# Articles

# Anaesthesia-related maternal mortality in low-income and middle-income countries: a systematic review and meta-analysis

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# Summary

**Background** The risk factors contributing to maternal mortality from anaesthesia in low-income and middle-income countries and the burden of the problem have not been comprehensively studied up to now. We aimed to obtain precise estimates of anaesthesia-attributed deaths in pregnant women exposed to anaesthesia and to identify the factors linked to adverse outcomes in pregnant women exposed to anaesthesia in low-income and middle-income countries.

Methods In this systematic review and meta-analysis, we searched major electronic databases from inception until Oct 1, 2015, for studies reporting risks of maternal death from anaesthesia in low-income and middle-income countries. Studies were included if they assessed maternal and perinatal outcomes in pregnant women exposed to anaesthesia for an obstetric procedure in countries categorised as low-income or middle-income by the World Bank. We excluded studies in high-income countries, those involving non-pregnant women, case reports, and studies published before 1990 to ensure that the estimates reflect the current burden of the condition. Two independent reviewers undertook quality assessment and data extraction. We computed odds ratios for risk factors and anaesthesia-related complications, and pooled them using a random effects model. This study is registered with PROSPERO, number CRD42015015805.

**Findings** 44 studies (632556 pregnancies) reported risks of death from anaesthesia in women who had an obstetric surgical procedure; 95 (32149636 pregnancies and 36144 deaths) provided rates of anaesthesia-attributed deaths as a proportion of maternal deaths. The risk of death from anaesthesia in women undergoing obstetric procedures was  $1 \cdot 2$  per 1000 women undergoing obstetric procedures (95% CI  $0 \cdot 8 - 1 \cdot 7$ ,  $I^2 = 83\%$ ). Anaesthesia accounted for  $2 \cdot 8\%$  ( $2 \cdot 4 - 3 \cdot 4$ ,  $I^2 = 75\%$ ) of all maternal deaths,  $3 \cdot 5\%$  ( $2 \cdot 9 - 4 \cdot 3$ ,  $I^2 = 79\%$ ) of direct maternal deaths (ie, those that resulted from obstetric complications), and  $13 \cdot 8\%$  ( $9 \cdot 0 - 20 \cdot 7$ ,  $I^2 = 84\%$ ) of deaths after caesarean section. Exposure to general anaesthesia increased the odds of maternal (odds ratio [OR]  $3 \cdot 3$ , 95% CI  $1 \cdot 2 - 9 \cdot 0$ ,  $I^2 = 58\%$ ), and perinatal deaths ( $2 \cdot 3$ ,  $1 \cdot 2 - 4 \cdot 1$ ,  $I^2 = 73\%$ ) compared with neuraxial anaesthesia. The rate of any maternal death was  $9 \cdot 8$  per 1000 anaesthetics ( $5 \cdot 2 - 15 \cdot 7$ ,  $I^2 = 92\%$ ) when managed by non-physician anaesthetists compared with  $5 \cdot 2$  per 1000 ( $0 \cdot 9 - 12 \cdot 6$ ,  $I^2 = 95\%$ ) when managed by physician anaesthetists.

**Interpretation** The current international priority on strengthening health systems should address the risk factors such as general anaesthesia and rural setting for improving anaesthetic care in pregnant women.

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# Introduction

A quarter of a million women die every year during or after pregnancy and childbirth, and 99% of these are from low-income and middle-income countries.<sup>1</sup> Anaesthetic interventions are an integral part of emergency obstetric care.<sup>2</sup> However, there is a paucity of physician anaesthetists in many of the poorest countries, with an estimated ratio of one physician anaesthetist per million women.<sup>3</sup> There is also a lack of infrastructure, drugs, and equipment.

The need for safe, affordable surgery and anaesthesia in low-income and middle-income countries is recognised, with perioperative death as a global safety indicator.<sup>4</sup> In high-income countries, very few maternal deaths are attributed to anaesthesia.<sup>5</sup> However, no robust estimates are available of maternal deaths from obstetric anaesthesia, or of overall maternal mortality attributable to anaesthesia, in low-income and middle-income countries. Factors that contribute to maternal and perinatal mortality in women exposed to anaesthesia in low-income and middle-income countries need to be identified.

Individual studies have provided varied and imprecise results, with up to a fifth of all direct maternal deaths attributed to anaesthesia-related procedures.<sup>6</sup> Systematic reviews report estimates of complications in all individuals exposed to anaesthesia, not specifically in pregnant women.<sup>7</sup>We undertook a systematic review to obtain precise estimates of anaesthesia-attributed deaths





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#### **Research in context**

#### Evidence before this study

Existing systematic reviews on global causes of maternal death have not previously assessed the role of obstetric anaesthesia. A recent systematic review of anaesthesia-related mortality in low-income and middle-income countries focused on risks to the general population, and not specifically to pregnant women, who are at high risk. Individual observational studies vary in their estimates for anaesthesia-related maternal deaths in low-income and middle-income countries and relevant risk factors.

## Added value of this study

We have provided robust estimates of risk of anaesthesiaattributed maternal death in pregnant women who have obstetric procedures in low-income and middle-income countries overall, and in various geographic regions grouped by income status. We have highlighted the contribution of

in pregnant women exposed to anaesthesia and to identify the factors linked to adverse outcomes in pregnant women exposed to anaesthesia in low-income and middle-income countries.

#### Methods

# Search strategy and selection criteria

In this systematic review and meta-analysis, we used a prospective protocol (PROSPERO CRD42015015805)<sup>8</sup> in line with current recommendations, and reported as per the PRISMA guidelines.<sup>9</sup>

We searched MEDLINE, Embase, Scopus, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Web of Science, and the WHO Library and Global Index Medicus from inception until Oct 1, 2015. We used MeSH headings, text words, and word variants for "pregnancy" and combined them with terms for low-resource countries such as "low-income" or "middle-income" or "developing country". We combined these with terms related to anaesthesia and surgery such as "an(a)esthesia" or "an(a)esthetist" or "nurse an(a)esthetist" or "c(a)esarean section" (appendix p 1). There were no language restrictions. Additionally, we searched the reference lists of the included studies and relevant reviews for eligible studies.

We selected studies in two stages. In the first stage, we screened the titles and abstracts of all citations for potentially relevant papers. In the second, we assessed the full texts of the retrieved papers. Two independent reviewers (SS, KD) selected the papers against prespecified inclusion criteria. Any discrepancies were resolved after discussion with a third reviewer (ST). Studies were included if they assessed maternal and perinatal outcomes in pregnant women exposed to anaesthesia for an obstetric procedure in countries categorised as low-income and middle-income countries by the World Bank.<sup>10</sup> We excluded studies in high-income

anaesthesia to overall maternal mortality, particularly in deaths related to caesarean section (13.8%). We identified the risk factors for maternal deaths related to anaesthetic exposure such as general anaesthesia and rural setting. We provided estimates of death related to anaesthesia according to the type of anaesthetic practitioner in low-income and middle-income countries. About two-thirds of reported deaths from anaesthesia were due to preventable complications related to airway management and pulmonary aspiration.

## Implications of all the available evidence

Ongoing and future efforts to improve the safety of obstetric anaesthesia in low-income and middle-income countries should target the risk factors identified in our review to improve training, infrastructure, and provision of resources.

countries, those including non-pregnant women, case reports, and studies published before 1990 to ensure that the estimates reflect the current burden of the condition.

We defined anaesthesia-attributed complications as those that occurred directly as a result of anaesthesia (as established by the primary study authors), and anaesthesia-related outcomes as those that were directly or indirectly associated with anaesthesia. Maternal mortality was defined as the death of a woman during pregnancy or at any time until 42 days after delivery, irrespective of the duration and site of the pregnancy, as defined by WHO. This definition included deaths from any cause related to or aggravated by pregnancy and its management, but not from accidental or incidental causes.11 Direct maternal deaths were those that resulted from obstetric complications; indirect maternal deaths from disorders aggravated by physiological effects of pregnancy, by pre-existing disease, or by diseases that developed during pregnancy." We grouped direct and indirect maternal deaths together as overall maternal death.

Perinatal death included any fetal death that occurred after 28 completed weeks of gestation, stillbirths, and early neonatal deaths up to 1 week after birth.<sup>12</sup> We classed Apgar scores as low if they were less than or equal to 7 at 1 and 5 min. We accepted the primary study authors' definitions for maternal and fetal complications such as post-partum haemorrhage, cardiac arrest, and admission to the intensive care unit.

# Study quality assessment and data extraction

Two independent reviewers (SS and KD) undertook study quality assessment and data extraction, and any discrepancies were resolved with input from the third reviewer (ST). For studies of rates of anaesthesiaattributed maternal death, we assessed the following criteria: representativeness of the population, sample

See Online for appendix

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