Caesarean delivery and neonatal mortality rates in 46 low- and middle-income countries: a propensity-score matching and meta-analysis of Demographic and Health Survey data

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Background Previous research on the association between caesarean delivery (CD) and neonatal mortality has had methodological limitations and given conflicting results. We conducted a study to: (i) estimate the association between CD at the individual level and neonatal mortality rates (NMR) in 46 countries; and (ii) examine whether this association varies among countries according to country-level rates of CD or gross domestic product (GDP).

Methods We obtained data from nationally representative Demographic and Health Surveys of women aged 15–49 years and their children aged 0–59 months (N = 392,883). Propensity-score matching, meta-analysis, and meta-regression were used to address the study objectives.

Results The pooled odds ratio (OR) for the association between individual level CD and NMR in 46 countries was 1.67 (95% confidence interval (CI) 1.48–1.89), with moderate heterogeneity ($I^2 = 39\%$). A meta-analysis of subgroups indicated that CD at the individual level was positively associated with NMR in countries with low (OR = 1.99, 95% CI 1.71–2.33, $I^2 = 8.5\%$) and medium (OR = 1.53, 95% CI 1.29–1.82, $I^2 = 24\%$) rates of CD. There was substantial heterogeneity of the effects of CD among countries with high rates of CD ($I^2 = 63\%$). Results of meta-regression showed that the association of individual-level CD with NMR depended upon country-level rates of CD. Compared with countries with high rates of CD, the OR of the NMR associated with individual-level CD in countries with low rates of CD was estimated to increased by a factor of 1.48 (95% CI 1.09–1.97).

Conclusions Studies are needed to better understand the risks posed by CD in countries with low and medium rates of CD and to identify possible reasons for the heterogeneity in effects of CD among countries with high rates of CD.

Keywords Caesarean delivery, neonatal mortality, low and middle income countries
Introduction

The rate of caesarean delivery (CD), defined as the proportion of all deliveries by CD in a geographical area, has been selected as an indicator of access to life-saving services for both mothers and newborns. Rates of CD vary widely among countries in the world, ranging from 0.4% to 40% of all deliveries. Both very low and very high rates of CD can be harmful, the former because they may reflect women’s lack of access to life-saving care, and the latter because they may indicate overuse of the CD procedure, with attendant unnecessary surgical risk. The recommended lower and upper limits for CD in any population are 5% and 15%, respectively, but there is no empirical evidence that these rates are optimal.

The rationale for the present study arose from the conflicting results and methodological limitations of previous research. For example, the three ecological studies of the association between CD and neonatal mortality rates (NMR) that are available for review yielded different findings for countries with relatively high rates of CD. One study showed no association between rates of CD and NMR in medium- and high-income countries, where rates CD were mainly >10%. A second study found a positive association between rates of CD and NMR in countries with CD rates >15%. Ecological data contain only marginal observations on the joint distribution of individually defined confounders and outcomes, and so identify neither contextual nor individual-level effects. This limitation can be addressed by studies of multi-level design that integrate individual and group-level data. Studies based on individual-level data have also reported conflicting results for the association between individual-level CD and NMR.

The conflicting findings of previous studies may be attributable to the dependence of the association between individual-level CD and NMR on country-level factors (e.g. country-level rate of CD or income). In countries with very low CD rates, poverty and clinical inexperience might increase the risk of NMR associated with individual-level CD, whereas in countries with higher rates of CD, this risk might be attenuated by expertise, affluence, and resources. However, no studies have attempted to examine this through the use of both country-level and individual-level data. Accordingly, the objectives of the present study were to: (i) estimate the association between individual-level CD and NMR in 46 low and middle income countries; and (ii) examine whether this association varies across countries according to country-level rates of CD or gross domestic product (GDP).

Methods

Data were obtained from nationally representative Demographic and Health Surveys (DHS) conducted in 46 developing countries from 2001–2008 (for a full list of countries see Supplementary Appendix 3, available as Supplementary data at IJE online). The detailed methodology of DHS is available at (http://www.measuredhs.com/What-We-Do/methodology.cfm), and is briefly outlined here. The DHS sampling frame is a list of non-overlapping area units (enumeration areas) that cover an entire country and serve as the primary sampling units or clusters in a DHS of that country. All households in the selected clusters are listed, and a fixed proportion is selected by systematic sampling. Eligible persons include all women aged 15–49 years in selected households, and their children aged 0–59 months, and interviews are conducted with these women about maternal and child health. The response rates ranged from 90% in Zimbabwe to 98% in Cambodia. The DHS uses standardized methodology, an identical core questionnaire, continuous training and monitoring of interviewers, and pre-testing of the core questionnaire to ensure the collection of data of high quality and the comparability of these data across countries.

The outcome variable in the present study was neonatal mortality, indicating whether a child born in the 5 years before the survey, survived its first 30 days of life as based on a maternal report of this. The independent variable, caesarean delivery (CD) (as compared with vaginal delivery (VD)), was also based on a maternal report. The co-variates used in the study included a wealth index (derived from an index of household assets), number of antenatal visits, mother’s education, maternal age at birth of child, maternal height-for-age, birth order of the index child, previous birth interval, birth size of the index child, the child’s gender, and urban or rural residence. Detailed descriptions of these variables are presented in Appendix 1. Household wealth, antenatal care, mother’s education, and urban or rural residence have been reported in previous studies to be important determinants of CD. One or more of the variables including short maternal stature, younger or older maternal age at child birth, short or long inter-pregnancy intervals, and extreme birth order of the index child have been linked to an extensive array of risk factors for CD or neonatal mortality or both, ranging from obstetrical emergencies (placental abruption and placenta previa) to common indications for CD (cephalopelvic disproportion, obstructed labour, prolonged labour, dystocia in labour, and malpresentations) and adverse perinatal outcomes (pre-term birth, low birth weight, and early neonatal death).

Country-level variables included: gross domestic product (GDP) per capita, converted to constant 2005 international dollars on the basis of parity of purchasing power, and country-level CD rates, obtained by aggregating individual-level CD to the country level. Country-level CD rates were stratified as low (<5%), medium (5%–15%), and high (>15%).
Data Analysis
After the exclusion of multiple births, 427,463 singleton births (97.5% of all births) were eligible for the study. Covariate information was missing for about 3.5% of the children (N=15,225) in these singleton births, and they were excluded from the analysis of the study data. First, propensity-score matching was done for each country in the study, to estimate the odds ratios (ORs) of NMR associated with individual-level CD. Second, a meta-analysis was done to obtain a summary OR of this association. Third, a meta-regression was done to examine whether the association between individual-level CD and NMR was dependent on country-level CD rates and GDP.

In the 46 countries in which DHS were conducted, maternal heights were fully measured in 28 countries, and were also measured in a random subset (one-third or half) of the study sample in 14 countries, but were not measured in 4 countries. Data on birth size were unavailable for 2 countries. When estimating propensity scores, birth size was not included as a variable in two countries (Bangladesh and Colombia), and maternal height was not included in four countries (Dominican Republic, Indonesia, Philippines and Pakistan) where data were unavailable. Data on antenatal care were collected only for the most recent births (72% of the sample). For our data analyses, we created a dummy variable to represent older children for whom antenatal care data were intentionally not collected, and another dummy variable to indicate whether data on maternal height were available.

Propensity-score matching
Because women with high-risk pregnancies might be more likely to undergo CD, and these risks might in turn affect the NMR, we used propensity-score matching to ensure that the CD and VD groups in the study were comparable in terms of important prognostic characteristics. The propensity score is the conditional probability of assignment of a variable to a particular group given a set of observed co-variates. Infant-specific propensity scores were estimated from a logistic regression model that included all covariates and quadratic terms for continuous covariates to predict the probability of an infant being delivered by CD in each country included in the study. The PSMATCH2 Stata module was used to conduct radius matching within a caliper distance of 0.01 on the probability scale of 0–1. Rosenbaum and Rubin (1985) suggested using a caliper distance of ≤1/4 standard deviation (SD) of the estimated propensity scores of a sample. (In our study, the SD of the propensity score was 0.12 and the chosen caliper distance of 0.01 was 1/12 of the SD.) All comparison infants (i.e., those delivered by VD) within the caliper distance of infants born by CD were considered a match. Matching with replacement was used because it minimizes the propensity-score distance between the matched comparison units and the treatment unit and is beneficial in reducing bias. Unmatched cases (N=202) and unmatched controls (N=19,153) were excluded from the analyses. The final sample for analysis included 392,883 children.

A logistic regression model was used to estimate the association between individual-level CD and NMR for each country, with adjustment for covariates to control for the remaining minor differences in the matched sample and to adjust for clustering within matched pairs.

Assessing the quality of matching
The ‘pptest’ command in Stata was used to check covariate balance after propensity-score matching in each country. It provides t-tests for equality of means in the individual-level CD and VD groups both before (unweighted) and after (weighted using the matching weight) matching. In the matched sample, there were no differences (P>0.05) in any co-variates between the CD and VD groups in each country. A sample checking of the quality of matching in one of the included countries (Cameroon) is presented in Appendix 2.

Meta-analysis
Meta-analyses were done to estimate summary ORs for the association between individual-level CD and NMR. Meta-analysis and subgroup meta-analyses were done with STATA/IC 12 (StataCorp, College Station, TX, USA), using the ‘meta’ command. Random-effects models were chosen to compensate for between-country variation in ORs.

Meta-regression
In our meta-regression analysis, an individual country was used as the unit of analysis, and the outcomes were the logarithms of the ORs of NMR based on individual-level data in the 46 countries in which DHS were conducted. The independent variables were country-level CD rates and GDP. An association between an independent variable (e.g. country-level CD rates) and the outcome indicates that the relation between individual-level CD and NMR depends on country-level CD rates. Meta-regression was conducted in STATA/IC 12 by using the ‘metareg’ command.

Sensitivity analysis for hidden bias
We checked the sensitivity of our results to hidden bias by using the bounding approach suggested by Rosenbaum (2002) and the mhbounds package in STATA/IC 12. The sensitivity analysis does not indicate the existence of hidden bias, but it does show how large this bias would have to be to cancel out the observed CD effect, by providing a test statistic named ‘gamma’, which is the ‘odds ratio of differential treatment assignment due to unobserved factors’. In this approach, the threshold value of gamma was
calculated at the point at which hidden bias would eliminate the CD effect. The closer the threshold value of gamma is to 1 (e.g. <1.05), the more likely it is that the effect can be explained by an unobserved factor.\(^4^3\) A threshold value of gamma between 1.25 and 1.30 can be considered relatively robust to bias caused by unobserved factors.\(^4^4\) A threshold value of gamma of 1.50 could be considered very robust, particularly when a study can show matching in many important observed co-variates. In addition, the effect of an unobserved variable (i.e. one that causes a 50% difference in the odds of CD) on the outcome (i.e., NMR) would have to be so strong as to almost perfectly predict the outcome in each pair of matched cases in a set of data.\(^4^4\)

### Sensitivity analysis after excluding complicated pregnancies and/or deliveries

Although information about complications during pregnancy and/or delivery is not routinely collected in DHS, country-specific information is available for the most recent births in 5 countries with medium rates of CD (Bangladesh, Honduras, India, Indonesia and Nicaragua) and 1 country with a high rate of CD (Colombia). Of the 82326 most recent births in these 6 countries, 40168 were reported to have had at least one complication during pregnancy and/or delivery. Relatively commonly reported complications included vaginal bleeding; prolonged labour; high blood pressure; swelling of the leg, face, or body; excessive fatigue or anemia; infection; fever with a foul-smelling vaginal discharge; and convulsions. In the sample remaining after the exclusion of complicated pregnancies/deliveries \(N=42\,158\), propensity-score matching was done for each country, with the same co-variates as in the main analysis. After the exclusion of unmatched cases and unmatched controls, the final sample for sensitivity analysis included 38811 children.

### Results

Table 1 presents the overall characteristics of the study sample. The number of countries that fell within the low-, medium-, and high-CD-rate groupings were 27, 13, and 6, respectively. Among all children, 7.7% were delivered by CD and 3.0% died during the neonatal period. The sample characteristics according to individual country appear in Appendix 3.

The pooled ORs for the association between individual-level CD and NMR in the 46 countries in which DHS were conducted was 1.67 (95% CI 1.48–1.89), with moderate heterogeneity \(I^2=39.4\%\) (not shown). This implies that children born by CD had a higher overall risk of dying during the neonatal period than did children born by VD, but this risk may vary across countries. The results of our subgroup meta-analysis (Figures 1 and 2) showed that individual-level CD was positively associated with NMR in countries with low (pooled OR=1.99, 95% CI 1.71–2.33, \(I^2=8.5\%\)) and medium (pooled OR=1.53, 95% CI 1.29–1.82, \(I^2=24\%\)) rates of CD. The pooled OR in countries with high rates of CD was 1.31 (95% CI 0.97–1.76), with substantial between-country heterogeneity \(I^2=63\%)\) (Figure 3). The ORs for the association of individual-level CD with NMR varied from 0.53(95% CI 0.20–1.38) in Turkey to 2.40 (95% CI 1.56–3.71) in Jordan.

Table 2 presents the results of our meta-regression. Model 1 showed that the association between individual-level CD and NMR depended on country-level CD rates: the log OR of NMR associated with individual-level CD was estimated to increase by 0.39 units
In countries with low rates of CD as compared with those with high rates of CD. In Model 2, GDP showed no association with NMR, and its inclusion led to no appreciable change in the log OR for NMR associated with a low country-level rate of CD. This implies that the effects of individual-level CD vary among countries according to country-level rates of CD and not GDP.

Sensitivity analysis for hidden bias
The results of our sensitivity analysis for hidden bias showed the following gamma threshold values for countries with low (gamma = 1.80), medium (gamma = 1.15), and high (gamma = 1.00) rates of CD. In countries with low rates of CD, the association between individual-level CD and NMR would remain even if there was a hidden bias to the degree that two matched individuals differed by 80% in their odds of having CD as a result of hidden bias. In countries with medium rates of CD, the association was relatively more sensitive to hidden bias. In countries with high rates of CD, an overall association between CD and NMR was unlikely even under the assumption of no hidden bias.

Sensitivity analysis after excluding complicated pregnancies and/or deliveries
Figure 4 shows the results of our sensitivity analysis after the exclusion of complicated pregnancies and/or deliveries.
deliveries. There was a positive association between CD and NMR in the 5 countries with medium rates of CD (pooled OR = 1.74, 95% CI 1.25–2.42), with minimal between-country variation ($I^2 = 0\%$). There was also a positive association between CD and NMR in Colombia (OR = 2.22, 95% CI 1.16–4.25). When the results were pooled across all 6 countries with medium or high rates of CD, the pooled OR was 1.83 (95% CI 1.36–2.46), with minimal heterogeneity ($I^2 = 0\%$).

### Table 1

<table>
<thead>
<tr>
<th>Countries</th>
<th>CD (n/N)</th>
<th>VD (n/N)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swaziland</td>
<td>11/194</td>
<td>58/2324</td>
<td>2.45 (1.21-4.98)</td>
</tr>
<tr>
<td>Philippines</td>
<td>13/523</td>
<td>84/5534</td>
<td>1.69 (0.74-3.84)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>38/568</td>
<td>380/8198</td>
<td>1.48 (0.98-2.22)</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>22/782</td>
<td>88/5566</td>
<td>1.84 (1.02-3.31)</td>
</tr>
<tr>
<td>Namibia</td>
<td>12/441</td>
<td>79/3915</td>
<td>1.34 (0.66-2.72)</td>
</tr>
<tr>
<td>Morocco</td>
<td>12/283</td>
<td>122/4799</td>
<td>1.67 (0.75-3.70)</td>
</tr>
<tr>
<td>Lesotho</td>
<td>6/169</td>
<td>124/3177</td>
<td>0.93 (0.39-2.27)</td>
</tr>
<tr>
<td>Kenya</td>
<td>15/345</td>
<td>126/4988</td>
<td>1.76 (0.95-3.27)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>45/1137</td>
<td>332/16380</td>
<td>1.99 (1.30-3.06)</td>
</tr>
<tr>
<td>India</td>
<td>198/5207</td>
<td>1527/44419</td>
<td>1.10 (0.90-1.35)</td>
</tr>
<tr>
<td>Honduras</td>
<td>32/1097</td>
<td>127/9201</td>
<td>2.16 (1.30-3.60)</td>
</tr>
<tr>
<td>Ghana</td>
<td>6/155</td>
<td>70/2404</td>
<td>1.26 (0.52-3.10)</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>26/488</td>
<td>193/5286</td>
<td>1.50 (0.78-2.88)</td>
</tr>
<tr>
<td>Overall</td>
<td>437/11389</td>
<td>3310/115921</td>
<td>1.53 (1.29-1.82)</td>
</tr>
</tbody>
</table>

**Figure 2** Adjusted numbers and odds ratios of neonatal mortality in caesarean delivery versus vaginal delivery groups in 13 countries with medium rates of caesarean delivery

<table>
<thead>
<tr>
<th>Countries</th>
<th>CD (n/N)</th>
<th>VD (n/N)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turkey</td>
<td>8/804</td>
<td>65/3406</td>
<td>0.53 (0.20-1.38)</td>
</tr>
<tr>
<td>Jordan</td>
<td>34/1674</td>
<td>72/8342</td>
<td>2.40 (1.56-3.71)</td>
</tr>
<tr>
<td>Egypt</td>
<td>43/2639</td>
<td>106/7602</td>
<td>1.18 (0.80-1.74)</td>
</tr>
<tr>
<td>DominicanR</td>
<td>73/3953</td>
<td>92/6506</td>
<td>1.32 (0.92-1.90)</td>
</tr>
<tr>
<td>Colombia</td>
<td>70/3555</td>
<td>137/10488</td>
<td>1.51 (1.06-2.16)</td>
</tr>
<tr>
<td>Bolivia</td>
<td>38/1462</td>
<td>184/6720</td>
<td>0.94 (0.59-1.50)</td>
</tr>
<tr>
<td>Overall</td>
<td>267/14087</td>
<td>656/43064</td>
<td>1.31 (0.97-1.76)</td>
</tr>
</tbody>
</table>

**Figure 3** Adjusted numbers and odds ratios of neonatal mortality in caesarean delivery versus vaginal delivery groups in six countries with high rates of caesarean delivery

_N = total number of children in the caesarean delivery (CD) or vaginal delivery (VD) groups; n = adjusted number of neonatal deaths; OR=adjusted odds ratio; CI=confidence interval._

$I^2$ describes the percentage of total variation in ORs across countries that is due to heterogeneity rather than chance. It was calculated as $I^2 = 100\% \times (Q-df)/Q$ where Q is the Cochran heterogeneity statistic.

### Discussion

Our study found positive associations between individual-level CD and NMR in countries with both low (<5\%) and medium (between the 5\%–15\% recommended limits) rates of CD. Sensitivity analysis indicated that these associations were robust. There was no overall association between CD and NMR in countries with high rates of CD, but there was substantial between-country heterogeneity in these associations.
In this study, the NMR was 3% (ranging from 1% in Jordan to 5.1% in Pakistan). Despite the high quality of DHS data in general, the ascertainment of neonatal mortality relied on retrospective maternal reports, which might create the risk of under-reporting. Nevertheless, a study in Ethiopia showed that the overall patterns of child mortality based on longitudinal estimates were similar to those of cross-sectional estimates based on maternal reports in the 2000 and 2005 DHS. Furthermore, the 2-year reliability of retrospective maternal reports of child mortality in 20 villages in Egypt was high (kappa = 0.90).

The present study is the first of its kind to: (i) estimate the strength of association between CD and NMR on the basis of integrated country- and individual-level data; (ii) mimic randomization using propensity-score matching based on observed prognostic variables; (iii) use sensitivity analysis to estimate the boundary at which unobserved factors could account
for the findings; and (iv) test the moderating influence of country-level CD rates on the association between individual-level CD and NMR. Although propensity-score matching provides a rigorous approach to ensuring group equivalence in observed prognostic variables, limited information about specific maternal and neonatal risk factors in DHS forced us to restrict our analyses to singleton births and to use proxy variables to develop propensity scores. On the basis of our successful matching of propensity scores, the robustness of our results to hidden bias in countries with low rates of CD, and the consistency of our findings after the exclusion of complicated pregnancies in medium CD rate countries, we believe that the effects of CD observed in countries with low and medium rates of CD are very robust. However, we cannot be sure that our co-variate adjustments were fully adequate, and we acknowledge that residual confounding by indication remains a plausible explanation for our results.

Factors contributing to the increased risk of neonatal mortality associated with CD might include poor infrastructure in health facilities, inadequate expertise in performing CD, poor neonatal care, and delayed initiation of breast-feeding. There is considerable variability among countries in the distribution of operating theatres: the estimated number of such facilities varies from 1.0 (95% CI 0.9–1.2) per 100,000 people in west sub-Saharan Africa to 25.1 (95% CI 20.9–30.1) per 100,000 people in eastern Europe. \(^4\) In Afghanistan, for example, it is not uncommon for health facilities to have a theatre containing a single operating table that is used both for general surgery and obstetric operations including CD. \(^4\) This could interfere with the timely performance of a CD. Proper sterilization of the operating theatre could be a challenge in low-resource settings, which could increase the risk of nosocomial infections in both mothers and newborns. The maintenance of clinical expertise and the confidence to perform CDs could also be a challenge in settings with a low volume of CDs. \(^4\) Although infants born by CD are more likely to have respiratory distress and be admitted to neonatal intensive-care units, \(^49\)–\(^51\) intensive-care services in poorer countries, especially in sub-Saharan Africa, are underdeveloped and described as ‘a novel concept’. \(^52\) Additionally, CD has been associated with delayed initiation of breast-feeding, \(^53\), \(^54\) which has been linked to an increased risk of neonatal mortality. \(^55\), \(^56\) Although several factors may contribute to this increased risk, studies are necessary to identify specifically contributing factors in particular countries.

Previous population-based studies of the effects of CD have been limited in number, scope, or methodology. In estimating the effects of CD, the integration of country- and individual-level data, combined with propensity-score matching to control for selection factors, are strengths of the present study not reflected in previous research. This study showed that as compared with countries having high rates of CD, the OR for NMR associated with individual-level CD was increased by an estimated factor of 1.48 in countries with low rates of CD. In attempting to understand the effects of CD at the individual level, it is important to consider overall practice levels within countries (e.g. quality of health facilities, expertise of physicians) and to be aware of heterogeneity among countries in the risks for neonatal mortality associated with CD. Indeed, the inconclusive findings in previous studies based on individual-level data are most likely a reflection of the differences between countries in the effects of CD observed in the present study.

Although the large, diverse sample in the present study, representing 46 countries, is an important strength of the study, only 6 countries fell into the category of having a high rate of CDs. The striking heterogeneity among these 6 countries in the strength of association between CD and NMR should focus the attention of health-policy analysts on this issue within their own countries. In Colombia, for example, CD was associated with an increased risk for NMR in both the main analysis (all births) and the sensitivity analysis (the most recent births without reported obstetric complications in our study) in Colombia. \(^57\) According to a previous study in four hospitals in Colombia, \(^57\) most CDs were unjustified. As an instance of this, about 84% of patients in that study who had diagnoses of dystocia did not meet the criteria for dystocia, which include ‘no progress of labour for >2 hours of regular and intense uterine contractions and no response to oxytocin or amniotomy.’ \(^57\) According to the World Health Report for 2010, \(^58\) the estimated cost of ‘excess’ CD (using 15% as a threshold rate) was approximately US$ 23 million in Colombia, where the rate of CD was 26.7% in 2008. Taken collectively, the evidence indicates that practices associated with CD in Colombia can not only increase the risk of neonatal death but also add to the burden of health-care costs in that country. Available evidence suggests that there may be unjustified CDs even in countries with low rates of CD. A study in two rural hospitals in Tanzania, \(^59\) for example, found that prolonged labour was the only indication for emergency CD in 144 of 303 women, and that in 52 (36%) of these 144 cases, the indication for CD seemed inappropriate because the partograph showed that labour progressed in a timely fashion and/or the membranes were intact.

Our study raises the following unanswered questions: (i) What are the factors associated with CD that increase risk for neonatal death especially in countries with low and medium rates of CD? (ii) In countries with low rates of CD, to what extent are women who would benefit from a CD being denied this procedure? (iii) Are there national-level phenomena that explain differences among countries in the
strength of association between CD and neonatal death, especially in countries with high rates of CD? The problems raised by CD constitute an important, poorly understood, and multifaceted challenge. The high cost and increased reliance on CD, and the potential adverse effects associated with it, provide a strong rationale for addressing these problems in future studies.

Supplementary Data
Supplementary data are available at IJE online.

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Conflict of interest: None declared.

KEY MESSAGES
- This study found positive associations between individual-level CD and NMR in countries with low (<5%) and medium (between the 5%–15% recommended limits) rates of CD and these findings were robust to sensitivity analyses.
- There was substantial between-country variability in individual-level effects of CD among countries in the study that had high rates of CD.
- Further studies are needed to explore possible reasons for: (i) the increased risk of neonatal mortality associated with individual-level CD in countries with low and medium rates of CD, and (ii) the variability in effects of individual-level CD in countries with high rates of CD.

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