38 accidental or violent deaths (1.06; 0.61 to 1.85)) were considerably smaller than those for cardiovascular mortality.

Discussion
The underlying causes of the variation in waiting times observed here are not explained by the audit data, and we do not suggest that there are “across the board” implications for clinical outcome in the waiting times reported. Clearly, these are clinical issues and would vary with specific types of cancer. However, the focus on reducing unnecessary delays in cancer treatment stems from the belief that the earlier disease is detected, the more quickly multidisciplinary care can be instigated and the better the outcome. Irrespective of the specific waiting times reported here, the key contribution of this study is in establishing baseline data which can be used to set targets for improvement and, crucially, to monitor such attempts.

Mortality was analysed by using Cox’s proportional hazards model in relation to birth weight, with adjustment for socioeconomic position and whether the birth occurred inside or outside marriage (with additional adjustment for sole registration or joint registration if outside marriage).

The table shows a substantial association between infants’ birth weight and mothers’ mortality from all causes and from cardiovascular disease. The relative risk of maternal cardiovascular mortality associated with a 1 kg lower birth weight in offspring was closely similar to that seen in the previous study of this issue (2.00 (1.18 to 3.35)); the corresponding associated risks for the other two major causes of death (153 deaths from cancer (1.33; 1.03 to 1.72) and 38 accidental or violent deaths (1.06; 0.61 to 1.85)) were considerably smaller than those for cardiovascular mortality.

Methods and results
In the longitudinal study, information from birth registrations of infants during 1976-97 is linked to data from the census and death registration (1976-97) for study members. Birth weight was collected from 1976 onwards, but during the 1970s the data were not complete. The first recorded birth weight of infants to 44 813 women aged 15-45 years at birth registration was used as the exposure measure. Mean birth weight was 3210 g (SD 566 g). The average birth weight changed little over the study period (4.6 g increase a year, 95% confidence intervals 3.6 g to 5.6 g). The difference between average male birth weight and average female birth weight (99 g) was subtracted from each male birth weight. The average birth weight of infants to mothers was associated with a doubling in the risk of parental cardiovascular disease among parents. So far only one small study has investigated this possibility. In that study each kilogram decrease in birth weight of the infant was associated with a doubling in the risk of parental cardiovascular mortality associated with offspring. We found a strong inverse relation between infants’ birth weight and mothers’ mortality from all causes and from cardiovascular disease. The relative risk of maternal cardiovascular mortality associated with a 1 kg lower birth weight in offspring was closely similar to that seen in the previous study of this issue (2.00 (1.18 to 3.35)); the corresponding associated risks for the other two major causes of death (153 deaths from cancer (1.33; 1.03 to 1.72) and 38 accidental or violent deaths (1.06; 0.61 to 1.85)) were considerably smaller than those for cardiovascular mortality.

Comment
We found a strong inverse relation between infants’ birth weights and mothers’ mortality from cardio-

<table>
<thead>
<tr>
<th>Infants’ birth weight (g)</th>
<th>No of births</th>
<th>Deaths of mothers</th>
</tr>
</thead>
<tbody>
<tr>
<td>From all causes (n=293)</td>
<td>From cardiovascular disease (n=41)</td>
<td></td>
</tr>
<tr>
<td>&lt;2500</td>
<td>3 891</td>
<td>3.06 (2.15 to 4.35)</td>
</tr>
<tr>
<td>2500-3499</td>
<td>27 360</td>
<td>1.27 (0.96 to 1.69)</td>
</tr>
<tr>
<td>≥3500</td>
<td>13 562</td>
<td>1.00</td>
</tr>
<tr>
<td>Per 1000 g</td>
<td>1.63 (1.37 to 1.94)</td>
<td>2.25 (1.48 to 3.41)</td>
</tr>
<tr>
<td>Per 1000 g (adjusted)*</td>
<td>1.61 (1.35 to 1.92)</td>
<td>2.22 (1.46 to 3.38)</td>
</tr>
</tbody>
</table>

*Adjusted for socioeconomic position (housing tenure and car access) at the start of the study in 1971 and marital status (sole or joint registration if unmarried) at birth registration.

We thank Dr Stephen Green for his advice on the development of the guidance notes used by the trusts in completing the survey instrument and the many trust staff who gave their time in the collection of the data.

Contributors: PS coordinated the study and helped design the survey instrument and write the report. FB analysed the data and helped write the report. DK helped initiate the research, interpret the data, and write the report.

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vascular disease. Three basic processes could generate this association. Firstly, poor social circumstances could lead to both lower birth weight and higher mortality risk. Secondly, maternal health, nutritional, and behavioural factors could influence both birth weight and cardiovascular mortality. Thirdly, intergenerational factors—such as genomic and epigenetic processes that lead to a positive correlation between the birth weights of mothers and their offspring—could influence cardiovascular risk.

Adjustment for socioeconomic position and marital status had little influence on the findings in either the current study or the previous investigation of this issue, rendering a simple explanation in terms of socioeconomic confounding unlikely. In the current study, we had no data on health status, but in the earlier study adjustment for a wide range of measures of health and health-related behaviours reduced only slightly the association between infants’ birth weight and mothers’ cardiovascular mortality. The magnitude of the association in the current study is too great to be generated plausibly by the known associations between birth weight and maternal smoking, alcohol drinking, or anthropometry.

The marked similarity between the current findings and those from the previous study—which related to an earlier generation of women living in widely different circumstances—suggests that an important influence is being uncovered by our analyses. Possible intergenerational influences on birth weight and cardiovascular risk therefore merit further investigation.

Contributors: GDS formulated the hypothesis regarding infants’ birth weight and mothers’ mortality. All authors discussed and specified the analyses, which were carried out by SH and MR. The first draft of the paper was written by GDS, with SH and MR contributing to the final draft. GDS is the guarantor of the paper. Funding: None. Competing interests: None declared.

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