Maternal mortality estimates 2000–2017

Summary of statistical methodology

Maternal Mortality Estimation Inter-Agency Group



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Acronyms and abbreviations

age-specific fertility rates
Bayesian Hierarchical Model
MMEIG Bayesian maternal mortality estimation model
completeness of the CRVS data (in terms of reporting all female deaths of reproductive age)
civil registration and vital statistics
Bayesian CRVS adjustment model
Demographic and Health Survey
gross domestic product (per capita)
general fertility rate
International statistical classification of diseases and related health problems, 10th edition
Multiple Indicator Cluster Surveys
Maternal Mortality Estimation Inter-Agency Group
maternal mortality ratio
odds ratio
proportion of deaths among women of reproductive age that are due to maternal causes
purchasing power parity
reproductive-age mortality study
skilled birth attendant
sensitivity
specificity
technical advisory group
Joint United Nations Programme on HIV/AIDS
United Nations Population Fund
United Nations Children's Fund
United Nations Population Division
World Health Organization

1. Introduction

The World Health Organization (WHO), the United Nations Children's Fund (UNICEF), the United Nations Population Fund (UNFPA), the World Bank Group and the United Nations Population Division have collaborated on a new round of country-level estimates of maternal deaths for WHO Member States up to 2017, summarized for your country in the accompanying "country profile" (PDF document).

The purpose of this technical document is to support the country consultation process with Member States by providing a detailed description of the Maternal Mortality Estimation Inter-Agency Group (1) processes and methods for estimating levels and trends of maternal mortality globally. During the consultation, Member States have an opportunity to review the draft estimates and their methods, to provide advice on primary data sources for respective countries that may not have been previously reported or used, and to build mutual understanding of the strengths and weaknesses of available data and estimation process.

Previously, in 2010, 2012, 2014 and 2015, the MMEIG published reports on maternal mortality trends with advice from an external technical advisory group (TAG) (2-5). The methods described here for constructing estimates of levels and trends of maternal mortality up to 2017 build upon the methods used in previous rounds (6, 7). The key change to the estimation methodology and resulting estimates in this round is described in section 5 and concerns the adjustment of data from civil registration and vital statistics (CRVS). CRVS data have been adjusted in previous rounds to account for missed/unregistered and/or misclassified maternal deaths. The MMEIG has considered concerns from Member States about how this adjustment was calculated, and how it may or may not have reflected improvements in data collection and data quality related to maternal mortality over time (see section 5).

The following sections of this technical document provide explanatory notes on data sources and methods used for constructing these estimates. The updated estimates draw on extensive databases compiled by MMEIG and on information provided by Member States. For example, for predictor variables/covariates used in the multilevel regression model, information on the gross domestic product (GDP) is based on the World Bank Group and the MMEIG series (1), data on coverage by skilled birth attendants (SBA) are derived from the joint WHO and UNICEF database (8), and general fertility rates (GFR) from UNPD estimates (9). Regarding the other data inputs, total numbers of deaths are from WHO (10), numbers of AIDS deaths are from the Joint United Nations Programme on HIV/AIDS (UNAIDS) (11), and numbers of live births are from UNPD (12).

For the proportion of maternal deaths (PM) and the maternal mortality ratio (MMR), there are multiple data sources. For most countries, however, the information comes from one or more of the following sources: CRVS data from the WHO Mortality Database

(http://www.who.int/healthinfo/mortality_data/en/), sisterhood data from population-based surveys (e.g. Demographic and Health Surveys [DHS] (13) and Multiple Indicator Cluster Surveys [MICS] (14)), and data from special studies of maternal deaths, including national surveillance systems available to WHO. Census analyses were carried out by the MMEIG and have benefited greatly from previous consultations and interactions with Member States.

Maternal mortality estimates were constructed for WHO Member States countries and territories.

Note that we have revised the estimates of the trend up to 2017. Differences between these estimates and earlier published estimates for 2010, 2012, 2014 and 2015 (2-5) should not be interpreted as representing time trends.

2. Concepts and definitions

In the International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10¹) (15), WHO defines **maternal death** 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.

This definition allows identification of a maternal death, based on the cause of the death being identified as either a direct or indirect maternal cause.

Direct obstetric deaths are those resulting from complications of the pregnant state (pregnancy, delivery and postpartum up to 42 days), from interventions, omissions or incorrect treatment, or from a chain of events resulting from any of the above. **Indirect obstetric deaths** are those resulting from previous or pre-existing disease, or diseases that developed during pregnancy and which were not due to direct obstetric causes but were aggravated by the physiological effects of pregnancy. **Late maternal deaths** are direct or indirect maternal deaths occurring from 42 days to 1 year after termination of pregnancy.

Accurate identification of the causes of maternal deaths by differentiating the extent to which they are due to direct or indirect obstetric causes, or due to accidental or incidental events, is not always possible – particularly in settings where deliveries occur mostly at home, and/or where civil registration systems with correct attribution of causes of death are inadequate. With the publication of ICD-10, WHO recommended to add a checkbox on the death certificate for recording a woman's pregnancy status at the time of death. This would help to identify indirect maternal deaths but has not been implemented in many countries to date. Historically, for countries using ICD-10 coding for registered deaths, the MMEIG counted all deaths coded to the maternal chapter (O codes) and A34 (maternal tetanus) as maternal deaths. Based upon ICD-10, maternal deaths up to 42 days postpartum are considered relevant for international reporting.^{2,3}

Any death while a woman is pregnant or within 42 days of termination of pregnancy is defined as a **pregnancy-related death** even if it is due to accidental or incidental causes. This alternative definition allows measurement of deaths that occur during pregnancy while acknowledging that such measurements do not strictly conform to the standard "maternal death" concept in settings where accurate information about causes of death based on medical certificates is unavailable. For instance, in maternal mortality surveys (such as those employing the sisterhood method), relatives of a woman of

¹ A preview version of ICD-11 was released by WHO in June 2018. The coding rules related to maternal mortality have not been revised at the time of this writing. Attention has been made to ensure that the definition used for international comparison of mortality statistics remain stable over time. For further information, see the ICD website: http://www.who.int/classifications/icd/revision/en/

² ICD-11, volume 2, section 5.8.2: International reporting. For the purpose of the international reporting of maternal mortality, only those maternal deaths occurring before the end of the 42-day reference period should be included in the calculation of the various ratios and rates, although the recording of later deaths is useful for national analytical purposes.

³ Late maternal deaths coded to O96 (late maternal deaths) and O97 (late maternal deaths due to sequalae of complications) are also of interest for international-level analysis, and are reported separately.

reproductive age who has died are asked about her pregnancy status at the time of death without eliciting any further information on cause of death. These surveys usually measure pregnancy-related deaths rather than maternal deaths.

Until 2010, **indirect maternal deaths due to HIV disease** should have been coded to Chapter 1 (Certain Infectious and Parasitic Disease) according to ICD-10 rule 5.8.3 (in Vol. 2) and included in the calculation of MMR. These are deaths of HIV-positive women who die because of the aggravating effect of pregnancy on HIV. Incidental HIV deaths in which the HIV-positive women happened to be pregnant would not be included in the calculation of MMR. From early 2010, an ICD-10 code O98.7 (human immunodeficiency virus [HIV] disease complicating pregnancy, childbirth and the puerperium) has been introduced for identifying indirect maternal deaths due to HIV disease.

The number of maternal deaths in a population is essentially the product of two factors: the risk of mortality associated with a single pregnancy, and the number of pregnancies or births that are experienced by women of reproductive age. The MMR is defined as the number of maternal deaths in a population per 100 000 live births; thus, it depicts the risk of maternal death relative to the number of live births. An alternate measure of maternal mortality, the proportion maternal (PM), is the proportion of deaths among women of reproductive age that are due to maternal causes, and is calculated as the number of maternal deaths in a given time period divided by the total deaths among women aged 15–49 years.

3. Data inputs used for the maternal mortality ratio estimation process

3.1 Data sources

MMR estimates are based upon a variety of methods and data sources – including data from CRVS systems, which are the preferred data source, population-based household surveys using the sisterhood method, reproductive-age mortality studies (RAMOS), confidential enquires, verbal autopsies, censuses and other maternal mortality studies conducted at the national level. The database has been updated since the last round of estimates in 2015, and the database for the draft estimates was closed in February 2019.

3.1.1 Civil registration and vital statistics (CRVS)

For countries with routine death registration, maternal deaths may be incorrectly reported due to missed/unregistered deaths and/or deaths that are misclassified in terms of ICD coding. To account for potential missed/unregistered deaths as well as misclassification in CRVS data, an adjustment is calculated for each CRVS input data point (see section 5.1) before it is included in the MMEIG Bayesian maternal mortality estimation model (BMat).

For each country with CRVS data, we estimate the completeness of the CRVS (in terms of reporting all female deaths of reproductive age) as follows.

- We calculate the annual ratio of female deaths reported in the CRVS over female deaths estimated by WHO for all years with CRVS data, based on a moving window of five-year periods (five-year periods are used to obtain smoothed estimates of completeness).
- If the ratio (in particular, its upper bound when accounting for uncertainty in the ratio) is greater than 0.95 for all years with CRVS data, we assume that the CRVS is complete in the country.
- If the ratio is less than 0.95 for one or more years, the completeness is given by the ratio for each individual year.
- After obtaining an estimate of completeness, we combine this estimate with the proportion of deaths assigned to an ill-defined code. We exclude observations for which the percentage of deaths that is estimated to be recorded with a well-defined code is lower than 60%. In other words, if completeness proportion*(1 – proportion ill-defined)*100% > 60%, the observation is included (5).

3.1.2 Specialized studies reporting on CRVS

The MMEIG is aware of efforts being undertaken in certain settings to document maternal deaths and to improve CRVS. In some of these situations, a specialized study is conducted precisely for the purpose of assessing the extent of misclassification within the CRVS and/or the extent of "missingness" of maternal deaths. In other situations, the purpose of the specialized study is to perform an independent assessment of cause of death classification among the true number of maternal deaths.

These data sources typically expand the scope of their reviews to the entire number of deaths among women of reproductive age and triangulate information from sources including, but not limited to: medical/hospital records, police records, surveillance systems, national registries, death certificates, census, medical autopsy, and administrative reviews between national statistical offices and ministries of

health. The information reported by these specialized studies greatly varies, and includes any combination of the following: total number of deaths to women of reproductive age and/or maternal deaths, all causes of death correctly documented among all women of reproductive age and/or maternal death, "missed" deaths to women of reproductive age and/or maternal deaths. In these situations, it is agreed that no adjustment factor needs to be applied, and so observations from specialized studies are included in the BMat model (see section 5.2) without adjustment.

3.1.3 Other data sources for maternal mortality

Other available data sources include data from surveillance sites or systems, population-based surveys and censuses. For these data sources, the observed proportion of maternal deaths (PM) among all deaths to women aged 15–49 years was taken as the preferred indicator for use in estimating maternal mortality.

The PM is preferred over observed MMRs or other summary outcomes because it is less affected by missed or unregistered deaths: deaths to women aged 15–49 that are missed or unregistered would potentially affect the numerator and the denominator of the PM proportionately if causes of death are not missed or unregistered differentially. Therefore, in processing maternal-mortality-related data, observed PMs took priority over observed MMRs and for each observed PM, the corresponding MMR is calculated based on the UNPD estimates of live births (12) and all-cause deaths among females aged 15–49 (WHO estimates) (10) for the respective country-period. If only the MMR was available from the data source, the observed MMR was converted into a PM, again using estimates of all-cause female deaths age 15–49 and live births. An adjustment of 10% was applied to the resulting PM (5).

The available data sources provide calculated PMs according to two definitions: "maternal" or "pregnancy-related" deaths. PMs for pregnancy-related deaths excluding accidents were taken as measures of maternal PM without further adjustment. Based on an analysis of measured levels of maternal versus pregnancy-related death from sources where both quantities were reported, and of injury death rates at reproductive ages using WHO estimates of cause-specific mortality for Member States, the MMEIG/TAG agreed to estimate "maternal" deaths from the PM for "pregnancy-related" deaths, based on assumptions that incidental or accidental deaths comprise 10% of pregnancy-related deaths (excluding AIDS deaths) in sub-Saharan African countries, and 15% in other low- and middle-income countries (2).

3.1.4 Uncertainty associated with observations and adjustments

All observed death counts and PMs are subject to random error, either in the form of sampling error (for PMs obtained from surveys), stochastic error (for PMs obtained from a small number of deaths) and/or non-sampling error (which are random errors that may occur at any point during the data collection process).

To account for the uncertainty associated with these errors, and thus the uncertainty associated with the PM, error variances were calculated. For observations from CRVS or confidential enquiries, stochastic error variances were obtained, which quantify the uncertainty associated with the true risk of a maternal death, based on the available data. For observed PMs from surveys and other maternal mortality studies, the error variance was a combination of the sampling variance associated with the survey and an additional non-sampling error. The non-sampling error was estimated based on the global database of surveys and other maternal mortality studies (6). For all observed PMs, the error variances were taken into account when obtaining PM and thus MMR estimates: observations with smaller error variances are more informative of the true PM and will thus carry a greater weight in determining the estimates as compared to observations with larger error variances. Additionally, uncertainty associated with adjustments (e.g. the CRVS adjustment as per the new approach described in section 5.1 and adjustment of observations which report pregnancy-related deaths) was accounted for.

4. Other data inputs to the model

4.1 Data on all deaths to women 15-49 years and AIDS-related mortality

We used a set of consistent external estimates for deaths due to HIV/AIDS from UNAIDS and estimates for deaths among females 15–49 years from WHO life tables (10). These various agencies revise their estimates on a regular basis to take into account new data and improved methods. Any comments regarding these input indicators should be addressed to the respective agencies.⁴

4.2 Live births data

For the draft MMR estimates shared during the country consultation, inputs for live births were taken from the UNPD *World population prospects: the 2019 revision* (12). In this publication, the UNPD produced estimates of population and related indicators (e.g. births and deaths) for countries or areas, covering five-year periods from 1950–1955 through to 2005–2010, as well as projections covering fiveyear periods from 2010–2015 through to 2095–2100. For countries with good CRVS systems, UNPD utilized information on births by age of the mother together with population by age and sex from censuses and official statistics to estimate age-specific fertility rates (ASFR) for each historical five-year period. The population estimation and projection procedure used the ASFR and other inputs such as ageand sex-specific mortality rates to generate a consistent time series of population size, age distribution, and the demographic components of population change (births, deaths and migration). Annual estimates of births are obtained by interpolating the five-year estimates of the number of births output by the population estimation and projection procedure. As a result, the annually interpolated estimates do not necessarily match the annual numbers of births reported in the CRVS.

For enquiries about the estimates in *World population prospects: the 2019 revision,* or to provide additional data, country representatives may email: <u>population@un.org</u>. This email address is monitored regularly and messages are dispatched to the appropriate analysts for each country or area of concern.

4.3 Predictor variables in the maternal mortality model

Time series of annual estimates for these three predictor variables (covariates) were constructed from 1985 to 2017:

- GDP per capita measured in purchasing power parity (PPP) equivalent dollars using 2011 as the baseline was generated based on data from the World Bank Group and the MMEIG (1).
- GFR computed from data on live births and population size (number of women aged 15–49) from the UNPD *World population prospects: the 2019 revision* (9).
- SBA data consist of time series derived using all available data from health surveys and other sources (database jointly maintained by WHO and UNICEF (8). Annual series were estimated for

⁴ For UNAIDS mortality estimates: Dr Peter Ghys, Chief, Epidemiology and Analysis Division(<u>ghysp@unaids.org</u>); for WHO life tables: Dr John Grove (grovej@who.int); for the estimates of live births from United Nations Population Division (<u>population@un.org</u>).

countries with any value of SBA less than 95% and with four or more observations by fitting a regression model with time as the sole predictor for the logit (or log-odds) of SBA; such a model was estimated separately for each country. For all other countries, including those with no available SBA data, the SBA annual series were estimated using a multilevel model. In the multilevel model, logit (or log-odds) of observed SBA proportions for all countries were regressed against time. The model included region- and country-specific intercepts and slopes.

5. Statistical methods

We use two models.

- 1. We use a Bayesian CRVS adjustment model to account for errors in reporting of maternal death in the CRVS ("CRVS model" for short) to obtain the CRVS adjustment factors; and
- 2. We use a Bayesian maternal mortality estimation model (known as "BMat") to estimate the MMR for each country-year of interest.

To estimate MMR for country-years, we first use the CRVS model to obtain the CRVS adjustment factors. These adjustment factors are then applied in the BMat to estimate the MMR for each country-year of interest (see Figure 1). The CRVS model is described in section 5.1, followed by the description of the BMat in section 5.2.



Figure 1. Overview of modelling steps for MMR estimation

5.1 Bayesian CRVS adjustment model to account for errors in reporting of maternal death in the CRVS (the CRVS model)

CRVS reported maternal deaths are subject to potential error due to missed/unregistered maternal deaths and/or misclassification of maternal deaths within the CRVS. Therefore, an adjustment factor is obtained for CRVS data before it is included in BMat (section 5.2).

This section explains:

- 1. the types of reporting errors;
- 2. summary metrics for the reporting errors, referred to as CRVS data-quality parameters, and how they relate to the adjustment needed for CRVS data; and
- 3. the model used to estimate the CRVS data-quality parameters, and corresponding adjustment factors for CRVS data in BMat.

5.1.1. Types of reporting errors

Definitions of reporting errors are summarized in Box 1 and discussed further below. More detailed examples are given in Appendix A.

Box 1. Definitions of misclassification, missed or unregistered maternal deaths

Missed or unregistered

Refers to incomplete death registration in the CRVS. Includes both the identification of individual deaths in each country and the national coverage of the register.

We distinguish between:

- U- = Non-maternal deaths not registered in the CRVS, and
- U+ = Maternal deaths not registered in the CRVS.

Misclassification

Refers to incorrect coding in the CRVS, due either to error in the medical certification of cause of death or error in applying the correct code. We distinguish between:

- F- (false negative): maternal death which is incorrectly classified as a nonmaternal death.
- **F+ (false positive):** true non-maternal death which is incorrectly labelled as a maternal death.

5.1.1.1 Reporting errors within the CRVS

Within the CRVS system, incorrect reporting of maternal deaths can be attributed to misclassified maternal deaths in two ways: maternal deaths reported as non-maternal; and non-maternal deaths reported as maternal. The remaining deaths are those that have been correctly classified: maternal deaths reported as maternal, and non-maternal deaths reported as non-maternal. The notations used are

- T+ (true positive) = maternal deaths correctly reported in the CRVS as maternal
- T- (true negative) = non-maternal deaths correctly reported in the CRVS as non-maternal
- F+ (false positive) = non-maternal deaths reported in the CRVS as maternal
- F- (false negative) = maternal deaths reported in the CRVS as non-maternal

The four-box diagram in Figure 2 summarizes what is reported correctly and incorrectly in the CRVS.

Figure 2. Four-box diagram of breakdown of the total number of deaths to females of reproductive age as reported into the CRVS, by CRVS-maternal-cause-of-death classification (see Box 1 for definitions)



The observed PM – the proportion of deaths among women of reproductive age that are due to maternal causes – reported in the CRVS is given by $\frac{T^+ + F^+}{T^+ + F^- + T^-}$ while the true PM from CRVS data is $\frac{T^+ + F^-}{T^+ + F^+ + T^-}$.

The MMEIG approach to adjust for this potential difference between true and observed PM is explained in sections 5.1.2 and 5.1.3.

5.1.1.2 Deaths that are not reported in the CRVS

In cases where the CRVS system does not capture all female deaths (i.e. the CRVS is incomplete), we classify these maternal and non-maternal deaths as missed (unregistered) female deaths. Notation used is as follows:

U- = Non-maternal deaths not registered in the CRVS, and

U+ = Maternal deaths not registered in the CRVS.

We extend the four-box representation to also incorporate missed maternal (U+) and non-maternal (U–) deaths (six-box diagram) as shown in Figure 3.

Figure 3. Six-box diagram of breakdown of the total number of deaths to females of reproductive age by CRVS cause-of-death classification and reporting status (see Box 1 for definitions)



5.1.2 Summary metrics for reporting errors

5.1.2.1 Reporting within the CRVS

We summarize the occurrence of misclassification errors in the CRVS into the following two metrics:

(1) Sensitivity (Se): proportion of correctly classified maternal deaths out of all true maternal deaths, and (2) Specificity (Sp): proportion of correctly classified non-maternal deaths out of all true non-maternal deaths.

These metrics combined summarize the ability of the CRVS system to correctly identify a true maternal and true non-maternal death. The formulas using the notation introduced in the previous section are as follows:

- Sensitivity = $\frac{T^+}{T^+ + F^-}$ Specificity = $\frac{T^-}{T^- + F^+}$

Examples of the calculation of sensitivity, specificity and PMs are provided in Appendix A.

The third metric related to reporting errors in the CRVS is the adjustment factor:

(3) CRVS adjustment factor: adjustment factor associated with CRVS-reported PM, to account for the difference between CRVS-reported PM and true PM.

For country-years with complete CRVS, CRVS adjustment factors can be calculated for all country-years using their respective estimates of Se, Sp, and true proportional maternal (true PM), based on the following relation:

Expected CRVS-reported PM = Se * true PM + (1- Sp) * (1 - true PM),

such that the CRVS adjustment factor is given by

CRVS adjustment factor = true PM/ (Se * true PM + (1- Sp) * (1 – true PM)).

5.1.2.2 Reporting in incomplete CRVS systems

Reporting errors related to missed maternal deaths are summarized in terms of the ratio between:

- true PM in (PM-in) = the true PM among deaths captured in the CRVS (so the true number of maternal deaths in the CRVS over the total number of deaths captured in the CRVS);
- true PM out (PM-out) = the PM among deaths not captured in the CRVS.

such that:

True PM among all deaths = COM*PM-in + (1-COM)*PM-out

where COM stands for completeness of the CRVS data (in terms of reporting all female deaths of reproductive age).

- If the ratio (in particular, its upper bound when accounting for uncertainty in the ratio) is greater than 0.95 for all years with CRVS data, we assume that the CRVS is complete in the country (COM =1).
- If the ratio is less than 0.95 for one or more years, the completeness is given by the ratio for each individual year (COM = ratio).

For country-years with incomplete CRVS, we investigated the feasibility of estimating the odds ratio of the two PMs, but data were too limited for inference on this ratio. Instead, we assumed that PM-in equals PM-out and accounted for additional uncertainty related to the unknown true ratio when deriving the CRVS adjustment for country-years with incomplete CRVS.

5.1.3 Deriving sensitivity, specificity and CRVS adjustments from the CRVS model *5.1.3.1 CRVS model estimates of sensitivity and specificity*

The CRVS model obtains estimates of sensitivity and specificity for all country-years with CRVS data. Based on these estimates, corresponding estimates of the adjustment factor for country-years with complete CRVS can be obtained.

For all countries with specialized studies to inform Se and Sp, we model Se as well as Sp with a countryspecific intercept in the midyear of their respective observation period. The country-specific intercept is estimated with a multilevel model, such that estimates for countries with specialized studies are informed by those data while estimates for countries with limited or no data are informed by information from other countries. Se and Sp values for the remaining years before and after the reference year were obtained through a so-called random walk model set-up. In the random walk set-up, point estimates of Se and Sp are kept constant. For countries with specialized studies, the estimates are data driven and informed by the combinations of Se and Sp as indicated by the studies.

In the model for Se and Sp, Se is constrained to be between 0.1 and 1 and Sp is constrained to be between 0.995 and 1. These bounds were chosen to avoid extrapolations for countries with limited data to values that are more extreme than those observed in the data.

We considered predictor variables to capture changes in sensitivity and specificity over time within countries, and differences across countries. The following predictor variables were considered as candidate covariates:

- GFR
- GDP per capita
- CRVS completeness (COM)
- proportion of causes in the CRVS that are ill defined ("R" codes in CRVS)
- ICD coding (use of ICD-9 or ICD-10)
- proportion of CRVS deaths that fall under noncommunicable disease causes of death.

However, none of the candidate predictor variables showed a substantively meaningful relationship with the parameters of interest, hence no covariates were used.

5.1.3.2 CRVS model estimates of CRVS adjustment factors

The CRVS model was fitted to specialized study data, collected by review (refer to Appendix B and C for review details and full citations), and CRVS data for the corresponding periods. The CRVS yields estimates of sensitivity and specificity based on two scenarios.

- (1) For countries with data from specialized studies, the model is fitted to those data, and the estimates for the CRVS adjustment in the corresponding years will be consistent with the data.
- (2) For countries without specialized studies, the estimates for sensitivity and specificity are equivalent to global estimates of sensitivity and specificity, obtained from fitting the model to the global database (the envelope of all specialized studies). The resulting estimates of Se and Sp are constant with time, as global estimates are also constant with time.

Figure 4 shows the relationship between true PM and the estimated CRVS adjustment factors, for specific values of Sp to illustrate their effect on the CRVS adjustment factor. When Sp = 1, the CRVS adjustment factor = 1/Se, hence lower Se results in a higher adjustment, conversely higher Se results in a lower adjustment. When Sp < 1, while keeping Se fixed, the adjustment factor decreases with decreasing true PM. This effect is due to an increasing share of false positive maternal deaths among all deaths, and a decreasing share of false negative deaths, or, in other words, as the true PM decreases, the proportion of non-maternal deaths reported as maternal increases while the proportion of maternal deaths reported as non-maternal decreases.

Figure 4 illustrates that keeping specificity and sensitivity constant in extrapolations in countries with specialized studies, or for countries without any studies, will result in changing adjustment factors as the true PM changes.

The CRVS model provides estimates for all countries with CRVS data, using available information from these countries. This implies that inclusion of additional data observations for any one country (perhaps as a result of this consultation) can potentially result in changes to estimates for other countries, especially those without specialized studies.





5.1.4 Comparison with previous MMEIG approach to estimate CRVS adjustment factors

The CRVS adjustment model, described in section 5.1.3, yields estimates of sensitivity, specificity and CRVS adjustments for all country-years without specialized study data. In the previous round of estimates, the MMEIG CRVS adjustment was set to 1.5 for countries without specialized studies. For countries with at least one specialized study, the adjustment was calculated for countries with specialized studies by the ratio of true PM reported in the study to CRVS-based PM, i.e. the ratio of the proportion of true maternal deaths out of all female deaths to the proportion of CRVS-reported maternal deaths out of all CRVS-reported female deaths. The CRVS adjustment ratio was kept constant in forward extrapolations.

Limitations of the previous approach include the following.

- The use of a constant CRVS adjustment factor in extrapolations results in an overestimation of the adjustment factor if, in reality, specificity is constant and the true PM decreases (as illustrated in Figure 4 for adjustments based on the CRVS model).
- The uncertainty in the adjustment factor had not been assessed. Instead, the uncertainty of the adjustment factor was assumed to be around 50% of the point estimate for all country-years. The

uncertainty is likely to vary across countries and with time, depending on data availability and the country-specific setting.

• The value of 1.5 was based on the median of a set of studies. The assessment did not account for differences that may be due to different settings (i.e. high fertility settings versus low fertility settings, completeness of CRVS). The set of studies included multiple observations from the same countries (so the 1.5 is not the median across countries).

The new approach improves upon these limitations through an assessment of variability across countries and within countries over time, in terms of the sensitivity and specificity of maternal death classification, extrapolations that are based on Se and Sp, and an assessment of uncertainty associated with these metrics and the resulting CRVS adjustment factor. We also explored the use of predictor variables to obtain more country-specific adjustments for countries with limited data, although, ultimately, no covariates were used.

5.2 Bayesian maternal mortality estimation model (the BMat model)

Estimation and projection of maternal mortality indicators was undertaken using the BMat model. This model is intended to ensure that the MMR estimation approach is consistent across all countries but remains flexible in that it: is based on covariate-driven trends to inform estimates in countries or country-periods with limited information; captures observed trends in countries with longer time series of observations; and takes into account the differences in stochastic and sampling errors across observations.

In the BMat, the MMR for each country-year is modelled as the sum of the AIDS MMR and the non-AIDS MMR:

MMR = Non-AIDS MMR + AIDS MMR,

where non-AIDS maternal deaths refer to maternal deaths due to direct obstetric causes or to indirect causes other than HIV, while AIDS maternal deaths are those AIDS deaths for which pregnancy was a substantial aggravating factor.

The estimation of the AIDS MMR follows the same procedure as used in the previous publication, explained in section 5.2.2 (5).

In the BMat model, the non-AIDS MMR is estimated as follows:

Non-AIDS MMR(t) = Expected Non-AIDS MMR(t) * Data-driven multiplier(t)

where the expected Non-AIDS MMR(t) is estimated from a hierarchical regression model using covariates and country-specific intercepts (described in section 5.2.1). The data-driven multiplier(t) allows for deviations away from the rate of change in MMR implied by the expected non-AIDS MMR, as indicated by country-year-specific data points. For example, if data suggested that the non-AIDS MMR decreased (or increased) much faster in year *t* than expected based on covariates, the data-driven multiplier for that year is estimated to be greater (or smaller) than 1. This data-driven multiplier is modelled with a flexible time-series model, which fluctuates around 1, such that the covariates in the regression model determine the estimated change when data are absent.

The model is fitted to all data available in the country (see Figure 1), taking into account adjustments and uncertainty associated with the data points. CRVS observations are adjusted using the estimates of sensitivity and specificity as described in section 5.1. Specialized studies are not adjusted. Other data are adjusted as described in section 3.1.2. In the model, standard and stochastic errors for observations, which reflect the uncertainty associated with observations, are taken into account when obtaining PM and thus MMR estimates (see section 3.1.3). Observations with smaller error variances are more informative of the true PM and will thus carry a greater weight in determining the estimates as compared to observations with larger error variances.

In countries with high-quality data with little uncertainty, the final BMat estimates will closely track the country data. However, in the absence of data, or when data are very uncertain, the predictor variables (covariates) play an important role and inform the estimated trend in MMR.

The BMat provides estimates for all countries, using available information from these countries. This implies that inclusion of additional data observations for any one country (perhaps as a result of this consultation) will potentially result in very slight changes to estimates for other countries. For all outcomes of interest, uncertainty was assessed and will be reported in terms of uncertainty intervals.



The figure in this box illustrates MMR estimates for Country 1, a country without any observed MMR data, and Country 2, which has data. For both countries, the red dashed line illustrates the final estimates for the MMR, and red shaded areas illustrate the uncertainty associated with the estimates. The blue dashed line illustrates the covariate-driven "expected MMR" that would be estimated by the model if a country did not have data to inform its trend. Black dots illustrate MMR data points (usually obtained from observed PMs as explained in the data section). For each data point, its corresponding "adjusted value", which is the data after accounting for biases, is plotted in purple, together with associated uncertainty about the true PM (purple vertical lines).

For countries such as Country 1 without data points, the country-specific multiplier for the change in the non-AIDS MMR is equal to 1 for the entire period, and so the final MMR estimate is given by the expected MMR estimate (the red and blue lines are identical). For Country 2, the available data points suggest a different trend in the MMR as compared to the trend suggested by the covariates in the regression model (blue line). The final estimates in red better reflect the observed trend in the country's data.

Projections beyond the most recent observation for all countries are determined by the rate of change in the expected MMR (blue line) and the country-specific multiplier: the latter converges slowly to one, thus the rate of change in the projections converges to the rate of change in the expected MMR.

5.2.1 Hierarchical regression model (non-AIDS PM)

A hierarchical regression model was used to obtain the expected number of non-AIDS maternal deaths for each country-year. The model predicts the proportion of deaths due to maternal causes using three predictor variables: the GDP per capita, the GFR, and the presence of a skilled birth attendant (SBA) as a proportion of live births. These specific covariates were chosen from a broader list of potential predictor variables which fell into three groups: indicators of social and economic development (such as GDP, human development index, life expectancy), process variables (SBA, antenatal care, proportion of institutional births, etc.) and risk exposure (fertility level).

The model is summarized as follows:

$$\log(PM^{NA}) = b_0 + b_1 \log(GDP) + b_2 \log(GFR) + b_3SBA + \gamma_i + \varphi_k$$

where

 PM^{NA} = the expected proportion of non-AIDS-related maternal deaths among all non-AIDS deaths for women aged 15–49 years GDP = gross domestic product per capita (in 2011 PPP dollars) GFR = general fertility rate (live births per woman aged 15–49 years) SBA = proportion of births attended by skilled health personnel' personnel γ_j = random intercept term for country j φ_k = random intercept term for region k

For countries with data available on maternal mortality, the expected proportion of non-AIDS-related maternal deaths was based on country and regional random effects, whereas for countries with no data available, predictions were derived using regional random effects only. The resulting estimates of the PM^{NA} were used to obtain the expected non-AIDS MMR through the following relationship:

Expected non-AIDS MMR = $PM^{NA*}(1-a)*E/B$,

where

a = the proportion of AIDS deaths to women of reproductive age

E = the total number of deaths to women of reproductive age

B = the number of births.

5.2.2 Estimation of indirect HIV-related maternal deaths

For countries with generalized HIV epidemics and high HIV prevalence, HIV/AIDS has become a leading cause of death during pregnancy and post-delivery. There is also some evidence from community studies that women with HIV infection have a higher risk of maternal death, although this may be offset by lower fertility. If HIV is prevalent, there will also be more incidental deaths among pregnant women. It is thus important to address the issue of incidental and indirect maternal deaths among HIV-positive women in estimating maternal mortality for these countries.

The MMEIG examined several approaches for dealing with this issue and adopted a strategy that involves estimating the number of *indirect* maternal deaths due to HIV/AIDS. In this approach, the number of AIDS maternal deaths, D^{AIDS} is given by:

$$D^{AIDS} = a \cdot E \cdot v \cdot u$$

where

- a*E are the total number of AIDS deaths among all deaths to women aged 15-49.
- v is the proportion of AIDS deaths to women aged 15-49 that occur during pregnancy. The value of v can be computed as follows: v = c k GFR / [1 + c(k-1) GFR] where GFR is the general fertility rate, and where c is the average exposure

time (in years) to the risk of pregnancy-related mortality per live birth (set equal to 1 for this analysis), and where k is the relative risk of dying from AIDS for a pregnant versus a non-pregnant woman (reflecting both the decreased fertility of HIV-positive women and the increased mortality risk of HIV-positive pregnant women). The value of k was set at 0.3 based on newly available information (16).

u is the fraction of pregnancy-related AIDS deaths assumed to be indirect maternal deaths. The MMEIG/TAG reviewed available study data on AIDS deaths among pregnant women and recommended using u=0.3.

For observed PMs, we assumed that the total reported proportion of maternal deaths are a combination of the proportion of non-AIDS maternal deaths and the proportion of AIDS-related deaths, where the latter is given by a*v for observations with a "pregnancy-related death" definition and a*v*u for observations with a "maternal death" definition.

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APPENDIXES

Appendix A. Reporting errors in civil registration and vital statistics (CRVS) systems: examples

Figure 1 gives an illustrative example of misclassification in a CRVS system.



Figure 1: Illustration of CRVS misclassification

From this information, sensitivity and specificity are calculated as follows: Sensitivity = $\frac{T+}{T+plus F-} = \frac{320}{370} = 0.865$, Specificity = $\frac{T-}{T-plus F+} = \frac{1390}{1430} = 0.972$

Figure 2 provides an illustrative example with unregistered female deaths. In this example, the PM-in is given by (40+1390)/(360+1440), and the PM-out is given by 30/(30+670).

Figure 2: Illustration of CRVS misclassification AND missed deaths



Appendix B. Misclassified and missed/unregistered maternal deaths in civil registration and vital statistics (CRVS) systems – review process

The objective of the review was to assess the level of misclassification and missed/unregistered maternal deaths reported by national official agencies for all WHO Member States. In other words, what is the level of incorrect reporting of maternal deaths in national official CRVS reporting? (e.g. what is the difference between the official reported number of maternal deaths versus the number of maternal deaths identified through special maternal mortality studies, confidential enquires and surveillance systems, etc.?) And to what extent is the incorrect reporting of maternal death due to misclassification versus missed or unregistered maternal deaths? This finding is used to inform the adjustment factor for countries and periods where empiric information is not available.

This review identified studies that fulfilled the inclusion criteria, as presented in Table 1.

	Inclusion criteria
Population	Women of reproductive age (15–49 years) who died during
	pregnancy, or up to 1 year after termination of pregnancy,
	irrespective of the duration and the site of the pregnancy, from
	any cause
Concept	Assessment of misclassification of maternal deaths by CRVS
	systems.
Study design	Cross-sectional studies and retrospective cohort
Context	All WHO Member States reporting CRVS data

Table A1: Inclusion criteria for identifying eligible studies

Articles were eligible for inclusion in the review:

- a. if nationally representative;
- b. if possible to determine whether the data refer to misclassification or missed/unregistered deaths;
- c. if mid-year of reported data is after 1990;
- d. if there is matched comparison CRVS data available in the study or in the WHO Mortality Database to calculate the CRVS adjustment factor.

Search strategy

The search strategy was conducted for all relevant existing literature based on search terms relevant to the research questions restricted to the years 1990–2016, using the following online bibliographic databases: PubMed/MEDLINE, Embase, Global Index Medicus, EBSCO, Web of Science and POPLINE. The searches were conducted without any language restrictions. A hand search was also conducted on all WHO Member States ministries of health (MoH) websites to identify pertinent MoH maternal mortality and confidential enquiries reports.

Data extraction

Data were extracted from full-text journal articles and reports which meet the inclusion of the above criteria. Data were extracted using a Microsoft Excel database. Information retrieved from the included studies were country, years assessed, study objectives, methodology/study design, number of maternal deaths, information on misclassification and incompleteness when available, etc. Specifically, extraction focused on the assessment of the following

- a. The process by which the study retrieved and reviewed information on maternal deaths, including data source descriptions, definitions used by study, and whether the study reviewed all deaths to women of reproductive age or a description of the subset of deaths collected.
- b. The number of maternal deaths, and any information pertaining to a breakdown of maternal deaths misclassified by the CRVS system.
- c. Breakdown of maternal deaths by cause of death was extracted if reported.

Data from this review was merged with the MMEIG 2015 data base to add any studies that were not available from the review, i.e. as obtained through country consultation.

The search identified 86 studies that included relevant information on maternal death reporting.⁵ The 86 studies comprised of 32 individual countries, which contributed a total of 185 country-years with observed maternal death data relevant to analysis of misclassification of deaths or missed/unregistered deaths. Information was extracted on the extent to which the study assessed misclassification of maternal deaths within CRVS data, and whether the study identified unregistered maternal deaths outside CRVS systems.

Maternal death information available from specialized studies is sparse and is reported in a wide variety of ways. Specifically, the majority of specialized studies only reported total maternal deaths, which were assessed by reviewing maternal deaths from sources outside CRVS systems.

Information on misclassification specifically, is sparse, a total of 43 country-years contributed data on breakdowns of misclassification within CRVS reported maternal deaths (from 9 countries)⁶. A total of 13 specialized studies from three countries incorporated unregistered maternal deaths in their assessment of the total number of maternal deaths.⁷

⁵ The number of studies, country-years of data, and numbers of countries included may be revised following inputs received during the country consultation, as additional documentation may become available. ⁶ Ibid.

⁷ Ibid.

Appendix C. Specialized studies examining misclassification or missed/unregistered maternal deaths in civil registration and vital statistics (CRVS) systems

Australia

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Australia

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Australia

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Australia

Australian Institute of Health and Welfare (AIHW): Humphrey MD, Bonello MR, Chughtai A, Macaldowie A, Harris K, Chambers GM. Maternal deaths in Australia 2008–2012. Maternal Deaths Series no. 5. CAT. No. PER 70. Canberra: AIHW; 2015.

Australia

Maternal deaths in Australia 2012–2014. Cat. No. PER 92. Canberra: Australian Institute of Health and Welfare (AIHW); 2017.

Austria

Beck A, Vutuc C. Die Entwicklung der mütterlichen Mortalität in Österreich. Frauenarzt. 2008;49:21-6.

Brazil

Technical Note of the Ministry of Health of Brazil. Maternal mortality in Brazil: estimates versus reality. From country consultation in 2015. Ministry of Health, Secretariat of Health Surveillance [Brazil]; 2015.

Brazil

PAHO maternal mortality data set (reflecting communication on data requests collected via questionnaire). November–December 2018.

Canada

Turner LA, Cyr M, Kinch RAH, Liston R, Kramer MS, Fair M, et al. Under-reporting of maternal mortality in Canada: a question of definition. Chronic Dis Can. 2002; 23(1):22–30.

Chile

PAHO maternal mortality data set (reflecting communication on data requests collected via questionnaire). November–December 2018.

Colombia

PAHO maternal mortality data set (reflecting communication on data requests collected via questionnaire). November–December 2018.

Costa Rica

Proceso de Búsqueda Intencional y Reclasificación de Mortalidad Materna [Intentional Search Process and Reclassification of Maternal Mortality (ISPRMM)]. San José: Ministerio de Salud, Instituto Nacional de Estadística y Censos (INEC) [Costa Rica]; 2014 (in Spanish).

Denmark

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Denmark

Bødker B, Hvidman L, Weber T, Møller M, Aarre A, Nielsen KM, et al. Maternal deaths in Denmark 2002–2006. Acta Obstet Gynecol Scand. 2009;88:556-62.

Ecuador

PAHO maternal mortality data set (reflecting communication on data requests collected via questionnaire). November–December 2018.

Finland

Gissler M et al. Pregnancy-associated deaths in Finland 1987-1994 – definition problems and benefits of record linkage. Acta Obstet Gynecol Scand. 1997;76(7):651-7.

France

Les morts maternelles en France: mieux comprendre pour mieux prévenir. 5e rapport de l'Enquête Nationale Confidentielle sur les Morts Maternelles (ENCMM) 2010-2012. France: Institut National de la Santé et de la Recherche Médicale (INSERM), Sante Publique France; 2017 (in French).

France

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Georgia

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Jamaica

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Slovenia

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