Levels and Trends of Maternal Mortality in the World:  
The Development of New Estimates by the United Nations

Technical Report

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by

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This report offers a summary of work that has led to the development of new estimates of maternal mortality by the United Nations, and describes in detail the procedures used to calculate the final set of numbers. In general, the goal of the project was to derive new estimates of maternal mortality levels and trends for 172 countries or populations, by measuring, modeling, and then predicting summary indicators (such as the maternal mortality ratio) from 1990 to 2008.

For this purpose, we have developed an intricate system for recording all available data used for measuring maternal mortality at a national level going back to the late 1980s, and we have compared a number of modeling strategies. In this report, we describe both the data and the methods used for deriving the final set of estimates. The report does not include detailed information about the comparative analyses we have performed in choosing the final model. A more complete discussion and justification of the methodology used here will soon become available in a separate paper that we are preparing for publication in an academic journal.

Data on maternal mortality

Measures of maternal mortality

Most data points on maternal mortality used as inputs to our estimation process consisted of the observed proportion classified as “maternal” among all deaths occurring to females aged 15-49 (PMDF). PMDF inputs were in some cases reported values taken from a published source, and in other cases based on new calculations performed as part of this analysis. In the latter case, the calculation methods are documented here. One example in the latter category is the use of age-standardized PMDFs derived from DHS surveys or other applications of the sisterhood direct method.

PMDFs are considered the favored quantity to retain from available data because the reported fraction of maternal deaths is considered more robust and reliable than the number of maternal deaths on its own or in relation to the number of live births. The advantages of using PMDFs are discussed in detail elsewhere.¹ In all cases where PMDF information was available, the number of maternal deaths was estimated by multiplying an observed PMDF value by a corresponding estimate of total female deaths for ages 15-49. This procedure is sometimes referred to as the “envelope adjustment” because it assures that the resulting estimate of maternal mortality is consistent with an established envelope of all-cause mortality. Total female deaths for the envelope adjustment were estimated by multiplying mortality rates from WHO life tables by population estimates from the UN Population Division.²³

Observed values of the maternal mortality ratio (MMR) were sometimes used as inputs to the regression model, but only when comparable PMDF values were not available. In such cases, the MMR was converted into a PMDF using estimates of all-cause births from the UN Population Division and estimated total deaths of females aged 15-49 derived as described above. Reported MMRs from various sources were also used for checking and comparing model predictions against underlying data or previous estimates.

**Classification of maternal deaths**

Both PMDF and MMR data inputs and previous estimates reflect different concepts and practices with regard to the recording of a “maternal death”. There are two key dimensions along which these deaths can be categorized: maternal versus pregnancy-related deaths, and AIDS-related versus non-AIDS-related deaths. By definition, pregnancy-related deaths (any death during pregnancy plus 42 days, or 2 months in some cases) are composed of “maternal” and “accidental or incidental” deaths. Thus, all pregnancy-related deaths can be classified within the following two-by-two table:

<table>
<thead>
<tr>
<th>Maternal, non-AIDS-related</th>
<th>Maternal, AIDS-related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accidental/incidental, non-AIDS-related</td>
<td>Accidental/incidental, AIDS-related</td>
</tr>
</tbody>
</table>

Estimates of maternal mortality should only include deaths in the two categories of the top row.

To account for the different classifications of maternal deaths, two columns were included in the data matrix. The “definition” column of the input data matrix notes whether a data point has a proper “maternal” definition (including both “direct” and “indirect” maternal causes) or whether it reflects the broader “pregnancy-related” definition (any death during pregnancy plus 42 days, or 2 months). A third category, “pregnancy-related, no accidents”, includes all pregnancy-related deaths minus those identified as “accidents”. The “util” column represents the fraction of AIDS deaths (as estimated by UNAIDS) that were presumably included in a PMDF or MMR observation. This fraction is discussed in more detail in a later section on the method of modeling maternal mortality.

**Adjustments for different categories of “pregnancy-related” death**

*Maternal versus pregnancy-related deaths.* Data representing pregnancy-related rather than true maternal deaths were adjusted by removing a fraction of deaths, representing deaths that occur during pregnancy but not from maternal causes (i.e., accidental or incidental deaths). Adjustment factors for this purpose were derived using two types of evidence: studies where both maternal and pregnancy-related deaths were counted in the same population (see Table 1), and registration data on injury deaths (see Table 2). The latter study involved assessing the risk of injury death among reproductive-age women and estimating what proportion of pregnancy-related deaths would be injury-related, assuming pregnant women experience the same risk of injury death as women who are not pregnant. Such evidence suggests that the fraction of accidental/incidental deaths occurring during pregnancy is around 10-15% of non-AIDS deaths for low- or middle-income populations.
The value appears to be at the low end of this range for countries in Sub-Saharan Africa and at the high end elsewhere. Therefore, the non-AIDS-related component of the PMDF was adjusted by a factor of 0.9 for countries of Sub-Saharan Africa and by 0.85 for all other populations.

Table 1
Ratio of maternal to pregnancy related deaths from data sources with both types of information available

<table>
<thead>
<tr>
<th>Country</th>
<th>Source</th>
<th>Ratio of maternal to pregnancy-related deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bangladesh</td>
<td>BMMS 2001</td>
<td>0.846</td>
</tr>
<tr>
<td>Honduras</td>
<td>RAMOS 1998</td>
<td>0.739</td>
</tr>
<tr>
<td>Iran</td>
<td>Census 1996</td>
<td>0.700</td>
</tr>
<tr>
<td>Republic of Korea</td>
<td>MMR/COD 1995-1996</td>
<td>0.935</td>
</tr>
<tr>
<td>Nepal</td>
<td>NMMS 2008/9</td>
<td>0.930</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>Official Statistics 1997</td>
<td>0.958</td>
</tr>
<tr>
<td>Suriname</td>
<td>Confidential enquiry 1991-1993</td>
<td>0.940</td>
</tr>
<tr>
<td>Tunisia</td>
<td>Mat mort study 1993-1994</td>
<td>0.921</td>
</tr>
<tr>
<td>Mean / Median</td>
<td></td>
<td>0.871 / 0.926</td>
</tr>
</tbody>
</table>

Table 2
Percentage of non-AIDS pregnancy-related deaths estimated to be injury-related by WHO region

<table>
<thead>
<tr>
<th>Region</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>9</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>14</td>
</tr>
<tr>
<td>The Americas</td>
<td>19</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>27</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>31</td>
</tr>
<tr>
<td>Europe</td>
<td>41</td>
</tr>
<tr>
<td>High Income</td>
<td>49</td>
</tr>
</tbody>
</table>
**AIDS-related maternal deaths.** We also used data on the proportion of total deaths of women aged 15-49 that are due to AIDS. Maternal deaths can be related to HIV/AIDS in two ways: an HIV-positive woman may die from direct maternal causes where HIV infection is an aggravating factor, or from indirect maternal causes because the pregnancy increases her susceptibility to opportunistic infections such as tuberculosis or malaria.

Before serving as the dependent variable of the regression model, all PMDF values were adjusted so that they correspond to maternal, non-AIDS-related deaths only. Thus, the model was used to determine non-AIDS-related maternal mortality only, and a component related to AIDS was added separately. The formula used for removing the AIDS-related portion of maternal (or pregnancy-related) deaths is described below along with other formulas used in relation to the regression model.

**Adjustments for data errors or study design**

PMDF/MMR data points come from various sources. Observed values were adjusted for incomplete reporting and/or misclassification of maternal deaths depending on the type of data. The categories of data type and associated adjustments were as follows:

- Vital registration data.
  - Data from civil registration were extracted primarily from the WHO mortality database for the years 1985 onwards. For civil registration data using ICD-9, deaths from chapter X: complication of pregnancy, childbirth and the puerperium (codes 630–676) were included. For civil registration data using ICD-10, the chapter XV: pregnancy, childbirth and the puerperium (codes 000-099) plus A34 (maternal tetanus) were extracted in order to match ICD-9. It should be noted that ICD-9 does not specifically identify late maternal deaths whereas ICD-10 does. To maintain comparability between civil registration datasets, maternal deaths coded as late maternal deaths (ICD-10 096, 097), were considered in the total numbers of maternal deaths. These late maternal deaths only accounted for between 1% and 2% of the deaths extracted from ICD-10 data.
  - Before computing a PMDF or MMR, maternal and all-cause deaths of unknown age from vital registration data were distributed proportionally over the age range and added to reported age-specific deaths.
  - PMDFs derived from vital registration (VR) data used in the modeling were adjusted upward by a factor of 1.5 in order to account for misclassification of maternal deaths except for countries with one or more studies pointing toward a different value. This 50% upward correction is the median of values derived from studies of data quality for several countries. Full details on country-specific adjustment factors are provided in the appendix.
  - For countries with time series of death registration data of reasonable quality, data from vital registration were used directly to estimate trends in MMR (see section below).

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• Sisterhood direct data. PMDFs derived from sisterhood direct data were adjusted by a simple age-standardization (imposing the age distribution of all females in sampled households at the time of survey rather than the age distribution implied by retrospective reports of sisters’ lives). We also assumed that the fraction of pregnancy-related deaths is understated and adjusted the age-standardized value upward by a factor of 1.1. (Note that the total number of deaths occurring to sisters of respondents may have been underreported as well, but that issue is addressed by using the observed proportion of maternal deaths as the input for analysis, rather than their absolute number.)

• Data on recent household deaths, including various surveys, censuses, and the Indian Sample Registration System. These data have been adjusted upward by a factor of 1.1 in order to account for underreporting of maternal deaths.

• Special studies of maternal mortality, including Reproductive Age Mortality Study (RAMOS), confidential enquiries, etc. An adjustment factor of 1.1 has also been applied to these data points.

Inclusion or exclusion of PMDF data points

The dataset constructed for use in modeling the PMDF contains a total of 680 observations, of which only 484 were used for estimating the regression model. Individual data points were excluded for a variety of reasons:

• A number of the observations included were duplicates, corresponding to redundant information from the same source. For example, in the case of sisterhood direct data sources, the dataset includes PMDFs computed as part of this analysis using observed age-specific mortality rates (both all-cause and maternal), as well as various summary measures (MMR, PMDF, etc.) computed earlier and available in some published source. In such cases the PMDFs derived from age-specific data were used as the main inputs for this analysis, whereas the various summary measures were retained only for comparison purposes.

• If a study provided estimates of both pregnancy-related mortality and maternal mortality, the estimate for maternal mortality was utilized in the model and the pregnancy-related observation was excluded.

• Some observations were excluded because a PMDF could not be calculated from the data available in the study (e.g., lacking information about live births) or because the reported PMDF was equal to zero.

• Information from vital registration for several countries were excluded from the analysis because the attribution of cause of death was not considered good enough to warrant use of the data in the model.

• In general, we did not collect data from studies based on the sisterhood indirect method for producing estimates of maternal mortality. Any observations using this method that were included in the dataset were excluded from the modeling.

• Observations representative of a subgroup of the national population were excluded.
Treatment of multiple observations

Some countries have no or very few data points, and few countries have five or more data points over the time period of this study. Note that our data are organized such that a VR observation refers to five-year time periods such as 1988-1992 or 2003-2007, and such observations each receive a weight of one in the regression model. Most other data sources (a single survey, census, special study, etc.) yield a single observation referring to some time period; such observations also receive a weight of one in the regression model. Some surveys, however, yield more than one data point for multiple time periods; in such cases all of the various observation are included in the model but with a combined weight of one.

Data for model covariates/predictors

Three covariates were included in the regression model used here to estimate maternal mortality: gross domestic product per capita (GDP), the general fertility rate (GFR), and the proportion of deliveries with a skilled attendant at birth (SAB). These specific covariates were chosen from a broader list of potential covariates falling into three categories:

- **Socioeconomic development indicators.** In addition to the per capita GDP, we considered using other indicators of the level of socioeconomic development in a country, including the HDI (Human Development Index), the life expectancy at birth (for women), and the probability of dying from birth to age 5 (for both sexes combined). The mortality variables are available over the full time period, but per capita income was deemed preferable as a broader and more direct measure of development. The HDI offers an even broader measure of development than GDP per capita (the latter is a component of the former), but it is not universally available going back in time to the 1980s and 1990s because of the lesser availability of information on education and literacy.

- **Process variables.** In addition to the SAB, we gathered data and constructed time series estimates regarding the proportion of deliveries where the mother received antenatal care (ANC) and the proportion of births delivered in an institutional setting (IDLV). The choice to favor the SAB over the other two variables was due largely by its greater availability across time and space.

- **Fertility level.** The GFR is the number of births in a population divided by the number of women at reproductive ages (technically, woman-years of exposure for ages 15-49). We used the GFR because it is a central part of simple formulas linking some common measures of maternal mortality. For example, the MMR (maternal deaths per live birth) and the MMRate (maternal deaths per woman aged 15-49) are related by the following formula: \(\text{MMR} \times \text{GFR} = \text{MMRate}\). In words, maternal deaths per live birth times births per woman equals maternal deaths per woman. An alternative choice, the total fertility rate (TFR), obscures this relationship but leads nevertheless to similar empirical results, since the two measures are highly correlated.

Virtually complete series of annual estimates for these three sets of covariates were constructed from 1985 to 2008, with projections forward to 2015 in many cases, using data from various sources. Here, we document only the data series used as part of the final model.
Gross Domestic Product per capita (GDP)

The GDP variable used here is expressed in constant 2005 international dollars, or units of purchasing power parity (PPP), with most data provide by the World Bank. For years 1985-2008, published data from the World Bank\textsuperscript{5} were used without any manipulation. For years 2009-2015, projected series in international dollars were not available. Therefore, the projected World Bank series of GDP per capita in constant 2005 US dollars\textsuperscript{6} was converted to international dollars (PPP) using PPP conversion factors.\textsuperscript{7} Furthermore, since the population figures used to calculate the projected GDP per capita differed from those used to calculate the estimates for the earlier years, we corrected for the inconsistency by multiplying the projected GDP per capita\textsuperscript{8} by the associated population estimates to obtain the total GDP, and then dividing the total GDP by population estimates from the same series used to estimate GDP per capita for the earlier period.\textsuperscript{9}

Data for countries not included in the World Bank dataset were obtained from other sources. Since the World Bank dataset used for most countries in the analysis did not contain estimates for Myanmar, data from an older set of World Bank estimates were used. For Afghanistan, Bahamas, Cuba, Iraq, Puerto Rico, Somalia, and Zimbabwe, GDP estimates were obtained from the Penn World Tables Version 6.3.\textsuperscript{10} For North Korea, estimates of total GDP obtained from the World Health Organization\textsuperscript{11} were divided by population estimates from the World Bank\textsuperscript{12} to obtain the values of GDP per capita used for this analysis.

In many cases, a complete annual series for the period between 1985 and 2015 was missing mostly because data from earlier years were lacking, or because the projected GDP estimates were not available, or both. In these cases, the data were interpolated to produce one-year estimates according to the following set of rules:

- Estimates before the first observation were assumed equal to the first observation.
- If the desired time reference fell between the reference points of two observations, the estimated value was calculated by linear interpolation between the two observations.
- Estimates after the last observation were assumed equal to the last observation.

\textsuperscript{10} Alan Heston, Robert Summers and Bettina Aten, Penn World Table Version 6.3, Center for International Comparisons of Production, Income and Prices at the University of Pennsylvania, August 2009.
\textsuperscript{11} Unpublished data, National Health Accounts Series, WHO.
We used the annual data series of GDP per capita for each country to compute

time-matched average values of this covariate for time intervals corresponding to
observation intervals for each of the 484 PMDF (or MMR) observations that provide the
dependent variable of the regression model. In general, each time-matched covariate
equals a weighted average of annual estimates, with weights equal to the fraction of the
total observation interval contained in the given year. For example, if the PMDF
observation interval extends from 1 June 2000 through 31 May 2003, the time-matched
GDP equals:

\[
(1/3)\left[ \left( \frac{7}{12} \right) GDP_{2000} + GDP_{2001} + GDP_{2002} + \left( \frac{5}{12} \right) GDP_{2003} \right].
\]

If the interval covered less than one year, the time-matched covariate equals the (annual)
estimate for the year that contains the interval mid-date (instead of an average value if the
interval straddles two years).

**General Fertility Rate (GFR)**

The GFR was calculated using data from the United Nations Population Division.\(^{13}\) As with
the GDP, annual series of live births and female population aged 15-49 were constructed
directly using the UN data, then weighted averages of annual values for both births and
female population were computed for each PMDF time interval. Finally, the time-matched
value of the GFR was obtained by dividing the average number of births by the average
female population size for the interval.

**Skilled Attendant at Birth (SAB)**

According to the MDG manual, the proportion of births attended by skilled health
personnel (SAB) is defined as “the percentage of deliveries attended by personnel trained
to give the necessary supervision, care and advice to women during pregnancy, labor and
the post-partum period; to conduct deliveries on their own; and to care for newborns.”\(^{14}\)
Furthermore, the manual limits the qualified health personnel to “those who are properly
trained and who have appropriate equipment and drugs. Traditional birth attendants, even
if they have received a short training course, are not to be included.”\(^{15}\) Available SAB data
originate from health surveys and other sources. The information used for this analysis
was obtained from a database maintained by UNICEF. Although other sources of SAB data
were consulted, only the UNICEF data were used because they adhere strictly to the
definition given above.

Multiple SAB observations are available for most countries. However, since the data are
collected only periodically through surveys or other means, they refer to various time
intervals. Annual data series were constructed by fitting a logit (or log-odds) model of the

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\(^{14}\) United Nations Development Group. Indicators for monitoring the millennium development goals:

\(^{15}\) United Nations Development Group. Indicators for monitoring the millennium development goals:
SAB proportion with time as the sole covariate. Such a model was estimated separately for each country. When a country had only one observation, it was assumed that the SAB proportion remained constant over time. For some countries where the logit model did not fit well (including Fiji, Guyana, Montenegro, New Zealand and Thailand), annual values were estimated using the interpolation algorithm described above for producing one-year GDP estimates for countries with limited data. For the following countries, we had no properly documented SAB data: Cyprus, Germany, Denmark, Greece, Iceland, Israel, Italy, Norway, Puerto Rico, Spain, Sweden, and Switzerland. We assumed access to a skilled attendant at birth was universal in these countries so we assigned a value of SAB=1 for all time points.

As with the GDP and GFR covariates, time-matched values of SAB for use in the regression model were obtained by computing weighted averages of annual values over the PMDF observation interval.

**Method of estimating MMR trends from death registration data**

For countries whose death registration data met the following criteria, the death registration data were used directly in the analysis to derive the MMR. For all other countries, the model discussed in the next section was used to estimate maternal mortality. The requirements for death registration data to be included in the analysis were as follows:

- Earliest year of available data is before 1996.
- Latest year of available data is after 2002.
- Data were available for more than half of the range of years (from the first year available to the last year available).
- Estimated completeness of death registration of at least 85% for all years, with at the most 1 or 2 exceptions.
- Deaths coded to ill-defined cause codes (ICD-10 R codes) did not exceed 20%, or exceeded 20% for only 1 or 2 years.

Death registration data for maternal mortality were adjusted for both completeness and misclassification. The completeness refers to completeness of the death registration. The methods of adjustment for misclassification of maternal deaths used here were identical to those used for constructing the PMDF, i.e., an adjustment factor of 1.5 by default or a country-specific adjustment factor if a study or other documentation was available.

For each of the target years, \( t = 1990, 1995, 2000, 2005 \), the maternal mortality death counts adjusted for completeness and misclassification and the corresponding live births from UN Population Division were pooled for the 5-year periods from \( t-2 \) to \( t+2 \). The pooled maternal deaths were divided by pooled live births to obtain the estimated MMR.

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16 Although we examined other models of SAB using time and GDP as predictors, we concluded that the simpler model with time alone was sufficient for the present application.
There are a few countries without data for the interval centered on 1990 and a few with only one year of observation in the interval 2003-2007. For these countries, the estimate from the multilevel regression model was used instead.\textsuperscript{19} If data were available for 2008 or 2009, the average of 2004-2008 or 2004-2009 was taken as the point estimate for 2008. When data were not yet available for 2008 or 2009, the point estimate for 2005 (based on the 2003-2007 average) was assumed to remain constant through 2008.

For four countries with complete registration systems but very small numbers of maternal deaths (Bahamas, Belgium, Iceland, and Malta), the multilevel regression model was used to generate estimates for all time periods in order to avoid unrealistic time trends.

**Method of modeling maternal mortality**

For countries lacking complete and reliable death registration systems, the core of our estimation strategy was a hierarchical/multilevel model with three main covariates (log of GDP per capita, log of the GFR, and SAB), plus random effects for countries and regions. For this part of the analysis, we referred frequently to the excellent discussion of such methods by Gelman and Hill.\textsuperscript{20}

Although we tried models with both fixed and random effects for countries and regions, we prefer the hierarchical/multilevel approach (i.e., random effects) because it offers a statistically well-grounded means of incorporating country data about levels and trends of maternal mortality within a global model that can also be used for predicting out of sample. The model was used to generate estimates both for those few countries with no available data on maternal mortality, and for those many countries where data on maternal mortality refer to a limited number of time intervals over the period from 1990 to 2008.

The general form of the regression model used for this analysis is as follows (omitting country/region effects for the moment):

\[
\log(\text{PMDF}) = \beta_0 + \beta_1 \log(\text{GDP}) + \beta_2 \log(\text{GFR}) + \beta_3 \text{SAB} + \text{offset} + \text{error}
\]

An offset term is an additional predictor variable with an assumed coefficient of one. In this case, the offset equals \(\log(1 - a)\), where log is the natural logarithm (in base \(e\)) and \(a\) is the proportion of AIDS deaths among all deaths of women aged 15-49 in the population. Such an offset changes the interpretation of the beta-portion of the regression model, which becomes a predictive model of \(\log(\text{AMDF})\) rather than \(\log(\text{PMDF})\), since in general:

\[
\text{AMDF} = \text{AIDS-adjusted PMDF} = \frac{\text{PMDF}}{1 - a}.
\]

The AMDF (AIDS-adjusted PMDF), defined in this manner, was used in the 2005 round of UN estimates for the purpose of minimizing the influence of the HIV epidemic on the regression model used to predict maternal deaths. It removes AIDS deaths from the

\textsuperscript{19} These include Barbados 2005, 2008; Serbia 1990, 1995. In addition, for Serbia, in order to take into account the fact that Kosovo is not included in data after 1998, the MMR derived from the PMDF was used for 2000, 2005 and 2008.

denominator but not from the numerator. However, deaths due to AIDS are often included in the numerators of data used here to measure maternal mortality. For example, observations of pregnancy-related mortality from sisterhood data include all deaths to pregnant women in the reported PMDF, including deaths due to AIDS.

The model used here goes a step further than the methods used for previous UN estimates by removing AIDS deaths from both the numerator and the denominator of the PMDF. Removal of AIDS deaths from the denominator is accomplished by means of an offset term as described above. Removal of AIDS deaths from the numerator is somewhat more complicated and requires a special set of formulas (see next section).

Using a non-AIDS PMDF, or $PMDF^{na}$, as the dependent variable with an offset of $\log(1 - a)$ as described above, we estimated a multilevel regression model with random effects for both country and region. Thus, assuming that observation $i$ refers to country $j$ located in region $k$, the regression model was as follows:

$$\log\left( PMDF^{na}_i \right) = \beta_0 + \beta_1 \log(GDP_j) + \beta_2 \log(GFR_i) + \beta_3 SAB_i + \alpha^c_{j[i]} + \alpha^R_{k[i]} + \log(1 - a_i) + \epsilon_i$$

Predicted values of this regression equation were computed for 5-year intervals centered around 1990, 1995, 2000, 2005, and 2008 for each country, and these were taken as estimates of the non-AIDS PMDF.

**Special treatment of AIDS-related maternal deaths**

Our estimation strategy was based on the assumption that a portion of AIDS deaths occurring among pregnant women should be counted as “maternal,” either because HIV infection was an aggravating cause of a death that occurred primarily due to direct obstetric causes, or because pregnancy was a substantial aggravating factor in a death due primarily to HIV.

As before, for a given population, let $a$ be the fraction of AIDS deaths (as defined and estimated by UNAIDS) among all deaths of women at ages 15-49. Also, let $v$ be the estimated proportion of such AIDS deaths that occur during pregnancy or within 42 days (or 2 months) after delivery. It follows that $v$ times $a$ represents the number of AIDS deaths that occur to pregnant women among all deaths of women at ages 15-49. Assuming that a fraction, $u$, of these are counted as maternal, we obtain the following formula for an AIDS-related PMDF:

$$PMDF^a = uva$$

The total PMDF equals the sum of its non-AIDS and AIDS-related components, and therefore:

$$PMDF = PMDF^{na} + PMDF^a = PMDF^{na} + uva$$

This formula was used at two points in the calculations leading to final estimates of maternal mortality. First, it was used to derive the dependent variable of the regression model, by adjusting observed data on maternal or pregnancy-related mortality so that such observations refer to a common definition or category of deaths (non-AIDS-related, maternal deaths only). Second, after using the regression model to estimate the non-AIDS
PMDF, the above formula was used to estimate the total PMDF, from which one can easily compute the total MMR and other quantities of interest.

There is an important difference between these two calculations, however. In the latter case, we use a value of $u = 0.5$, reflecting an assumption about the fraction of AIDS deaths during pregnancy that should be counted as “maternal” in our final estimates. In the former case, we use $\tilde{u}$ in place of $u$, as $\tilde{u}$ is a characteristic of a particular data point and represents the fraction of pregnancy-related AIDS deaths that presumably were included in a given PMDF observation – after any adjustments for misclassification of maternal deaths have already been made.

Although we considered various options, in the end we used only two values of $\tilde{u}$ for this analysis. For PMDF observations with a “pregnancy-related” definition (with or without accidents), we assumed that $\tilde{u} = 1$ in all cases. For PMDF observations with a “maternal” definition, we assumed that $\tilde{u} = 0.5$. For vital registration data, in particular, we assumed that the corrected data (after application of adjustment factors as shown here in Appendix 1) included the proper fraction of deaths due to AIDS during pregnancy (i.e., $u = \tilde{u} = 0.5$). In such cases, the two assumptions cancelled out, as we assumed that any corrections to underlying data yielded adjusted values that capture, implicitly, maternal deaths that are related to HIV/AIDS as well as those (the vast majority in most cases) that are not.

Prior to fitting the multilevel regression model, we converted each observed or adjusted PMDF value into a non-AIDS PMDF by the following formula:

$$
PMDF_{i}^{na} = \begin{cases} 
PMDF_{i}^{adj} - \tilde{u}_i \nu_i \alpha_i & \text{if definition = "maternal"} \\
(PMDF_{i}^{adj} - \nu_i \alpha_i)(1 - \pi_i) & \text{if definition = "pregnancy-related"} \\
PMDF_{i}^{adj} - \nu_i \alpha_i & \text{if definition = "pregnancy-related, no accidents"}
\end{cases}
$$

where $\delta_i$ is indicator variable that equals 1 if the observation’s definition is “pregnancy-related” and 0 otherwise. In theory, the resulting quantity includes only non-AIDS-related maternal deaths in the numerator (and all deaths of women at ages 15-49 in the denominator, including deaths due to HIV/AIDS).

Note that this definitional adjustment also corrects the over-counting of incidental or accidental deaths due to causes other than HIV/AIDS for pregnancy-related observations. Thus, the only adjustments that preceded this calculation were those related to the incomplete recording of events due to misclassification of maternal (or pregnancy-related) deaths.

The parameter, $\nu$, in the above equations is computed as follows:

$$
\nu_i = \frac{k c GFR_i}{1 + (k - 1) c GFR_i}
$$

---

21 Because so little evidence was available, we agreed to count exactly half of the estimated number of AIDS deaths that occur during pregnancy as “maternal” deaths in this evaluation.
where \( c \) equals the average exposure-to-risk (in years) of pregnancy-related mortality per live birth, \( k \) equals the relative risk of dying from AIDS for a pregnant versus a non-pregnant woman. The formula can be derived easily by noting that each woman-year of exposure to the risk of a maternal death can be divided into two parts: a portion where she is pregnant (on average, \( c \cdot GFR \)) and a portion where she is not pregnant (on average, \( 1 - c \cdot GFR \)). If the risk of death due to HIV/AIDS when a woman is pregnant is \( k \) times the same risk when a woman is not pregnant, then the fraction of AIDS deaths occurring to pregnant women is \( k \cdot c \cdot GFR \) divided by \( k \cdot c \cdot GFR \) plus \( 1 - c \cdot GFR \), which equals \( v \).

For this analysis, we have assumed that \( c = 1 \) and \( k = 0.4 \). The assumption of \( c = 1 \) allows for a typical gestation of 39 weeks, plus 42 days (or 2 months) after delivery, plus a small allowance for pregnancies that do not result in a live birth.

Although there was no strong \textit{a priori} basis for choosing \( k = 0.4 \), there seemed to be agreement among the experts we consulted that its value is almost certainly below one (reflecting a belief that the selection against pregnancy for HIV-positive women has a stronger effect compared to the elevated mortality experienced by such women during pregnancy). The chosen value of 0.4 resulted from an analysis of model output, suggesting that the multilevel regression model fit the data more closely for values of \( k \) in the range of around 0.3 to 0.6. Within this range, most results of interest are not highly sensitive to the specific choice of \( k \).

**Uncertainty of Estimates**

We have broken down the components of uncertainty as follows:

1. Remaining bias in adjusted PMDF values;
2. Imprecise knowledge of model parameters (\( c, k, u \), and \( \pi \));
3. Variability as reflected within the PMDF model;
4. Errors in data used for the AIDS adjustments (\( a \), the proportion of AIDS deaths among women aged 15-49) or for the MMR conversion (estimated live births and total deaths of women aged 15-49);
5. Alternative specification of model, choice of covariates, etc.

We performed calculations to quantify the uncertainty implied by (1) through (4). Although there was inadequate time to consider (5) in any detail, we believe that this would be a useful topic for further analysis. We made a distinction between uncertainty that is reflected within the multilevel regression model used for estimating the non-AIDS PMDF and uncertainty that is due to calculations that occur outside that model, and labeled these “internal” and “external” uncertainty, respectively.

For the external components, or (1), (2), and (4), we chose a set of \textit{a priori} distributions based on our own intuition (following discussions with various experts), but in all cases without the benefit of strong evidence to guide the specific choices. The assumed distributions were used to generate a large number (\( N_r = 100 \)) of model replicates. For each replicate the model was re-estimated using the slightly altered set of data and input
parameters. Then, within each replicate, an additional number \( (N_2 = 10) \) of simulations were performed to assess the impact of the internal component of uncertainty, or (3). Thus, each simulation yielded a total of 1000 distinct outcomes \( (N_1 \times N_2 = 100 \times 10 = 1000) \).

Proceeding in this manner, simulated data were used to compute full sets of model estimates (for each time period in every country, region, and the world), reflecting the uncertainty implied by (1), (2), (3), and (4). From these distributions we derived 95% uncertainty intervals using the 2.5 and 97.5 percentiles.

Creating replicates of dataset and input parameters

As noted above, the first step of these calculations was to create by simulation a large number of replicates \( (N_1 = 100) \) of the dataset, adjustment factors, and model parameters. Such distributions are depicted in graphs found at the end of this report. The model was estimated separately and a second set of simulations was then performed using each replicate.

Adjustment factors for PMDF data. Each adjustment factor, \( F \), was represented by a log-normal distribution with a mean located at the assumed value (as noted earlier, these factors differ by data type). We assumed that the standard deviation of \( \log(F) \) was 0.05, and thus that likely errors in the adjustment factors fall in a range of plus or minus 10%.

Input parameters \( (c, k, u, \text{ and } \pi) \). Input parameters were represented by log-normal or beta distributions. The beta was used for parameters with values between 0 and 1 only, either by definition as with \( u \) and \( \pi \), or by choice as with \( k \). A log-normal distribution for \( k \) seemed overly lopsided, so we used a beta distribution for greater symmetry around the assumed mean value of 0.4. Although in theory \( k \) could have any positive value, there was wide agreement among the experts we consulted that it is almost certainly below one.

Additional data inputs \( (a, \text{Births, and Deaths}) \). The number of live births and the number of deaths among women aged 15-49 are additional data inputs needed for converting an estimate of PMDF into an estimate of MMR. In addition, the estimated proportion of AIDS deaths among all deaths of women aged 15-49 (the variable \( a \) in the equations shown here) was another necessary data input for calculations that occur outside the regression model. For all three of these data inputs, simulated values were generated for each replicate. The birth and death counts were assumed to follow a bivariate log-normal distribution, with means equal to the logarithm of the estimated values, standard deviations equal to 0.05 (like the adjustment factors), and a correlation of 0.7 (reflecting the fact that both quantities were derived using the same set of population estimates from the UN Population Division). Similarly, we assumed that \( \logit(a) \) had a normal distribution, with a mean equal to the logit of the estimated value and a standard deviation of 0.05.

Correlation of errors across countries. The types of errors described by these various distributions are likely to be correlated across countries. That is, if our assumed value is too high for one country, it is likely to be too high for other countries as well. It seems very unlikely that there is either no correlation or perfect correlation across countries in the errors of our assumed values for adjustment factors and input parameters. However, these two cases are the most convenient to compute: either we sample separate (independent)
values for each country, or we sample one value and apply it to all countries (within a given replicate).

Simulating correlated values in a more general way was not attempted. Rather, in the absence of evidence about the actual degree of correlation of errors in these assumed values across countries, we took the midpoint of the two extremes (i.e., no or perfect correlation) as our best estimate for all uncertainty intervals. It is important to note that this choice has no effect on uncertainty estimates at the country level but only for regional and global aggregates. When we assume no correlation across countries, then the errors made at the country level tend to cancel out in the aggregate, implying less uncertainty for regional and global estimates. When we assume perfect correlation, the regional and global uncertainty is much greater because country errors are tied together and do not cancel out.

Whereas it seems very likely that there is some positive correlation of errors across countries for individual parameters (or adjustment factors), it seems less likely that there is a significant correlation of errors across these items. On the other hand, there is probably a very strong correlation over time within countries for a given item. Therefore, we have sampled each parameter independently of the others and have assumed constant values over time for a given country.

**Propagating uncertainty through the model and estimates**

After creating a set of replicates as described above, the second step of the uncertainty evaluation involved estimating the PMDF model using each replicate. Then, using standard model outputs (estimated coefficients, variance-covariance matrix, etc.), we simulated distributions of model coefficients. Using these simulated results, we approximated the distribution of the estimated \( \log(\text{PMDF}) \) in order to quantify the inferential uncertainty. We did not include the predictive uncertainty related to each individual data point.

In a standard picture of a regression model (multilevel or otherwise), the inferential uncertainty is represented by a band of regression lines or curves representing the plausible range of best estimates given the covariates, whereas the predictive uncertainty refers to the spread of data points around an individual regression line. Since our concern was to represent the uncertainty of the estimated regression equation, not the variability of individual data points, we included only the inferential component of the uncertainty from the regression analysis.

**Notation and key equations used for these calculations are as follows:**

- **Beta coefficients**: \( \beta_0, \beta_1, \ldots, \beta_p \) - \( p \) covariates (\( p \) equals 3)
- **Country random effects**: \( \alpha_i^C, \alpha_j^C, \ldots, \alpha_i^C \) - \( J \) countries
- **Region random effects**: \( \alpha_i^R, \alpha_k^R, \ldots, \alpha_k^R \) - \( K \) regions
- **Variance components**: \( \sigma_c \) (countries), \( \sigma_R \) (regions), \( \sigma_y \) (data)

**Multilevel regression model:**

\[
y_i = \beta_0 + \alpha_i^C + \alpha_i^R + \beta_1 \log(\text{GDP}) + \beta_2 \log(\text{GFR}) + \beta_3 \text{SAB} + \log(1 - a_i) + \epsilon_i
\]
where:

\( y_i \) is a shorthand for the dependent variable, \( \log(\text{PMDF}^{na}) \), for \( i = 1, \ldots, n \)

\( \text{PMDF}^{na} \) is an adjusted “non-AIDS, maternal only” PMDF, as described earlier

\( j \) and \( k \) of \( \alpha_{ji}^c \) and \( \alpha_{ki}^k \) refer to the country and region of the \( i \)-th observation

\( \alpha_j^c \sim N(0, \sigma_j^c), \quad \alpha_k^k \sim N(0, \sigma_k^k), \) and \( \epsilon_i \sim N(0, \sigma_i^2) \)

Distributions of parameters given the estimated coefficients (used for simulation):

\[
\begin{align*}
\sigma_j^c &\sim \tilde{\sigma}_j^c \cdot df_j / \chi^2_{df_j} \\
\sigma_k^k &\sim \tilde{\sigma}_k^k \cdot df_k / \chi^2_{df_k} \\
\sigma_i^y &\sim \tilde{\sigma}_i^y \cdot df_i / \chi^2_{df_i} \\
\beta &\sim N(\hat{\beta}, V_p) \\
\alpha_j^c &\sim N(\hat{\alpha}_j^c, V_j^c) \\
\alpha_k^k &\sim N(\hat{\alpha}_k^k, V_k^k)
\end{align*}
\]

where:

\( V_p \) is the variance-covariance matrix for \( \beta \) given \( \hat{\beta} \)

\[
V_j^c = \frac{1}{\frac{n_j}{\sigma_j^c} + \frac{1}{\sigma_j^c}} \quad \text{is the variance of} \quad \alpha_j^c \quad \text{given} \quad \hat{\alpha}_j^c, \quad \text{for} \quad j = 1, \ldots, J
\]

\[
V_k^k = \frac{1}{\frac{n_k}{\sigma_k^k} + \frac{1}{\sigma_k^k}} \quad \text{is the variance of} \quad \alpha_k^k \quad \text{given} \quad \hat{\alpha}_k^k, \quad \text{for} \quad k = 1, \ldots, K
\]

\( n_j \) and \( n_k \) are the number of obs. (or total weight) per country or region

\( \chi^2_v \) is a chi-square random variable with \( v \) degrees of freedom

As described earlier, we began by simulating \( N_1 \) replicates of the dataset and input parameters. Then, using the equations given here, for each replicate we simulated \( N_2 \) values of all parameters of the regression model, creating \( N = N_1 \times N_2 \) values in total to represent the distribution of each parameter. Note that the sigma parameters must be simulated first, as they are used to derive the beta and alpha parameters. The latter are used to derive a simulated distribution of estimates, depicting the inferential uncertainty.
## Appendix 1
Country-specific adjustment factors used for this analysis:

<table>
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<th>Country</th>
<th>Interval</th>
<th>Misclassification adjustment</th>
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Sources (by country):
Albania
Australia
Austria

Brazil

Canada


Colombia
Registros de Certificados de Defunción del Sistema de EEEV. 2008: Cifras preliminares.

El Salvador

Finland

France


Georgia

Japan


Netherlands


Taiwan

United Kingdom


United States of America


Uzbekistan
State department of statistics.
Assumed distribution (log-normal) for PMDF adjustment factor

Note: adjusted PMDF is observed value multiplied by adjustment factor

Assumed distribution (log-normal) for PMDF adjustment factor

Note: adjusted PMDF is observed value multiplied by adjustment factor

Assumed distribution (log-normal) for PMDF adjustment factor

Mean = 2
SD = 0.1

Note: adjusted PMDF is observed value multiplied by adjustment factor

Assumed distribution (beta) for \( u \) parameter

Mean = 0.5
SD = 0.2

Note: \( u \) is the proportion of AIDS deaths among pregnant women with indirect maternal causes
Assumed distribution (log-normal) for $c$ parameter

- Mean = 1
- SD = 0.04

Note: $c$ is the mean exposure to the risk of pregnancy-related death per live birth

Assumed distribution (beta for $k$ parameter

- Mean = 0.4
- SD = 0.15

Note: $k$ is the relative risk of AIDS mortality among pregnant vs. non-pregnant women aged 15-49

Assumed distribution (beta for $\pi$ parameter, SSA countries

- Mean = 0.1
- SD = 0.04

Note: $\pi$ is the proportion incidental or accidental among non-AIDS deaths to pregnant women

Assumed distribution (beta for $\pi$ parameter, non-SSA countries

- Mean = 0.15
- SD = 0.06

Note: $\pi$ is the proportion incidental or accidental among non-AIDS deaths to pregnant women