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

Soha Sobhy\*, Javier Zamora\*, Kuhan Dharmarajah, David Arroyo-Manzano, Matthew Wilson, Ramesan Navaratnarajah, Arri Coomarasamy, Khalid S Khan, Shakila Thangaratnam



## 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 (632 556 pregnancies) reported risks of death from anaesthesia in women who had an obstetric surgical procedure; 95 (32 149 636 pregnancies and 36 144 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 1.2 per 1000 women undergoing obstetric procedures (95% CI 0.8–1.7,  $I^2=83\%$ ). Anaesthesia accounted for 2.8% (2.4–3.4,  $I^2=75\%$ ) of all maternal deaths, 3.5% (2.9–4.3,  $I^2=79\%$ ) of direct maternal deaths (ie, those that resulted from obstetric complications), and 13.8% (9.0–20.7,  $I^2=84\%$ ) of deaths after caesarean section. Exposure to general anaesthesia increased the odds of maternal (odds ratio [OR] 3.3, 95% CI 1.2–9.0,  $I^2=58\%$ ), and perinatal deaths (2.3, 1.2–4.1,  $I^2=73\%$ ) compared with neuraxial anaesthesia. The rate of any maternal death was 9.8 per 1000 anaesthetics (5.2–15.7,  $I^2=92\%$ ) when managed by non-physician anaesthetists compared with 5.2 per 1000 (0.9–12.6,  $I^2=95\%$ ) 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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\*Joint first authors

Women's Health Research Unit (S Sobhy MBBS, Prof J Zamora PhD, Prof K S Khan MSc, Prof S Thangaratnam PhD), Multidisciplinary Evidence Synthesis Hub (mEsh) (Prof J Zamora, Prof S Thangaratnam), Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK; Clinical Biostatistics Unit, Hospital Ramon y Cajal (IRYCIS, CIBERESP), Madrid, Spain (Prof J Zamora, D Arroyo-Manzano MSc); Northwick Park Hospital, Harrow, Middlesex, UK (K Dharmarajah MRCCOG); School of Health and Related Research, University of Sheffield, Sheffield, UK (M Wilson MD); Barts Health NHS Trust, Whitechapel, London, UK (R Navaratnarajah MRCCOG); and School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK (Prof A Coomarasamy MD)

Correspondence to: Prof Khalid S Khan, Women's Health Research Unit, Multidisciplinary Evidence Synthesis Hub (mEsh), Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London E1 2AD, UK  
k.s.khan@qmul.ac.uk

### 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 anaesthesia-attributed 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

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.

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

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.<sup>11</sup> 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.<sup>11</sup> 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 anaesthesia-attributed maternal death, we assessed the following criteria: representativeness of the population, sample

See Online for appendix

selection, outcome assessment, adequacy of sample size, and ascertainment of the cause of maternal death to anaesthesia.<sup>13,14</sup> We deemed a study to be adequate for representativeness if it included institutions from various settings such as rural and urban hospitals in a region or country, and to be inadequate if it included only one hospital or unit. We classed sample selection as adequate if all deliveries or maternal deaths were included, and as inadequate if a particular group of women were excluded. We deemed outcome assessment to be adequate when a confidential inquiry, verbal autopsy, or professional panel established the cause of death and inadequate when there was no special effort or use of registry data from only one source. An adequate sample size included data for at least 10 000 births. We regarded studies that accounted for the cause of death in at least 95% of maternal deaths to be adequate for ascertainment of cause of death. A study was classed as high quality if three of the above five criteria were met.<sup>13</sup>

For comparative studies, we used the Newcastle-Ottawa scale to establish the risk of bias in selection, comparability of cohorts, and outcome assessment.<sup>15</sup> Studies that scored four stars for selection, two stars for comparability, and three stars for ascertainment of the outcome were regarded to have a low risk of bias. Studies with two or three stars for selection, one for comparability, and two for outcome ascertainment were considered to have a medium risk of bias. We deemed any study with a score of one for selection or outcome ascertainment, or zero for any of the three domains, to have a high risk of bias.<sup>15</sup>

To compute corresponding proportions for individual studies, we extracted data for the number of women exposed to anaesthesia, total and direct maternal deaths, and deaths during or after caesarean section. We obtained information about the number of events (anaesthesia-related maternal death and pregnancy complications) in women exposed and unexposed to risk factors such as type of anaesthesia (neuraxial or general), setting (urban or rural), and practitioner (physician or non-physician).

### Data analysis

We computed odds ratios for various risk factors and anaesthesia-related complications in individual studies, and pooled them using a random effects model.<sup>16</sup> We used Peto odds ratios when the numbers of events were too few.<sup>17</sup> We assessed heterogeneity with the  $I^2$  statistic. When comparative data were not available, we reported the proportion of complications for each risk factor separately, and provided summary estimates.

Summary rates of risk of death from anaesthesia in pregnancy were reported as deaths per 1000 women undergoing obstetric procedures. We also reported anaesthesia-attributed deaths as a proportion of all maternal deaths (direct and indirect). We did subgroup analysis and meta-regression for the following factors that were prespecified before the analysis: geographical location (World Bank classification), country income (low, lower

middle, or upper middle), setting (urban or rural), and year of publication (before and after 2000). We assessed the effects of study quality (low or high) and design (prospective or retrospective) on the maternal mortality rates. We used multilevel random effects logistic models, and included the above factors. The meta-regressions were run as separate univariate analyses. We did sensitivity analysis by limiting our findings to only direct maternal deaths. We also assessed the proportion of all maternal deaths during or after caesarean section attributed to anaesthesia.

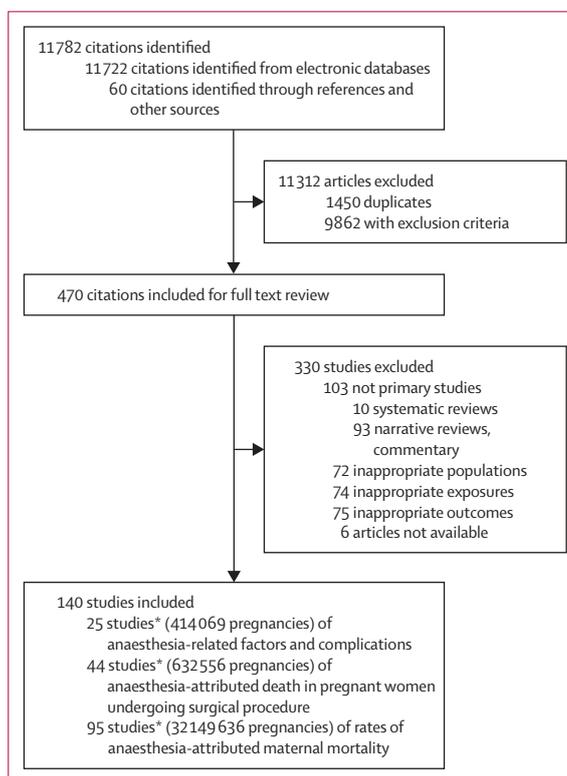
We assessed for publication bias and the effects of small studies using funnel plots, and Begg's<sup>18</sup> and Egger's tests.<sup>19</sup> All analyses were done with Stata (version 13).<sup>20</sup>

### Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

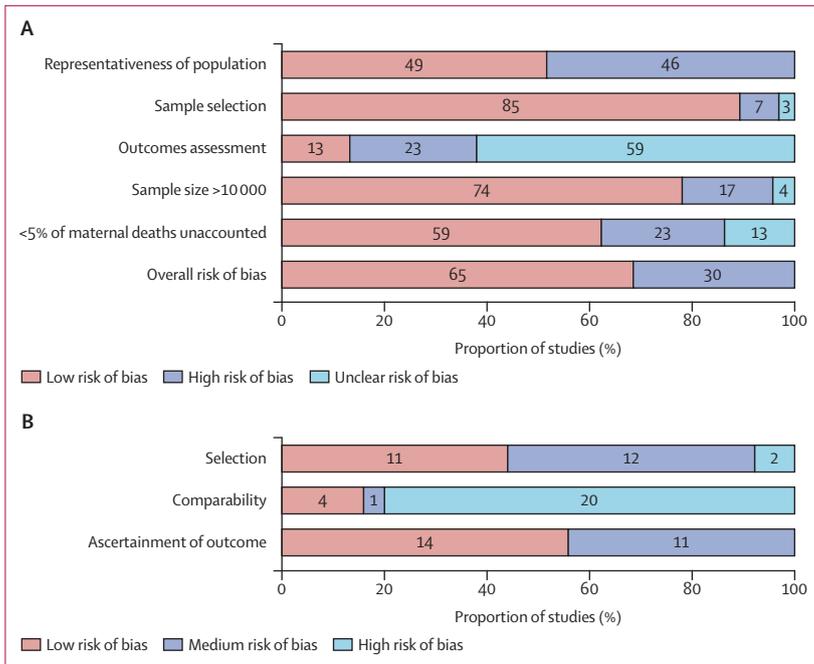
### Results

From 11 782 citations, we included 140 studies. 44 studies (632 556 pregnancies) provided data for risk of death from anaesthesia in women undergoing obstetric surgical procedures, and 95 studies (32 149 636 pregnancies, 36 144 deaths) reported anaesthesia-attributed maternal mortality as a proportion of maternal deaths. 25 studies



**Figure 1: Study selection**

\*Some studies have been used in more than one category.



**Figure 2: Risk of bias assessment** (A) Studies of anaesthesia-attributed maternal mortality rates. (B) Studies evaluating anaesthesia-related risk factors and maternal and fetal complications.

	Number of studies	Number of deaths	Number of women undergoing surgical procedures	Maternal deaths per 1000 women undergoing surgery	95% CI	I <sup>2</sup>	Meta-regression p value
Overall	44	264	632 556	1.2	0.82–1.7	83%	..
World Bank regions							
South Asia	4	16	37 132	0.34	0.13–0.90	71%	0.004
Sub-Saharan Africa	38	237	567 431	1.5	1.1–2.2	85%	
East Asia and Pacific	2	11	27 993	0.40	0.22–0.71	..	
Year							
<2000	17	55	49 232	1.2	0.76–1.7	50%	0.74
≥2000	27	209	583 324	1.2	0.74–2.1	86%	
Setting							
Urban	31	85	72 203	1.5	1.0–2.3	67%	0.02
Rural	1	1	69	14.5	0.00–42.7	..	
Both	12	178	560 284	0.67	0.37–1.2	89%	
Country income							
Low	13	53	33 431	1.5	0.84–2.8	63%	0.003
Lower middle	27	90	80 295	1.4	0.92–2.2	72%	
Upper middle	4	121	518 830	0.23	0.20–0.28	24%	

**Table 1: Mortality rates from anaesthesia in women undergoing obstetric surgical procedures in low-income and middle-income countries**

(414069 pregnancies) assessed the association between anaesthesia-related risk factors and complications in women undergoing obstetric procedure (figure 1).

The risk of maternal death directly attributed to anaesthesia after obstetric procedures was reported in 44 studies from 15 low-income and middle-income countries, which were grouped into the following regions: sub-Saharan Africa (n=38 studies), south Asia (n=4), and east Asia and the Pacific (n=2). Most studies were facility based (42 of 44) and in nearly three-quarters of studies (31 of 44), women were managed in an urban setting. Of the 95 studies (31 countries) that reported anaesthesia-attributed mortality as a proportion of all maternal deaths, 52 provided facility-based data, and 29 provided countrywide data. In 45 studies, women were managed in an urban setting (appendix p 3 and p 20).

Studies compared the odds of adverse maternal and fetal outcomes for risk factors such as the type of anaesthesia (25 studies, 414069 pregnancies), setting (one study, 8070 pregnancies), and anaesthesia provider (one study, 8070 pregnancies). Rates of any maternal death in anaesthesia administered by a non-physician were assessed in eight studies (27714 pregnancies), and by a physician anaesthetist in six studies (20 313 pregnancies). Both high-risk and low-risk women were studied, and caesarean section was the most common surgical procedure. Studies ascertained the cause of maternal deaths and exposure to anaesthesia from theatre records, patient notes, facility and countrywide maternal death reviews, and verbal autopsies.

65 (68%) of 95 included studies of anaesthesia-attributed maternal mortality had low risk of bias. About half had high risk of bias for representativeness of the population and setting, and 90% had adequate sample selection, and a quarter had high risk of bias for outcomes reporting (figure 2A). Three-quarters of all studies had adequate sample size and about two-thirds adequately accounted for maternal deaths (figure 2A).

Four-fifths of studies of risk factors for complications in women exposed to obstetric anaesthesia had high risk of bias (figure 2B). Nearly half of the included studies had low risk of bias for study selection; a fifth of studies had low or medium risk of bias for comparability of the cohorts, and more than half of studies had low risk of bias for ascertainment of the outcome (figure 2B).

In women undergoing an obstetric procedure, the risk of death attributed to anaesthesia was 1.2 per 1000 women (95% CI 0.82–1.7, I<sup>2</sup>=83%), with the highest rates in sub-Saharan Africa (1.5 per 1000 women, 1.1–2.2, I<sup>2</sup>=85%; table 1). The appendix provides estimates for individual countries (appendix p 14). Caesarean section was the surgical procedure done in 37 studies, comprising 97% (611 291/632 556) of the included women. Seven studies either reported other obstetric procedures (eg, cervical cerclage, laparotomy for ectopic pregnancy, dilatation and curettage, and removal of retained placenta), or failed to specify the type of obstetric surgery.

Subgroup analysis and meta-regression showed a significant difference between regions (p=0.004). The risks of death from anaesthesia were higher in rural than

urban settings ( $p=0.02$ ), and in low-income and lower-middle-income than upper-middle-income countries ( $p=0.003$ ). There were no differences for year of publication ( $p=0.74$ ; table 1).

Anaesthesia was reported as the main cause of death in 2.8% (95% CI 2.4–3.4,  $I^2=75%$ ) of all maternal deaths (direct and indirect), with the highest rates in Middle East and north Africa (6.2%, 3.9–9.7,  $I^2=86%$ ), and the lowest in east Asia and Pacific (1.5%, 0.9–2.3,  $I^2=63%$ ; table 2). The appendix provides estimates from individual countries (appendix p 14). Anaesthesia was reported as the cause of death in 3.5% (95% CI 2.9–4.3,  $I^2=79%$ ) of direct maternal deaths (76 studies, 20780 deaths, 26750727 pregnancies), and 13.8% (95% CI 9.0–20.7,  $I^2=84%$ ) of all deaths that occurred during or after caesarean section (31 studies, 1028 deaths; appendix pp 17–18).

Meta-regression showed a significant difference in the overall anaesthesia-attributed mortality rates by geographical region ( $p=0.004$ ) and year of publication ( $p=0.002$ ). We noted no significant differences by setting, study design, income level, or study quality (table 2).

Compared with neuraxial anaesthesia, administration of general anaesthesia tripled the odds of maternal death (OR 3.3, 95% CI 1.2–9.0,  $I^2=58%$ ), with mortality rates of 5.9 per 1000 and 1.2 per 1000 for general and neuraxial anaesthesia, respectively. General anaesthesia also doubled the odds of perinatal death (odds ratio [OR] 2.3, 95% CI 1.2–4.1,  $I^2=73%$ ) compared with neuraxial anaesthesia. There was an increase in other complications such as post-partum haemorrhage (OR 9.4, 95% CI 5.1–17.2,  $I^2=65%$ ), low Apgar score at 1 min (6.3, 2.9–13.6,  $I^2=64%$ ) and at 5 min (3.2, 2.3–4.4,  $I^2=0%$ ) with general compared to neuraxial anaesthesia (figure 3). There were no differences in cardiac arrest (OR 3.6, 95% CI 0.6–20.6,  $I^2=71%$ ) between the two groups. Management in a rural setting was associated with an increase in the odds of maternal death (2.1, 1.2–3.7) compared with an urban setting.<sup>21</sup>

No direct comparative data were available for physician versus non-physician providers of anaesthetic care. The overall risk of any maternal death when non-physicians provided care was 9.8 per 1000 (95% CI 5.2–15.7,  $I^2=92%$ ), and the rates of anaesthesia-attributed maternal deaths was 1.8 per 1000 (0.25–4.3,  $I^2=85%$ ). The corresponding estimates for physician anaesthetists were 5.2 per 1000 (0.9–12.6,  $I^2=95%$ ) for any maternal death, and 1.3 per 1000 (0.16–3.1,  $I^2=79%$ ) for anaesthesia-attributed maternal deaths, respectively (appendix p 13). One study reported an increase in the odds of maternal deaths (OR 2.7, 95% CI 1.6–4.6) when maternal care was managed by non-physician anaesthetists without formal structured training compared to those with training.<sup>21</sup>

The underlying causes were reported for 124 maternal deaths (24 studies). 56 (45%) of all deaths resulted from airway complications such as difficult or failed tracheal intubation, oesophageal intubation, bronchospasm,

	Number of studies	Number of deaths from anaesthesia	Total number of maternal deaths	Anaesthesia-attributed mortality	95% CI	$I^2$	Meta-regression p value
Overall	95	987	36144	2.8%	2.4–3.4	75%	
World Bank regions*							
Sub-Saharan Africa	50	675	24873	2.9%	2.3–3.6	61%	0.004
South Asia	18	89	4317	2.4%	1.5–3.8	79%	
Middle East and north Africa	10	136	2555	6.2%	3.9–9.7	86%	
East Asia and Pacific	9	49	3276	1.5%	0.9–2.3	63%	
Europe and central Asia	4	14	455	3.0%	1.3–6.7	64%	
Latin America and the Caribbean	4	24	668	3.6%	2.4–5.3	0%	
Year							
<2000	28	250	6589	4.1%	3.0–5.5	77%	0.002
>2000	67	737	29555	2.4%	1.9–2.9	72%	
Setting							0.29
Rural	8	14	894	1.9%	0.9–3.8	38%	
Urban	45	245	7987	3.3%	2.5–4.2	72%	
Both	42	728	27263	2.5%	1.9–3.4	80%	
Study design							0.68
Prospective	9	35	1819	2.5%	1.1–5.6	77%	
Retrospective	86	952	34325	2.9%	2.4–3.4	75%	
Country income							0.57
Low	17	89	3171	2.6%	1.9–3.6	35%	
Lower middle	38	199	8130	2.6%	1.9–3.6	78%	
Upper middle	40	699	24843	3.1%	2.4–4.1	78%	
Study quality							0.12
High	65	859	32099	2.6%	2.1–3.2	79%	
Low	30	128	4045	3.6%	2.6–4.8	59%	

\*Based on 2015 World Bank data.

Table 2: Anaesthesia-attributed maternal mortality in low-income and middle-income countries

ventilation difficulties, and hypoxia; 38 (31%) from pulmonary aspiration; 34 (27%) from issues related to staff competency, poor pre-assessment, intraoperative monitoring, and equipment failure. Other causes included cardiac arrest at induction or during the procedure (seven [6%]), high spinal anaesthesia (eight [6%]), and drug overdose or adverse reactions (seven [6%]).

With regard to publication bias and small studies effects, a funnel plot of studies reporting risk of death from anaesthesia in women undergoing obstetric procedure showed significant asymmetry (Egger's test  $p=0.001$ ), although Begg's test failed to confirm this effect. There was no asymmetry in a funnel plot of studies that reported anaesthesia-attributed mortality as a proportion of all maternal deaths (Egger's and Begg's tests  $p>0.05$ ; appendix p 19).

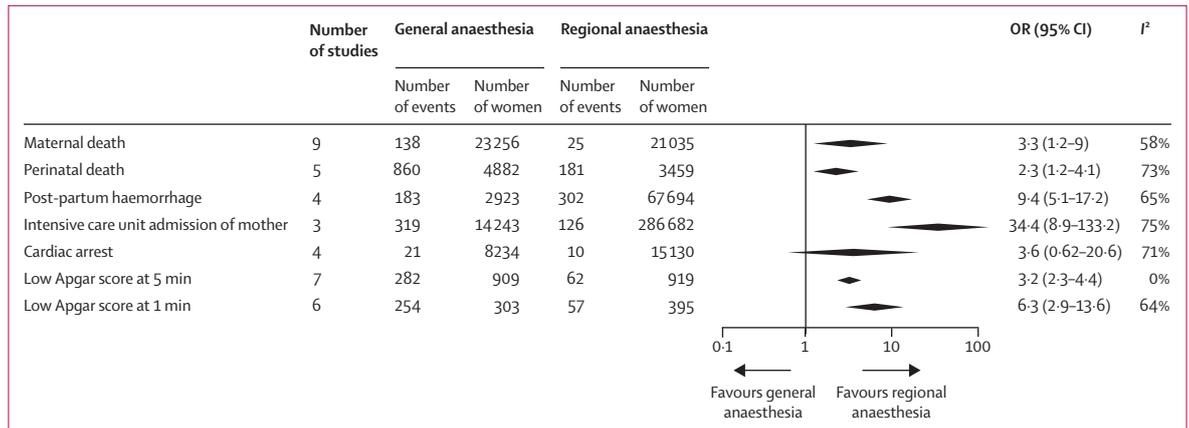


Figure 3: Maternal and fetal complications in women exposed to general versus neuraxial anaesthesia in low-income and middle-income countries

**Discussion**

Anaesthesia contributes disproportionately to maternal mortality in low-income and middle-income countries. About one in seven maternal deaths during or after caesarean section was due to anaesthesia, a very high mortality rate compared with developed countries.<sup>5</sup> Exposure to general anaesthesia, and administration of anaesthesia by non-physicians, especially those with no formal training, were major risk factors for maternal deaths from anaesthesia. We have mapped the safety of obstetric anaesthesia across various economic regions and individual countries. Most studies were from the sub-Saharan African region, which also had the highest risk of deaths from anaesthesia in women undergoing surgery.

Ours is the first review, to our knowledge, to comprehensively assess the risk factors for maternal and perinatal deaths and complications from anaesthesia in low-income and middle-income countries, and the overall risk of maternal death from anaesthesia. Our estimates of the risk in low-income and middle-income countries are significantly higher than those reported in high-income countries such as the USA, where the case fatality rate from general and regional anaesthesia given for caesarean section were 6.5 and 3.8 per million anaesthetics, respectively.<sup>22</sup> We assessed the extent of the problem in detail by assessing rates of death in women who had surgery, and as a proportion of any, direct, and caesarean-section-related maternal deaths. We reported the effects of study quality on mortality estimates. We looked for variations in anaesthesia-attributed maternal mortality rates according to economic regions, individual countries, setting, year, and anaesthesia provider.

Our findings were limited by the differences in quality and reporting of outcomes in the studies. Studies focused mainly on assessing the risks associated with type of anaesthesia, and less on other factors, which limited our synthesis, and we could only provide rates for these risk factors separately. Fewer studies were published in low-income countries that are outside sub-Saharan Africa. The actual rates of anaesthesia-attributed deaths are probably

higher than current estimates because of scarce data from these low-income and middle-income countries with high maternal mortality and poor health-care resources. We used the 2015 World Bank atlas for classification of a country’s income status, and adjustment for year of publication could have resulted in some differences in classification. We noted significant heterogeneity in our findings despite adjusting for various factors because of variations in the characteristics of population, setting, type of anaesthesia, availability of caesarean section, and provider. Few studies provided detailed reports on the underlying cause of death from anaesthesia.

The asymmetry recorded in the funnel plot was the result of high rates of maternal deaths in small studies making them more likely to be published, similar to the effect reported in many non-comparative reviews on proportions.<sup>23</sup> This asymmetry could have slightly overestimated the recorded maternal death rates. However, the magnitude of the bias is probably small in view of the low weight of these studies in the analysis.

Pregnant women requiring general anaesthesia need tracheal intubation to ensure the airway is secure from aspiration. Compared with the general surgical population, pregnant women are at increased risk of complications from general anaesthesia, with eight times higher risk of failed intubation and its associated hazards.<sup>24,25</sup> Our findings support existing data for the role of airway complications, and pulmonary aspiration of gastric contents as major causes of death from anaesthesia, and the need for specific training.<sup>26</sup>

The increased mortality and morbidity that we identified with general anaesthesia could be due to the following reasons: inadequate training and resources, poor general condition of the mother, or concomitant complications such as post-partum haemorrhage. The low Apgar scores associated with general anaesthesia exposure could be indicators of neonatal and anaesthetic facilities, including limited access to modern, volatile anaesthetic agents that minimise fetal respiratory depression.<sup>27</sup> The increased blood loss associated with

exposure to general anaesthesia is similar to the findings of the Cochrane review, which reported higher blood loss with general than regional anaesthesia in pregnant women undergoing caesarean section.<sup>28</sup>

In high-income countries such as the USA, no measured differences were recorded in anaesthetic complications between physician and non-physician anaesthetists.<sup>29–31</sup> However, compared with the rigorous additional training provided to non-physician anaesthetists in the USA, their counterparts in low-income and middle-income countries have very little training, which varies between countries. This discrepancy could have contributed to the recorded increase in maternal mortality when anaesthesia was given by non-physician anaesthetists than their physician counterparts; the risks were also high for non-physicians without adequate training.<sup>21</sup> Many of the reported causes of anaesthesia-attributed deaths such as complications of airway management, pulmonary aspiration with general anaesthesia, and hypotension and high spinal with neuraxial anaesthesia are preventable with appropriate training and resources.<sup>32</sup>

The global definition and classification of anaesthesia-attributed deaths need standardisation to identify the real burden. Anaesthetists should be part of the panel analysing the causes of maternal deaths, and the level of contribution of anaesthesia to the death should be reported clearly.<sup>33</sup> Strategies to reduce maternal mortality should include increasing the number of anaesthetic practitioners managing pregnancy, enhancing the resources available to them, and increasing their level of training in low-income and middle-income countries. Implementation of simple measures, such as the WHO Safer Surgery checklist before and during surgery, and access to simple monitoring technology such as pulse oximetry, could potentially reduce adverse outcomes.<sup>34</sup> The introduction of these measures in anaesthesia providers in high-income countries has reduced maternal death from anaesthetic complications to very low levels. Recent global initiatives such as Lifebox,<sup>35</sup> and training courses done in partnership with non-profit organisations such as Kybele,<sup>36</sup> have focused efforts to improve the safety of surgical procedures. Governmental and non-governmental organisations should prioritise investment in obstetric anaesthesia, to implement the World Health Assembly's resolution to include emergency and essential surgical care and anaesthesia as a component of universal health coverage.<sup>37</sup>

In conclusion, anaesthesia is a major contributor to maternal deaths in pregnant women undergoing surgery in low-income and middle-income countries. Targeted efforts are needed to provide safe obstetric anaesthesia by improving training, infrastructure, and resources.

#### Contributors

ST, JZ, and SS came up with the research question and designed the protocol. SS and KD did the literature search, study selection, and data extraction with the help of ST. JZ and DA-M did statistical analysis. SS designed the tables, figures, and appendices, with input from ST.

MW provided expert anaesthetic advice. SS and ST prepared the initial drafts of the manuscript, with additional input from KSK, AC, MW, and RN. All authors contributed to the drafts and final version of the manuscript.

#### Declaration of interests

We declare no competing interests.

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For more on Kybele see <https://www.oaa-anaes.ac.uk/Kybele>

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