Estimating causes of maternal death in data-sparse contexts

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Abstract

Understanding the underlying causes of maternal death across all regions of the world is essential to inform policies and resource allocation to reduce the mortality burden. However, in many countries there exists very little data on the causes of maternal death, and data that do exist do not capture the entire population at risk. In this paper, we present a Bayesian hierarchical multinomial model to estimate maternal cause of death distributions globally, regionally, and for all countries worldwide. The framework combines data from various sources to inform estimates, including data from civil registration and vital systems, smaller-scale surveys and studies, and high-quality data from confidential enquiries and surveillance systems. The framework accounts for varying data quality and coverage, and allows for situations where one or more causes of death are missing. We illustrate the results of the model on three case-study countries that have different data availability situations.

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1 Introduction and Motivation

Maternal mortality is an important indicator of the health and development of a country. It is explicitly linked to child health and development outcomes, and is strongly associated with women’s education, rights and access to adequate healthcare (McAlister and Baskett 2006; Alvarez et al. 2009; Muldoon et al. 2011; Mbizvo and Say 2012; Alkema et al. 2016; Briozzo et al. 2016). Reducing maternal deaths is a public health priority, with Sustainable Development Goal (SDG) 3.1 aiming to reduce the global maternal mortality ratio (MMR) to less than 70 deaths per 100,000 live births by the year 2030 (UNDESA 2020). Over the past several decades, substantial progress towards this goal has been made, with the global estimate of maternal deaths in 2017 being 35% lower than deaths in 2000 (295,000 compared to 451,000) (WHO et al. 2019). However, substantial disparities exist across countries; in particular, Sub-Saharan African countries account for around 66% of all maternal deaths worldwide.

An important part of understanding differences in levels and trends in overall mortality is determining the main causes of maternal death. Understanding the main causes of death would help to guide how best to improve conditions in regions of the world that are making relatively slow progress towards the 2030 goals, offering direct insight into how resources could be most effectively allocated to reduce overall mortality. As such, the aim of this project was to estimate, for all regions in the world, the proportion of maternal deaths due to major causes, including hemorrhage, sepsis, hypertension, embolism, abortion, indirect causes and other direct causes.

If data existed on every maternal death and the underlying and associated causes, then it would be a simple tabulation exercise to calculate the maternal cause of death distributions for regions worldwide. However, as is the case with most other population statistics and indicators, the degree of data availability on maternal deaths, and the quality of such data, varies substantially across countries. One of the main sources of data on deaths are civil registration and vital statistics (CRVS) systems, which aim to record all vital events (such as births and deaths) for a population. While well-functioning CRVS systems exist in most high-income countries, many lower- and middle-income countries (LMIC) have no such systems in place. Indeed, only 26% of the world’s population lives in countries with complete registration of deaths (CDC 2015). Countries that lack CRVS systems are
concentrated in regions where the overall mortality burden is highest, such as Sub-Saharan Africa and Southern Asia. In such countries, other data sources on maternal mortality may be available, such as data from surveys, or local-level administrative records from hospitals or community health centers. Such data are generally of lower quality and unlikely to be representative of the broader population of interest.

Data issues are further exacerbated when considering the estimation of causes of death. Even if data exist on the total number of maternal deaths in a population, we may not have information on some or all of the causes of maternal death. In a particular population or country, the causes of maternal death reported may vary by year or data source. In addition, the quality of reporting of causes of death varies substantially across populations, even within CRVS systems, and is dependent on factors such as country-level practices and policies, and physician and health official training (Messite and Stellman 1996; Salanave et al. 1999; Eriksson et al. 2013; MacDorman et al. 2016). While cause of death information has a standardized classification system — the International Classification of Diseases (ICD), currently in its 10th revision (ICD-10) — it is not always the case that deaths are reported according to ICD-10 classifications, particularly when data are sourced from surveys or single institution studies.

Data quality and sparsity issues are particularly pertinent in the case of maternal deaths compared to deaths at other ages (for example, child mortality). Although the MMR is much higher than is acceptable in many countries, the absolute number of maternal deaths relative to the number of live births (the measure of exposure to risk) is relatively small. In addition, an important cause of maternal death — deaths due to abortion — are substantially under-reported in many countries, due to definition, cultural and legality issues (Gerdts, Vohra, and Ahern 2013; Gerdts et al. 2015; Abouchadi, Zhang, and De Brouwere 2018). All these data characteristics make the goal of estimating a maternal cause of death distribution particularly challenging.

In this paper we present a Bayesian hierarchical modeling framework to estimate maternal cause of death distributions in contexts of varying data availability and quality. The model estimates a set 14 sub-categories within 7 main categories of maternal death, for each country of interest. The model accounts for varying data quality and coverage, thereby allowing for many different types of data sources to be included to inform estimates. The modeling framework can be easily adapted to
estimate maternal cause of death distributions in a variety of different populations and time periods, in varying data availability contexts.

The remainder of the paper is structured as follows. We first briefly discuss the use of Bayesian modeling in global health estimation in general, and specific efforts to model causes of death. We then outline the goals of estimation and introduce the 14 different categories that make up the cause of death distributions. Section 4 outlines the data sources and availability and how these were processed into the main cause of death categories. Section 5 describes in detail the modeling framework and computational aspects. We then illustrate some key features of the model through illustrative results, and present results from validation exercises in Section 6. Finally, we discuss possible extensions to the modeling framework and future work in Section 7.

2 Background

Statistical modeling frameworks used in demographic and global health estimation have increasingly shifted to using Bayesian methods over the past decade. The introduction of Bayesian methods by the United Nations Population Division to estimate world population trends from 2010 (Raftery, Alkema, and Gerland 2014) paved the way for other UN organizations to follow suit. Many of the global health indicators related to mortality, health, fertility, and family planning are modeled using Bayesian methods (Alkema and New 2014; Alkema et al. 2017; Alexander and Alkema 2018; Cahill et al. 2018; Wakefield et al. 2019).

The majority of models used in these contexts are Bayesian hierarchical frameworks, with a combination of systematic components capturing theoretical relationships or relationships with key covariates, and a temporal component which allows for trends over time to be smoothed and projected forward. For example, Cahill et al. (2018) presents the Family Planning Estimation Model (FPEM), a country-level model of contraceptive use rates among married women of reproductive age from 1990-2020. The model is based on a logistic curve, which assumes that adoption of contraception is expected to start slowly, speed up, then slow down before reaching an asymptote. Specific parameters of the curve are data-driven and modeled hierarchically, with deviations from the expected rate of change modeled with an AR(1) process.
Another example is the ‘Bmat’ model, discussed in Alkema et al. (2017), which describes the estimation method used by the United Nations Maternal Mortality Estimation Interagency Group (MMEIG) to produce country-level trends in the all-cause maternal mortality ratio (MMR). The model consists of a hierarchical model which models the non-HIV/AIDS MMR as a function of the general fertility rate, average number of skilled attendants at birth, and gross domestic product. In addition, country-time-specific deviations are modeled as an ARMA(1,1) process, allowing for noisy observed trends to be smoothed and projected forward. The Bmat model is particularly relevant to this work, as the estimates of all-cause maternal mortality are used as the ‘envelope’ for our cause-specific estimates, meaning that we constrain the total number of maternal deaths to be consistent with those produced by the MMEIG.

In general, Bayesian hierarchical models are particularly suited to problems of estimating global health indicators for a set of multiple populations with varying data quality and availability. For example, the use of informative priors, based on substantive and theoretical knowledge of the process being modeled, is useful to obtain estimates in populations where the level of missing data are high. In addition, hierarchical structures allow for information about mortality and other health trends to be shared across similar populations that may have varying amounts of data availability. Finally, Bayesian models aid in the combination of multiple data sources with varying types of data quality.

2.1 Estimation of cause-specific mortality

In terms of efforts to model and estimate specific causes of death, and with multiple causes being estimated in the same model (that is, the estimation of cause of death distributions), the existing literature mostly focuses on estimating cause-specific child mortality or maternal mortality. This is probably partly driven by research agendas in the Millennium Development (MDG) and Sustainable Development Goal (SDG) eras, of which two important indicators are child and maternal health (as part of SDG 3).

A range of different statistical approaches have been used to model cause of death distributions. For example, Liu et al. (2016) uses a multinomial logistic regression to model cause proportions of under-five child mortality, while making various data adjustments to account for varying data quality and underlying cause profiles. The resulting cause proportions are then applied to the
‘envelope’ (all-cause) estimates produced by the methodology described in Alkema and New (2014) to get death counts. Other approaches to modeling causes of death tend to model causes separately and then rescale or perform post-hoc adjustments to ensure the sum of the deaths by causes adds up to some predefined total. In particular, published estimates of causes specific deaths produced as part of the Global Burden or Disease Study (Naghavi et al. 2017; Wang et al. 2017) rely on a multi-stage ensemble modeling technique which models each cause of death in a similar but separate way. In contrast, Schumacher et al. (2020) present a model that allows for cause- and age-specific child mortality to be estimated from sample registration data, with cause-specific and total deaths being estimated all within the one framework.

Say et al. (2014) present estimates of maternal deaths by cause based on a Bayesian hierarchical framework which models the underlying proportions of death as a multivariate logistic Normal distribution. Assumptions about data quality and coverage are based on the source of the data, and HIV/AIDS maternal deaths are modeled separately. The model we propose in this paper improves on Say et al. (2014) in several ways; in particular, we explicitly account for the type of data, down-weighting data sources of lower quality, and include a much larger data set of observations of causes of maternal deaths, including those from subnational sources, single-causes studies, and potentially multiple data sources for the same country-year.

3 Goals of estimation

A maternal death is defined by the World Health Organization as ‘the death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes’ (WHO 2020). We are interested in obtaining estimates of the proportion of total maternal deaths in a particular country and year by each of the 7 main cause categories (as defined below), including additional breakdowns of 3 main categories into sub-cause categories. Once estimates of the cause of death distribution for each country-year are obtained, they are aggregated across both geographic and time dimensions to obtain estimates of cause of death distribution by SDG region for a specific time period of interest (2009-2017).
3.1 Main cause of death categories

There are many potential cause of death group classifications that we could consider estimating. Motivated by previous work and priorities of health policy agendas (Say et al. 2014), we estimate the proportion of maternal deaths from each of the following seven cause categories:

- Abortion (ABO)
- Embolism (EMB)
- Hypertension (HYP)
- Hemorrhage (HEM)
- Sepsis (SEP)
- Other direct causes (DIR)
- Other indirect causes (IND)

Of particular note are maternal deaths related to HIV/AIDS, which are encompassed in the indirect causes category. However, due to the substantially different epidemiological profile of this death category, as well as vastly different trends over time, we follow previous work on mortality estimation (Alkema and New 2014; Say et al. 2014; Alkema et al. 2017) in restricting our goal to be estimating the proportion of non-HIV/AIDS maternal deaths by cause. Estimates of HIV/AIDS maternal deaths produced elsewhere (UNAIDS 2017; WHO et al. 2019) are then incorporated into the final cause of death distributions (as part of the indirect cause group). See Section 5.5 for more details.

3.2 Cause of death subcategories

In addition to the 7 main cause of death categories listed above, we are interested in estimating further sub-cause breakdowns of hemorrhage, sepsis and other direct cause groups. For hemorrhage (HEM) and sepsis (SEP) deaths, we estimate the following breakdowns based on the timing of death:

- Ante-partum (ANT)
- Intra-partum (INT)
- Post-partum (POS)

For other direct maternal deaths (DIR), we further break down the category into four sub-categories:

- Anesthesia (ANE)
• Obstructed labour (OBS)
• Obstetric trauma (OBT)
• Other causes (OTH)

Thus, a total of 14 separate causes of death categories are estimated. Figure 1 summarizes the classification of data available on maternal deaths, and the cause of death categories to be estimated. Maternal deaths are first classified as either deaths due to HIV/AIDS or non-HIV/AIDS. Of the non-HIV/AIDS deaths, these can be further classified into one of the 7 main cause of death categories. For deaths due to hemorrhage (HEM), sepsis (SEP), and other direct causes (DIR), we further classify into one of 10 sub-cause categories. In each stage of the classification process, if no further information is available, these deaths are excluded from the analysis.

Figure 1: Organization of maternal deaths into analysis categories. Non-HIV/AIDS deaths are classified into 7 main cause of death categories, of which hemorrhage (HEM), sepsis (SEP), and other direct causes (DIR) are classified further. After estimation of the main distribution using only non-HIV/AIDS observations, externally obtained estimates of HIV/AIDS are added to the other indirect causes (IND) category to give the complete distribution.
4 Data

4.1 Overview of data sources

Data on maternal deaths by cause come from three main sources: Civil Registration and Vital Statistics (CRVS) systems; ‘grey literature,’ which refers to government reports, technical reports and other non-peer-reviewed publications; and ‘studies,’ which were the result of a large-scale systematic literature review. CRVS systems and grey literature provide national-level data. Data from studies, on the other hand, can be from a number of different geographic levels. While some may be at the national level, many refer to subnational areas, for example Administrative 1 level (ADM1, state/province), Administrative 2 level (county), or lower. Indeed, in many cases, studies may only report observation from a single hospital or group of hospitals or other health institutions.

4.2 Overview of data availability

| SDG Region                      | Number of countries | Number of observed country-years | CRVS | Grey Literature | Studies ADM1 or higher | Studies Below ADM1 | Prop. country-years missing 2+ causes |
|---------------------------------|---------------------|---------------------------------|------|-----------------|------------------------|-------------------|-----------------------------------|
| Central and Southern Asia       | 12                  | 122                             | 31   | 16              | 2                      | 73                | 0.533                             |
| Europe and Northern America     | 36                  | 260                             | 252  | 8               | 0                      | 0                 | 0.738                             |
| Northern Africa and Western Asia| 18                  | 91                              | 81   | 6               | 0                      | 4                 | 0.538                             |
| Oceania excl. Australia and New Zealand | 3     | 7                               | 4    | 1               | 0                      | 2                 | 0.714                             |
| Sub-Saharan Africa              | 28                  | 151                             | 18   | 20              | 15                     | 98                | 0.642                             |
| Latin America and the Caribbean | 31                  | 218                             | 207  | 10              | 0                      | 1                 | 0.339                             |
| Australia and New Zealand       | 2                   | 26                              | 16   | 10              | 0                      | 0                 | 0.846                             |
| Eastern and South-Eastern Asia  | 12                  | 75                              | 46   | 9               | 2                      | 18                | 0.467                             |

Over the period of interest (2009–2017), at least one observation of cause-specific maternal mortality were available for 142 of the 183 UN member countries. Table 1 provides a breakdown of the available data by SDG region. The majority of available country-year observations, roughly 70%, come from CRVS data. Most notably these are observations from Europe and Northern America or
Latin America and the Caribbean. In other regions, data from the grey literature and studies play a particularly important role. For instance, as Table 1 demonstrates, the vast majority of available data for Sub-Saharan Africa and Central and Southern Asia come from various subnational studies.

It is worth noting that it is not uncommon for a country-year to report maternal mortality counts for only a subset of the cause categories that we are interested in estimating. As illustrated in the rightmost column of Table 1, the majority of the country-year observations in each region have two or more causes missing.

### 4.3 Classification into cause of death groups and subgroups

Where possible, deaths are assigned into one of the 14 cause categories listed in Section 3.1 and 3.2 above. This is straightforward when deaths are classified according to ICD-10 codes, which is the case for the majority of data (encompassing all CRVS and some studies and grey literature data). The assignment of ICD-10 codes to each of the 14 cause categories is summarized in Appendix A.

However, for the studies and grey literature data, classification into cause categories is more complex. In many studies the cause of death is referred to using a free text description, rather than an ICD-10 code. Sometimes the free text can be clearly translated into an ICD-10 code or be identified as one of the broader level ICD-10 cause groups defined by the WHO (WHO 2012) and, hence, designated into one of the seven main cause categories. Other times, the free text describes more than a single ICD-10 code or cause group associated with a number of maternal deaths. In such cases we rely on the clinician’s expert interpretation of the correct proportion of maternal deaths corresponding to each code or cause group. Cases where the cause of death could not be assigned (for example, instances where only the likely organ system causing the death could be identified from free text) were excluded from the analysis.

### 4.4 Other data sources

In addition to data on causes of maternal death, we make use of a number of other data sources in the model. We use annual all-cause female mortality estimates from the UN World Population Prospects (WPP) 2019 edition to assess the coverage, and subsequently the ‘usability,’ of death data observed by country (UNPD 2019). We also employ the UN Maternal Mortality Estimation
Inter-Agency Group’s (MMEIG) 2019 estimates on maternal mortality to obtain an estimate for
the total number of maternal deaths, and the number of maternal deaths due to HIV/AIDS (WHO
et al. 2019).

Additional information on data adjustments related to the treatment of zero reported deaths,
HIV/AIDS deaths, and multi-year studies are detailed in Appendix B.

5 Model

5.1 Overview

We begin with grouping the observed non-HIV/AIDS cause-specific death counts for each country
into 7 main cause of death categories, and we model these as coming from a multinomial distribution
with 7 categories. The relative proportions in the multinomial distribution then depend primarily
on regional and country-level differences. Additionally, we include an error term applied only to
lower quality data to allow for deviation from the assumed true country mean to lessen the impact
of potentially misrepresentative observations.

As detailed in Section 3, subdistributions for certain categories are also calculated. The DIR, HEM,
and SEP counts are further divided into separate multinomial distributions representing more
granular classifications of cause of death. Similar to the main cause distribution, these are modeled
as the sum of regional and country-level differences.

The true main cause of death distribution and the subcause distributions for each country are
calculated using the estimated regional and a weighting of the estimated country-level differences.
In order to reflect increased uncertainty in countries where data coverage is low, the weight given to
the country’s specific estimated term depends on the coverage of the available data in that country.

5.2 Notation

For \( i = 1, \ldots, N \), let \( y_i = (y_{i,1}, \ldots, y_{i,7}) \) be the observed non-HIV/AIDS maternal deaths by
cause, where \( y_{i,j} \) is the number of deaths in the \( i \)th observation attributed to cause group \( j \),
for \( j \in \{ABO, EMB, HEM, SEP, DIR, IND, HYP\} \). Define the total number of observed non-
HIV/AIDS maternal deaths for the \( i \)th observation to be \( d_i \).
Point estimates from the MMEIG of the HIV/AIDS-omitted total number of maternal deaths in a country-year $ct$ are denoted as $\hat{d}_{ct}$.

5.3 Model for observed cause proportions

Deaths in each observation are modeled using a multinomial distribution. The log-ratios of proportions are taken to be the sum of an intercept, region effect, and country effect. However, for observations from CRVS or studies data, an additional adjustment is applied to allow for deviation from the true country mean. This adjustment allows us to partially mitigate the impact of potentially misrepresentative observations that arise from lower quality data.

For observation $i$, the multinomial proportions $(p_{i,1}, \ldots, p_{i,7})$ are modeled as

$$y_i \sim \text{Multinomial}(d_i, p_i)$$

$$p_i = (p_{i,1}, \ldots, p_{i,7})$$

$$\log \left( \frac{p_{i,j}}{p_{i,7}} \right) = \beta_{0,j} + \beta_{r(c(i)),j} + u_{c(i),j} + q_{i,j},$$

where $c(i)$ refers to country of observation $i$, and $r(c(i))$ corresponds to the region of that country. The log-ratio of proportions for category $j$ relative to category 7 (HYP) is taken to be the sum of an intercept term $\beta_{0,j}$, a region effect $\beta_{r(c(i)),j}$, a country effect $u_{c(i),j}$ and a data quality adjustment term $q_{i,j}$.

The region effects are pooled with a global variance term. For all regions $r = 1, \ldots, R$,

$$\beta_{r,j} \sim \text{Normal}(0, \sigma_\beta^2)$$

$$\sigma_\beta \sim \text{Normal}(0, 1^2).$$

The regions $r = 1, \ldots, R$ are the same as those used by Say et al. (2014), which broadly aim to group countries that are believed to be epidemiologically similar. This region classification is distinct from the SDG region system used for aggregating and reporting results. More details on the modeling region classification are given in Appendix C.
5.3.1 Multinomial likelihood and missing values

In an ideal situation where counts for all categories are recorded, each \( y_i \) is treated as a 7-category multinomial observation with probabilities \((p_{i,1}, \ldots, p_{i,7})\). For observation \( i \), let the ratio of proportion \( j \) to the reference category be denoted \( g_{ij} \). That is,

\[
p_{i,j} = g_{i,j} = \exp(\beta_{0,j} + \beta_{r(c(i))},j + u_{c(i),j} + q_{i,j}).
\]

The probabilities can then be expressed

\[
p_{i,j} = \frac{g_{i,j}}{\sum_{k=1}^{7} g_{i,k}},
\]

and the corresponding multinomial likelihood \( L_M \) for all \( N \) observations is

\[
L_M = \left( \prod_{i=1}^{N} \prod_{j=1}^{7} p_{i,j}^{y_{i,j}} \right) = \left( \prod_{i=1}^{N} \prod_{j=1}^{7} \left( \frac{g_{i,j}}{\sum_{k=1}^{7} g_{i,k}} \right)^{y_{i,j}} \right).
\] (1)

However, as stated in Section 4, there are observations for which certain categories’ counts are considered to be missing. In such cases where we believe an apparent zero count is some category \( k \) is unreliable, we wish to treat \( y_{i,k} \) as unknown instead.

We can accomplish this by treating the observation as a multinomial observation with a reduced number of categories. For example, if \( j = 1 \) (ABO) is missing for observation \( i \), then the likelihood contribution for that observation would instead be

\[
\prod_{j=2}^{7} \frac{g_{i,j}^{y_{i,j}}}{\sum_{k=2}^{7} g_{i,k}^{y_{i,j}}}.
\]

where the probabilities \((\hat{p}_{2,j}, \ldots, \hat{p}_{i,7})\) are the original probabilities rescaled to sum to 1.

An appropriately reduced multinomial is used for every observation with any combination of missing categories.
5.3.2 Country-specific effect and correlations across causes

We allow for the possibility of correlations between death categories in countries’ cause of death distributions. Intuitively, because of co-morbidities and common, systematic underlying factors affecting maternal health, we would expect certain death categories to co-occur.

In order to capture correlations in countries’ cause of death distributions, the country effects $u_{c,j}$ are modeled as multivariate normal with a common 6x6 covariance matrix $\Sigma$. We decompose $\Sigma$ into its correlation matrix $\Omega$ and diagonal matrices of variance terms, $\Sigma = \text{diag}(v) \Omega \text{diag}(v)$. An LKJ(1) prior is used for $\Omega$ (Lewandowski, Kurowicka, and Joe 2009; Stan Development Team 2019). For each country $c = 1, \ldots, C$,

$$(u_{c,1}, \ldots, u_{c,6}) \sim \text{MVN}(0, \Sigma)$$

$$\Sigma = \text{diag}(v) \Omega \text{diag}(v)$$

$$\Omega \sim \text{LKJ}(1)$$

$$v \sim \text{Normal}(0, 3).$$

5.3.3 Data-quality adjustment

Even where cause of death data are available, the data may be misrepresentative due to systematic deficiencies and biases in data collection processes. In our model, we classify observations into 4 data quality ‘types’, and incorporate this information into the model by including an extra error term for observations from lower quality types, partially mitigating the impact of these observations on the country means.

The data quality type classification of each observation depends on the source and estimated coverage of the observation. Type 1 observations consist only of observations arising from grey literature. These are considered to be of the highest quality, and no additional adjustment is applied to these data.

Observations collected from studies are assigned to be Type 4, the lowest quality, since the included studies may from subnational regions, and also may not aim to be a comprehensive surveying of all causes of maternal death.
Observations from CRVS data can be classified as Type 2, 3, or 4, depending on the estimated coverage of the data. We follow a similar approach to Say et al. (2014) in defining a ‘usability’ index, which is a function of the presence of ill-defined deaths, the coverage of the observed number of deaths, and the presence of contributory-cause misclassification.

For observations where the number of observed maternal deaths is no more than 5, the usability index is calculated using the proportion of ill-defined deaths denoted $p_{i}^{\text{ill}}$, and the all-cause (maternal and otherwise) female death coverage $C_{i}$ of the observation. This is calculated as the ratio of all-cause death count in the CRVS system to the all-cause death count estimate from WPP 2019 (UNPD 2019). In particular, the usability for CRVS observation $i$, $\nu_{i}$ is calculated as

$$
\nu_{i} = \frac{d_{i}}{d_{ct(i)}} (1 - p_{i}^{\text{ill}}).
$$

If there are more than 5 maternal deaths in an observation, then we also consider the proportion $p_{i}^{\text{contr}}$ of maternal deaths attributed to contributory causes. Maternal deaths should always be classified with a main ICD-10 code that is an underlying cause of death, not a contributory cause of death. If contributory causes are listed as the main cause of death, then this suggests CRVS systems of a lower quality. In particular, where there are more than 5 maternal deaths observed, $\nu_{i}$ is calculated as

$$
\nu_{i} = \frac{d_{i}}{d_{ct(i)}} (1 - p_{i}^{\text{ill}})(1 - p_{i}^{\text{contr}})
$$

The usability index $\nu_{i}$ is then used to classify CRVS data into types 2, 3, or 4 as follows:

- the observation is classified as type 2 if $\nu_{i} > 85\%$ and is one of three consecutive years with $\nu_{i} > 60\%$,
- type 3 if $65\% < \nu_{i} \leq 85\%$ and is one of three consecutive years with $\nu_{i} > 60\%$, and
- type 4 otherwise.

For observations arising from type 2, 3, or 4 data sources, a data adjustment term $q_{i,j}$ is individually realized from a Normal distribution for each observation, with an estimated variance term dependent
Table 2: Summary of data quality type classification. Highest quality data is classified as type 1, and lowest quality data is classified as type 4. Data quality is assessed based on data source and a calculated usability index.

| Type | Sources                                      |
|------|----------------------------------------------|
| 1    | most grey literature observations            |
| 2    | some grey literature observations; high usability CRVS |
| 3    | medium usability CRVS                        |
| 4    | low usability CRVS; studies                  |

on the type of data source. For each observation \(i\) and cause \(j\),

\[
q_{i,j} = \begin{cases} 
0 & \text{if type}(i) = 1 \\
\sim \text{Normal}(0, \sigma_{\text{type}(i)}^2) & \text{if type}(i) = 2, 3, 4 
\end{cases}
\]

\[\sigma_{\text{type}} \sim \text{Normal}(0, 0.25^2).\]

5.4 Estimation of true proportions

Although some observations may have large death counts, they may only represent a fraction of the true number of maternal deaths in that country-year, which we take to be the MMEIG point estimate \(\hat{d}_{ct}\). In these cases where a large fraction of the deaths are unrecorded or unclassified, we may have an unduly high degree of certainty in our estimate of \(p_{i,j}\). We therefore apply a weighting scheme to better reflect our uncertainty where data coverage is low. For country \(c\), let \(w(c) \in [0, 1]\) be the maximum coverage among its observations. If \(ct(i)\) refers to the country-year of observation \(i\), then

\[w(c) := \max_{i:ct(i)=c} \frac{d_i}{\hat{d}_{ct(i)}}.\]

The weight \(w(c)\) is then used to regulate the contribution of the estimated country effect \(u_{c,j}\). For countries with only low-coverage observations (\(w(c)\) is low), the country-specific information is considered incomplete, and the estimate should therefore lean more heavily towards the region mean rather than the observed country mean. The estimate of the true HIV/AIDS-omitted cause of death
distribution is calculated as
\[
\log \left( \frac{p_{c,j}^*}{p_{c,7}^*} \right) = \beta_{0,j} + \beta_{r(c),j} + w_c \cdot u_{c,j} + (1 - w_c) \cdot \tilde{u}_{c,j}
\]
\[
\tilde{u}_c \sim \text{MVN}(0, \Sigma),
\]
where \( \tilde{u}_c \) is a new generic realization of the country effect.

### 5.5 Incorporating HIV/AIDS deaths

Deaths from HIV/AIDS are treated separately. Recall that \( \hat{d}_{ct} \) denotes the HIV/AIDS-omitted MMEIG estimate of maternal deaths in country-year \( ct \). Let \( \hat{d}_{ct,HIV} \) denote the MMEIG point estimate of the number of HIV/AIDS deaths in country-year \( ct \), and let \( \hat{p}_{ct,HIV} = \hat{d}_{ct,HIV}/(\hat{d}_{ct,HIV} + \hat{d}_{ct}) \) denote the MMEIG-estimated proportion of maternal deaths attributed to HIV/AIDS.

Similarly, let \( \hat{p}_{i,HIV} = d_{i,HIV}/(d_i + d_{i,HIV}) \), where \( d_i \) and \( d_{i,HIV} \) denote the analogous quantities from observation \( i \).

Define \( \sigma_{HIV} = \text{sd}(\hat{p}_{i,HIV} - \hat{p}_{ct(i),HIV}) \). Then
\[
\hat{p}_{ct,HIV} \sim \text{Normal}(\hat{p}_{ct,HIV}, (\hat{p}_{ct,HIV} \cdot \sigma_{HIV})^2) T(0,1)
\]
\[
d'_{ct,HIV} = \hat{p}_{ct,HIV} \cdot (d_{ct,HIV} + \hat{d}_{ct}).
\]

We then add the HIV/AIDS deaths \( d'_{ct,HIV} \) to the to the IND group, and recalculate proportions to obtain the final HIV/AIDS-inclusive country-year distributions \( (p'_{ct,1}, \ldots, p'_{ct,7}) \). We do this by converting the HIV/AIDS-omitted proportions \( p_{c,j}^* \) into counts \( d_{ct,j}^* \), adding the estimated HIV/AIDS counts appropriately, and rescaling these counts into proportions:
\[
d_{ct,j}^* = p_{c,j}^* \cdot \hat{d}_{ct}
\]
\[
d'_{ct,j} = \begin{cases} 
  d_{ct,j}^* + d'_{i,HIV} & \text{if } j = \text{IND} \\
  d_{ct,j}^* & \text{otherwise}
\end{cases}
\]
\[
p'_{ct,j} = \frac{d'_{ct,j}}{\sum_{l=1}^{7} d'_{ct,l}}.
\]
5.6 Calculating regional and global cause of death distributions

Regional cause of death distributions are obtained by aggregating country death counts. For (SDG) regions \( h = 1, \ldots, H \) (distinct from regions \( r = 1, \ldots, R \) used above in the model), the countries’ HIV/AIDS-inclusive counts \( d'_{ct,j} \) are aggregated accordingly to obtain regional counts for each cause

\[
d'_{h,j} = \sum_{h(c)=h} d'_{ct,j}. 
\]

The counts are then normalized to give proportions

\[
p'_{h,j} = \frac{d'_{h,j}}{\sum_{l=1}^{7} d'_{h,l}}. 
\]

Similarly, global estimates are obtained by aggregating regional death counts and normalizing

\[
d'_{\text{global},j} = \sum_{h=1}^{H} d'_{h,j}, 
\]

\[
p'_{\text{global},j} = \frac{d'_{\text{global},j}}{\sum_{l=1}^{7} d'_{\text{global},l}}. 
\]

5.7 Subcause distribution estimation

Within the cause groups HEM, SEP, and DIR, we are interested in a finer classification of cause of death. For each of these three main categories \( j \), let \( K_j \) denote the number of subcategories. These categories can be further subdivided as follows.

1. Within the hemorrhage (HEM) category, deaths can be classified as antepartum (HEM\(_{\text{ante}}\)), intrapartum (HEM\(_{\text{intra}}\)), and postpartum (HEM\(_{\text{post}}\)) hemorrhage. \( K_{\text{HEM}} = 3 \).
2. The sepsis (SEP) category can similarly be divided into antepartum (SEP\(_{\text{ante}}\)), intrapartum (SEP\(_{\text{intra}}\)), and postpartum sepsis (SEP\(_{\text{post}}\)). \( K_{\text{SEP}} = 3 \)
3. The direct cause (DIR) category can be divided into (DIR\(_{\text{obs}}\)), (DIR\(_{\text{ane}}\)), (DIR\(_{\text{obt}}\)), and other direct causes (DIR\(_{\text{oth}}\)). \( K_{\text{DIR}} = 4 \).

The subcategory estimation procedure is similar to the main categories’ procedure, with some key differences. First, there is no data quality error term \( q \) in the estimation of the log ratio of
proportions. Second, in the estimation of true proportions, we modify the weights that balance the estimated country effect \( u \) and the new realization of the country effect, \( \bar{u} \). In the main category model, we use the \( w_c \) and \( 1 - w_c \), where \( w_c \) is defined as the maximum coverage of any single country-year observation for country \( c \). This was to reflect the uncertainty that arises from not observing up to a proportion of \( 1 - w_c \) of the maternal deaths in a country-year. An analogous statistic for the subcategory distributions is not readily available, since we don’t know specifically the coverage of deaths in some category \( j \). For simplicity, we continue to use \( w_c \) for the purpose of reflecting unobserved deaths in the HEM, SEP, and DIR subdistributions. However, an additional complication is that more granular information is unavailable for some observations. For instance, some deaths may be attributed to hemorrhage but no further information is given about the timing, and therefore do not hold useful information about the subdistribution.

To account for this the subcategory model, we use the weight \( z_{c,j}w_c \) and \( 1 - z_{c,j}w_c \), where \( z_{c,j} \) is defined as the maximum proportion, among observations for country \( c \), of deaths in category \( j \) that have subcategory information available.

5.8 Implementation and Computation

5.8.1 Equivalent Poisson Likelihood

We implement the multinomial model using an equivalent Poisson likelihood. The Poisson implementation speeds up computation, and easily allows for arbitrary combinations of missing values. We rely on a result presented by Ghosh, Zhang, and Mukherjee (2006) which states that the multinomial likelihood in Equation (1) is equivalent to the Poisson likelihood

\[ L_P = \prod_{i=1}^{N} \prod_{j=1}^{7} (g_{ij} \exp(\phi_i)^{y_{ij}} \exp(-g_{ij} \exp(\phi_i)) \]

where \( \phi_i \) have independent improper priors \( p(\phi_i) \).

Note that if, for each observation \( i \), some arbitrary subset of categories \( J_i \subset \{1, \ldots, 7\} \) is missing, and the desired reduced multinomial is across the categories \( \{1, \ldots, 7\} \setminus J_i \), then the likelihood
reduces to

\[ L_P = \prod_{i=1}^{N} \prod_{j \in \{1,...,7\}\setminus J_i} (g_{ij} \exp \phi_i)^{y_{ij}} \exp(-g_{ij} \exp \phi_i). \]

in which the unused terms in \( J_i \) can simply be omitted from the likelihood while the other terms remain unchanged.

In practical terms, this means we treat non-missing count \( y_{ij} \) as coming from a Poisson distribution,

\[ y_{ij} \sim \text{Poisson}(g_{ij} \cdot \exp \phi_i), \]

omitting missing counts from the likelihood evaluation. Importantly, this means we do not have to rescale the probabilities to 1 for the reduced multinomial likelihood, which would require recalculation of the denominator \( \sum_{j \notin K_i} g_{ij} \) for each observation.

5.8.2 Computation in Stan

Posterior samples were obtained using Hamiltonian Monte Carlo implemented in Stan via the cmdstanR R package version 0.2.0, with 4 parallel chains of 6000 warmup iterations and 4000 sampling iterations (Stan Development Team 2019; Gabry and Češnovar 2020). Standard checks for \( \hat{R} \) and effective sample size were performed. This computation was enabled in part by resources provided by Compute Ontario (https://computeontario.ca/) and ComputeCanada (https://www.computecanada.ca/).

6 Results

In this section we illustrate some results of the estimation process at the regional level and also for the three case-study countries. We also present results of model validation exercises.

6.1 Results by region

Figure 2 illustrates the estimates and 95% credible intervals for the maternal cause of death distributions (showing the seven main causes of death categories) for the seven SDG regions. The results show substantial differences in the both the cause of death distributions by region and also the uncertainty around the resulting estimates.
The estimates for the Europe and North America, and Australia and New Zealand regions, which both encapsulate high income countries, are fairly similar. In particular, the proportion of deaths due to indirect causes is relatively high, which is expected given these countries are in the late stage of the epidemiological transition (Nair, Nelson-Piercy, and Knight 2017). Additionally, the uncertainty around the estimates in these regions is relatively low, which is a consequence of the large amount of data available in these countries. The Latin American and the Caribbean region also has a relatively high proportion of indirect deaths and low uncertainty, but additionally has a high proportion of deaths due to hypertension.

In other regions, such as in Africa and Asia, the proportion of deaths due to hemorrhage is much higher, which partly reflects lack of access to high quality health care and skilled attendants at birth (Prata et al. 2011; Montgomery et al. 2014; Maduka and Ogu 2020). Larger uncertainty intervals are mostly due to a lack of data available, apart from in Oceania where the uncertainty is mostly driven by small population sizes.

Figure 2: Estimates and 95% credible intervals for the maternal cause of death distributions for SDG regions
6.2 Case studies

Figure 3 illustrates the observed and estimated cause of death distributions for the three case-study countries under three different model set-ups, to illustrate the effect of different model components. Country A is a country with relatively low maternal mortality levels, with good-quality CRVS data available. Country B is a country with relatively high maternal mortality but only has data available from subnational studies. Country C has CRVS data with some issues, in particular there are a high number of mis-classified ‘other direct’ maternal deaths. In addition, Country C also has one high-quality data observation available from a maternal mortality surveillance study.

In each of the graphs, the dots represent the observed proportions by cause sequentially over 2009–2017. If the particular data source of interest contained sequential years then the dots are joined together with a line (for example, CRVS data in countries A and C). Note that the multiple proportions equal to one observed in country B refer to single-case studies, i.e. studies where only one cause of death was reported.

The columns of the figure show the implied estimates for three different modeling set-ups. The first, shown on in the left-hand column shows the results from a model with no quality adjustment and no weighting to account for under-coverage. The middle column shows the results based on a model with a quality adjustment but no weighting. And finally, the right-hand column shows the results from a model with both the quality and coverage adjustments, which is equivalent to the model described above.

There are several observations to note. Firstly, the estimates for Country A do not change substantially across the three model alternatives. This reflects the fact that Country A’s CRVS system is considered of good quality and high coverage.

Secondly, looking at Country B, the addition of the quality term (from the left to middle column) increases the uncertainty around the estimates only slightly, after accounting for the study data being of relatively poor quality. However, the addition of the weighting (from the middle to right column) changes both the point estimates and uncertainty intervals substantially. This is a consequence of the severe under-coverage of the available data in Country B. Although there is one relatively large study available in Country B with approximately 1400 deaths reported, this is still substantially
lower than the estimated 66000 total number of maternal deaths here in 2015. As a consequence, the final estimates for this country are weighted more heavily towards its regional distribution (possibly away from its own observed proportions), and the uncertainty around the estimates is much larger.

Finally, Country C is an example where the CRVS data have known issues, but available data is supplemented with high-quality surveillance data (‘grey literature’). Going from left to right, the inclusion of a data quality term has a substantial effect on the point estimates, as the estimates are pulled to be more in line with the grey literature (in particular for other direct deaths). The final step of weighting has minimal impact as the coverage of both these data sources is relatively high.

6.3 Validation: sensitivity to data exclusion

To assess the sensitivity of the cause of death distribution estimates, we performed a series of validation exercises leaving out certain types of data. Firstly, we were interested in sensitivity to exclusion of all data from studies, as these data represented a large amount of additional information compared to previous efforts (Say et al. 2014). Additionally, we assessed the change in the estimates when data from high-income countries were left out. These countries have relatively large amounts of data available and therefore run the risk of being overly influential in the hierarchical model set-up. Finally, we assessed the sensitivity of estimates to an exclusion of 20% of the data of each type (CRVS, studies and grey literature).

Table 3 shows the mean absolute difference between estimates by cause across SDG regions when the model was rerun excluding any information from studies. Similar results for the other two exercises (leaving high-income country data out and 20% of the data out) are shown in Appendix D. In general, differences in estimates are small across all causes and regions, particularly in Europe and North America, Australia and New Zealand, and Latin America and the Carribean. In these regions the availability of CRVS data is high and little information comes from studies. The mean absolute differences are by far largest in Sub-Saharan Africa, with the mean difference in embolism, hemorrhage and sepsis proportions being at least 0.02. The relatively larger differences in Sub-Saharan Africa are expected, given the lack of other data available in this region means the data from studies is quite influential.
Figure 3: Observed proportions (shown as points), and estimates (shown as bars) with 95% credible intervals for three case study countries, using three different model set-ups. The final model, shown in the right-most column, accounts for data coverage and data quality.
Table 3: Mean absolute difference in estimated country proportions, leaving out observations from studies

| Cause | Central and Southern Asia | Europe and Northern America | Northern Africa and Western Asia | Oceania excl. Australia and New Zealand | Sub-Saharan Africa | Latin America and the Caribbean | Australia and New Zealand | Eastern and South-Eastern Asia |
|-------|---------------------------|----------------------------|---------------------------------|----------------------------------------|-------------------|-------------------------------|--------------------------|--------------------------------|
| ABO   | 0.009                     | 0.001                      | 0.001                           | 0.007                                  | 0.007             | 0.001                         | 0.001                    | 0.001                           |
| DIR   | 0.007                     | 0.002                      | 0.003                           | 0.008                                  | 0.016             | 0.003                         | 0.002                    | 0.009                           |
| EMB   | 0.006                     | 0.003                      | 0.005                           | 0.012                                  | 0.027             | 0.002                         | 0.001                    | 0.008                           |
| HEM   | 0.009                     | 0.002                      | 0.006                           | 0.010                                  | 0.021             | 0.002                         | 0.003                    | 0.011                           |
| SEP   | 0.014                     | 0.002                      | 0.003                           | 0.011                                  | 0.020             | 0.002                         | 0.003                    | 0.008                           |
| IND   | 0.005                     | 0.003                      | 0.004                           | 0.010                                  | 0.010             | 0.003                         | 0.003                    | 0.009                           |
| HYP   | 0.008                     | 0.002                      | 0.003                           | 0.009                                  | 0.017             | 0.002                         | 0.001                    | 0.007                           |

7 Discussion

In this paper we presented a Bayesian hierarchical framework to estimate maternal cause of death distributions at the global, regional and national levels. A total of 14 cause groups are estimated, encompassed within the 7 main categories of causes of death: abortion, embolism, hemorrhage, hypertension, sepsis, other direct causes and indirect causes. The framework allows for data from various sources to be combined, and accounts for the fact that we usually do not have data on all cause of death categories. The framework pools information across regions, accounts for correlation between cause groups, and includes adjustments for data quality and coverage of the observed deaths, utilizing information on total maternal mortality and all-cause mortality more broadly. We illustrated the model on three cases of varying data availability and quality. While our motivation was to estimate causes of maternal death, the framework could easily be adapted and applied to estimate cause of death distributions for other key population sub-groups, such as under-five mortality or premature mortality.

The model framework has several advantages over previous efforts to estimate causes of maternal death. Firstly, while previous efforts chose the one ‘best data source’ available for each country, we account for data quality in the model, which in turn allows data from multiple sources for a particular country to be included in the model (Say et al. 2014). Secondly, we account for under-coverage of available data by weighting the final estimate by the observed number of total maternal deaths. This means the final estimate for a particular country is informed not only by the available data but also mortality trends in the broader region. Finally, the model accounts for missing observations of causes of death and allows for studies where only a single cause of death is observed to be included in the estimation process.
There are, however, some limitations to our approach. One of the main limitations is that we do not adjust for non-representativeness or bias of data sources. For example, many of the smaller studies that were included where CRVS data do not exist come from single institutions or a group of healthcare institutions from residential areas that are relatively urban. However, women included in these studies may not be representative of the broader population. In addition, causes of maternal death that are observed in healthcare facilities are likely to be different to causes of maternal death that happen in community centers or if the death occurs at home. While we include a data quality term in the model, this only adds uncertainty to the data, rather than adjusting the proportions of a particular cause up or down. In addition, the re-weighting of estimates based on under-coverage implicitly assumes the data we have is a representative sample of the broader population, and also assumes cause of death distributions are similar within geographical regions. In practice, is it usually very difficult or impossible to know the types of women captured within a study (in terms of their age, socioeconomic status, pre-existing conditions, etc) and how this differs from the broader population, and thus how it could be post-stratified to be more representative. Future work will aim to explore options to better account for non-representative samples, and include adjustments for countries where possible.

A second limitation is that we do not account for the uncertainty in cause of death classifications. Much of the data that came from studies had to be translated into one of the cause of death categories from ‘free text’ descriptions of cause. In some cases it may have not necessarily been clear which cause of death category observations belong to (there may be one or two possibilities). In these cases we split deaths equally based on possible categorizations and did not account for the relative likelihood or observing one cause over another.

Reducing maternal mortality continues to be an integral part of the Sustainable Development Goal agenda. The latest report from the MMEIG on maternal mortality suggests that many countries are not on track to reach the goal of less than 70 deaths per 100,000 live births by 2030. In particular, the 10 countries with the highest MMRs in 2017 have seen a stagnation or slowing of the annual rate of reduction of maternal mortality, and therefore remain at the greatest risk (WHO et al. 2019). Understanding the underlying causes of maternal death is necessary to evaluate progress and aid resource allocation. The importance of reducing maternal mortality as a public health priority
justifies continued efforts to improve not only estimates but also the data collected on causes of death.

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### Assignment of ICD-10 codes to cause of death categories

Table 4 gives the classification of ICD-10 codes into the seven main cause of death categories. Where appropriate, the classification is further broken down by sub-categories.

**Table 4: ICD-10 codes corresponding to the seven main cause categories.**

| Main Cause      | Sub-cause | ICD-10 Codes                                      |
|-----------------|-----------|---------------------------------------------------|
| Abortion        |           | O00, O00.0, O00.1, O00.2, O00.8, O00.9, O01, O01.0, O01.1, O01.9, |
|                 |           | O02, O02.0, O02.1, O02.8, O02.9, O03, O03.0, O03.1, O03.2, O03.3, |
|                 |           | O03.4, O03.5, O03.6, O03.7, O03.8, O03.9, O04, O04.0, O04.1, |
|                 |           | O04.3, O04.5, O04.6, O04.7, O04.8, O04.9, O05, O05.0, O05.1, |
|                 |           | O05.2, O05.3, O05.4, O05.5, O05.6, O05.7, O05.8, O05.9, O06, |
|                 |           | O06.0, O06.1, O06.2, O06.3, O06.4, O06.5, O06.6, O06.7, O06.8, |
|                 |           | O06.9, O07, O07.0, O07.1, O07.2, O07.3, O07.4, O07.5, O07.6, |
|                 |           | O07.7, O07.8, O07.9                                 |
| Embolism        |           | O22, O22.3, O22.5, O22.8, O22.9, O87, O87.1, O87.3, O87.9, O88, |
|                 |           | O88.0, O88.1, O88.2, O88.3, O88.8, O87.0, O87.2, O87.8     |
| Hemorrhage      | Ante-partum| O20, O20.0, O20.8, O20.9, O44, O44.1, O45, O45.0, O45.8, O45.9, |
|                 |           | O46, O46.0, O46.8, O46.9, O71.0                  |
|                 | Intra-partum| O43, O43.2, O67, O67.0, O67.8, O67.9, O71.1, Rupture NOS |
|                 | Post-partum| O72, O72.0, O72.1, O72.2, O72.3                    |
|                 | Timing Unknown| O71.3, O71.4, O71.7, Hemorrhage NOS                |
| Hypertension    |           | O11, O12, O12.0, O12.1, O12.2, O13, O14, O14.0, O14.1, O14.2, |
|                 |           | O14.9, O15, O15.0, O15.1, O15.2, O15.9, O16        |
|                 | Anaesthesia| O29, O29.0, O29.1, O29.2, O29.3, O29.5, O29.6, O29.8, O29.9, O74, |
|                 |           | O74.0, O74.1, O74.2, O74.3, O74.4, O74.6, O74.7, O74.8, O74.9, |
|                 |           | O89, O89.0, O89.1, O89.2, O89.5, O89.6, O89.8, O89.9, O74.5, O89.4 |
|                 | Obstetric Trauma| O71.2, O71.5, O71.6, O71.8, O71.9                  |
|                 | Obstructed Labor| O33, O33.0, O33.3, O33.4, O33.5, O33.9, O62, O62.0, O62.1, O62.2, |
|                 |           | O62.3, O62.4, O62.8, O62.9, O63, O63.0, O63.1, O63.2, O63.9, O64, |
|                 |           | O64.0, O64.1, O64.2, O64.4, O64.5, O64.8, O64.9, O65, O65.1, |
|                 |           | O65.4, O65.5, O65.9, O66, O66.0, O66.1, O66.2, O66.3, O66.4, O66.9 |
### Other Direct Causes

| Other          | O21.1, O24.4, O26.6, O44.0, O73, O73.0, O73.1, O75.4, O75.8, O75.9, O90, O90.0, O90.1, O90.2, O90.3, O90.4, O90.5, O90.8, O90.9, C58, O21, O21.0, O21.9, O22.0, O22.1, O22.2, O25, O26, O26.0, O26.1, O26.3, O26.5, O26.8, O26.9, O28, O28.5, O28.8, O30, O30.0, O30.1, O30.9, O31, O31.2, O31.8, O32, O32.1, O32.2, O32.4, O32.8, O32.9, O34, O34.0, O34.1, O34.2, O34.3, O34.4, O34.5, O34.6, O34.8, O34.9, O35, O35.0, O35.1, O35.5, O35.8, O35.9, O36, O36.0, O36.1, O36.2, O36.3, O36.4, O36.5, O36.6, O36.7, O36.8, O36.9, O40, O41, O41.0, O41.8, O41.9, O42, O42.0, O42.1, O42.2, O42.9, O43.0, O43.1, O43.8, O43.9, O47.0, O47.9, O48, O60, O60.0, O60.1, O60.2, O60.3, O61, O61.0, O61.9, O68, O68.0, O68.1, O68.2, O68.8, O68.9, O69, O69.0, O69.1, O69.2, O69.4, O69.5, O69.8, O69.9, O70, O70.0, O70.1, O70.2, O70.3, O70.9, O75, O75.0, O75.1, O75.2, O75.6, O75.7, O92, O92.2, O92.3, O92.5, O92.6 |

### Other Indirect Causes

| Other Indirect Causes          | O10, O10.0, O10.1, O10.2, O10.3, O10.4, O10.9, O24, O24.0, O24.1, O24.2, O24.3, O24.9, O98, O98.0, O98.1, O98.3, O98.4, O98.5, O98.6, O98.8, O98.9, O99.0, O99.1, O99.2, O99.3, O99.4, O99.5, O99.6, O99.7, O99.8 |

### Ante-partum

| Ante-partum | O23, O23.0, O23.1, O23.2, O23.3, O23.4, O23.5, O23.9, O41.1 |

### Intra-partum

| Intra-partum | O75.3 |

### Post-partum

| Post-partum | O85, O86, O86.0, O86.1, O86.2, O86.3, O86.4, O86.8, O91, O91.1, O91.2 |

### Sepsis

| Sepsis         | Timing Unknown | A34 |
B Data adjustments

B.1 Treatment of missing versus zero-reported deaths

For a number of country-years we encounter missing observations for some of the main causes. Sometimes however, zero counts are explicitly reported in the data for a given cause. In the current analysis we attempt to make a distinction between a death count for which we have no information, and hence treat as missing, and one where we are implying that the true count is, indeed, equal to zero. More specifically, for a particular country-year we consider an observation of zero maternal deaths for a particular main cause to be a true zero, if the observation is of data quality type 1 or 2 (quality type distinction is explained in more detail in Section 5.3.3), if the data source for that observation has previously observed non-zero maternal deaths for that main cause, and if the estimated maternal death count for that country (2019 UN MMEIG estimates) is less than 7. Put differently, we are willing to assume that in a country with low estimated maternal mortality and high quality data a zero maternal death count for a particular cause that has been previously reported is a true zero.

B.2 HIV/AIDS deaths

As indicated earlier maternal death due to HIV/AIDS were not part of the estimation process and HIV/AIDS-inclusive cause of death distributions were obtained only after incorporating HIV/AIDS estimates produced elsewhere (see Section 5.5 for more details). To exclude maternal deaths due to HIV/AIDS, observations classified as ICD-10 code O98.7 were explicitly excluded from the analysis. However, we believe this exclusion does not fully account for the possible number of HIV/AIDS deaths present among deaths from indirect (IND) causes in our data. For instance, HIV/AIDS deaths could be reported among maternal deaths classified more broadly as ICD-10 Group 7 or could be reported under ICD-10 code O98. To account for this, we consider each country-year observation reporting any maternal deaths as ICD-10 Group 7 or using ICD-10 code O98 and adjust that observation’s total deaths from IND causes by subtracting an appropriately scaled MMEIG estimate of HIV/AIDS maternal deaths for that country-year, where the scaling is based on a measure of completeness, or coverage, of the maternal deaths data.
B.3 Multi-year studies

A proportion of studies report maternal deaths as aggregate values over the entire study period. In such cases, where corresponding yearly maternal deaths are unavailable and the data cannot otherwise be disaggregated, to prevent such observation from having disproportionate weight in the model, the total number of maternal deaths reported are scaled down to a single-year equivalent. This, however, is done only for those studies where the total number of deaths reported is more than five times the number of years of the study.
C   Modeling regions

The organization of countries into regions $r = 1, \ldots, R$ used in the estimation model follow the classification used by Say et al. (2014). Table 5 shows the countries included in each of these regions.

| Model region          | Countries                                                                 |
|-----------------------|---------------------------------------------------------------------------|
| Central Asia          | Kazakhstan; Kyrgyzstan; Tajikistan; Turkmenistan; Uzbekistan              |
| Eastern Asia          | China; Democratic People's Republic of Korea; Mongolia; Republic of Korea |
| Eastern Africa        | Burundi; Comoros; Djibouti; Eritrea; Ethiopia; Kenya; Madagascar; Malawi; Mauritius; Mozambique; Rwanda; Seychelles; Somalia; South Sudan; Sudan; United Republic of Tanzania; Uganda; Zambia; Zimbabwe |
| South-Eastern Asia / Oceania | Brunei Darussalam; Cambodia; Fiji; Indonesia; Kiribati; Lao; People’s Democratic Republic; Malaysia; Micronesia (Federated States of); Myanmar; Papua New Guinea; Philippines; Samoa; Singapore; Solomon Islands; Thailand; Timor-Leste; Tonga; Vanuatu; Viet Nam |
| Southern Africa       | Botswana; Lesotho; Namibia; South Africa; Eswatini                       |
| Western Africa        | Benin; Burkina Faso; Cabo Verde; Côte d’Ivoire; Gambia; Ghana; Guinea; Guinea-Bissau; Liberia; Mali; Mauritania; Niger; Nigeria; Senegal; Sierra Leone; Togo |
| Central America       | Belize; Costa Rica; El Salvador; Guatemala; Honduras; Mexico; Nicaragua; Panama |
| Developed regions     | Australia; Austria; Belarus; Belgium; Bulgaria; Canada; Czechia; Denmark; Estonia; Finland; France; Germany; Greece; Hungary; Iceland; Ireland; Italy; Japan; Latvia; Lithuania; Luxembourg; Malta; Netherlands; New Zealand; Norway; Poland; Portugal; Republic of Moldova; Romania; Russian Federation; Slovakia; Slovenia; Spain; Sweden; Switzerland; Ukraine; United Kingdom of Great Britain and Northern Ireland; United States of America |
| Western Asia          | Armenia; Azerbaijan; Bahrain; Cyprus; Georgia; Iraq; Israel; Jordan; Kuwait; Lebanon; West Bank and Gaza Strip; Oman; Qatar; Saudi Arabia; Syrian Arab Republic; Turkey; United Arab Emirates; Yemen |
| South America         | Argentina; Bolivia (Plurinational State of); Brazil; Chile; Colombia; Ecuador; Guyana; Paraguay; Peru; Suriname; Uruguay; Venezuela (Bolivarian Republic of) |
| Region                        | Countries                                                                 |
|------------------------------|---------------------------------------------------------------------------|
| Caribbean                    | Antigua and Barbuda; Bahamas; Barbados; Cuba; Dominican Republic; Grenada; Haiti; Jamaica; Puerto Rico; Saint Lucia; Saint Vincent and the Grenadines; Trinidad and Tobago |
| Middle Africa                | Angola; Cameroon; Central African Republic; Chad; Congo; Democratic Republic of the Congo; Equatorial Guinea; Gabon; Sao Tome and Principe |
| Northern Africa              | Algeria; Egypt; State of Libya; Morocco; Tunisia                           |
| Transition countries of      | Albania; Bosnia and Herzegovina; Croatia; Montenegro; Serbia; Republic of North Macedonia |
| South-Eastern Europe         | Afghanistan; Bangladesh; Bhutan; India; Iran (Islamic Republic of); Maldives; Nepal; Pakistan; Sri Lanka |
Table 6: Mean absolute difference in estimated country proportions, leaving out observations from 'Developed regions'

| Cause | Central and Southern Asia | Europe and Northern America | Northern Africa and Western Asia | Oceania excl. Australia and New Zealand | Sub-Saharan Africa | Latin America and the Caribbean | Australia and New Zealand | Eastern and South-Eastern Asia |
|-------|---------------------------|------------------------------|----------------------------------|----------------------------------------|-------------------|---------------------------------|---------------------------|-------------------------------|
| ABO   | 0.003                     | 0.012                        | 0.001                            | 0.001                                  | 0.001             | 0.001                           | 0.033                     | 0.002                         |
| DIR   | 0.001                     | 0.047                        | 0.002                            | 0.001                                  | 0.001             | 0.001                           | 0.055                     | 0.004                         |
| EMB   | 0.004                     | 0.116                        | 0.008                            | 0.003                                  | 0.002             | 0.003                           | 0.139                     | 0.011                         |
| HEM   | 0.003                     | 0.045                        | 0.003                            | 0.008                                  | 0.004             | 0.002                           | 0.103                     | 0.009                         |
| SEP   | 0.002                     | 0.018                        | 0.002                            | 0.001                                  | 0.001             | 0.002                           | 0.005                     | 0.004                         |
| IND   | 0.003                     | 0.070                        | 0.003                            | 0.007                                  | 0.003             | 0.004                           | 0.177                     | 0.009                         |
| HYP   | 0.004                     | 0.040                        | 0.006                            | 0.005                                  | 0.007             | 0.002                           | 0.089                     | 0.008                         |

Table 7: Mean absolute difference in estimated country proportions, leaving out 20 percent of observations from each data quality type.

| Cause | Central and Southern Asia | Europe and Northern America | Northern Africa and Western Asia | Oceania excl. Australia and New Zealand | Sub-Saharan Africa | Latin America and the Caribbean | Australia and New Zealand | Eastern and South-Eastern Asia |
|-------|---------------------------|------------------------------|----------------------------------|----------------------------------------|-------------------|---------------------------------|---------------------------|-------------------------------|
| ABO   | 0.002                     | 0.003                        | 0.001                            | 0.009                                  | 0.002             | 0.008                           | 0.001                     | 0.006                         |
| DIR   | 0.005                     | 0.010                        | 0.004                            | 0.004                                  | 0.002             | 0.007                           | 0.004                     | 0.014                         |
| EMB   | 0.003                     | 0.028                        | 0.003                            | 0.004                                  | 0.002             | 0.004                           | 0.037                     | 0.003                         |
| HEM   | 0.004                     | 0.011                        | 0.004                            | 0.004                                  | 0.006             | 0.006                           | 0.017                     | 0.005                         |
| SEP   | 0.003                     | 0.005                        | 0.003                            | 0.005                                  | 0.003             | 0.003                           | 0.009                     | 0.006                         |
| IND   | 0.004                     | 0.021                        | 0.008                            | 0.009                                  | 0.007             | 0.009                           | 0.008                     | 0.010                         |
| HYP   | 0.002                     | 0.008                        | 0.003                            | 0.005                                  | 0.001             | 0.006                           | 0.010                     | 0.003                         |

D Additional validation results

Tables 6 and 7 show the mean absolute differences between estimates by region and main cause of death when excluding all data from high-income countries, and 20% of the data from each data quality type (1, 2, 3, 4) respectively. Removing data from high-income countries has a relatively large affect on estimates in Europe and North America, and Australia and New Zealand, but minimal effects in all other regions. This suggests that high-income regions, that have large amounts of data available, are not overly influential on estimates in other regions. Leaving out 20% of the available data by type at random has minimal effect on estimates across all regions and cause groups.
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