Maternal mortality in high HIV prevalence countries:

A critical analysis of the MMEIG methodology for

estimating maternal mortality

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Thesis submitted to the Faculty of Commerce in partial fulfilment
of the requirements for the Degree of Master of Philosophy
In Demography

September 2012
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PLAGIARISM DECLARATION

This research is my original work, produced with supervisory assistance from my supervisor. I have used the Harvard convention for citation and referencing. Each contribution to this dissertation from the works of other people has been duly acknowledged, cited and referenced. In addition, this dissertation has not been submitted for any academic or examination purpose to any other university.

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ABSTRACT

The main objective of this research is to analyse critically the methodology used by the Maternal Mortality Estimation Inter-Agency Group (MMEIG) to estimate maternal mortality in countries with high HIV/AIDS prevalence. This study interrogates each of the assumptions (implicit and explicit) in the MMEIG method by reviewing literature/studies that investigated each assumption.

This research has clearly demonstrated that there are differences in the effect that HIV/AIDS has on maternal mortality between regions and among countries. This research has shown that for southern African countries, the mortality rate of pregnant women infected with HIV/AIDS is lower than the mortality rate of non-pregnant women infected with HIV/AIDS, but appears to be significantly higher than the 40% assumed by the MMEIG. Consequently, the proportion of HIV/AIDS deaths in women aged 15-49 years last birthday occurring during the pregnancy-related period is higher than that estimated from the MMEIG's method for estimating v. The research has also shown that the estimated number HIV/AIDS deaths due to indirect maternal causes is more than the 50% assumed by the MMEIG, and consequently, HIV/AIDS deaths due to maternal causes estimated by the MMEIG are lower than expected. In spite of interventions to reduce mortality among women infected with HIV/AIDS (and hence lower estimates of deaths rates than estimated by the WHO life tables), HIV/AIDS is shown to increase the number of AIDS deaths due to maternal causes collectively through higher levels of v, k, and u, than is assumed by the MMEIG.

Through increases in GDP and SAB, and decreases in GFR, the covariates used by the MMEIG in its model of non-AIDS maternal mortality are associated with maternal mortality in a way that tends to predict lower levels of maternal mortality. Underlying observations of maternal mortality data and corollary adjustments to these data, on the other hand, suggest increasing levels of maternal mortality. Based on the assumption that countries with complete vital registration require a 50% adjustment for misclassification of maternal deaths, southern African countries with vital registration less complete than South Africa are likely to require an adjustment higher than the additional 50% assumed by the MMEIG. This research has also clearly shown that the 10% adjustment made by the MMEIG to account for the proportion of pregnancy-related deaths due to unnatural causes understates the expected proportion of

pregnancy-related deaths due to unnatural causes for South Africa, and possibly for the southern African region. Even though there is much uncertainty about maternal mortality estimates, based on the findings of this research, it is evident that the MMEIG approach to estimating maternal mortality understates the level and trend of maternal mortality estimates for countries with high HIV prevalence.

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1.1   Background

The United Nations, through its Maternal Mortality Estimation Inter-Agency Group (MMEIG) initiative with the World Health Organization (WHO), United Nations Children's Fund (UNICEF), United Nations Population Fund (UNFPA) and The World Bank, have developed numerous global, regional, and country estimates of maternal mortality (WHO, UNICEF and UNFPA 2001; 2004; 2007; 2010; 2012). The estimates of maternal mortality levels and trends produced by the MMEIG for the period 1990 to 2010 (WHO, UNICEF, UNFPA *et al.* 2012) are an updated version of the estimates for the period 1990 to 2008 (WHO, UNICEF, UNFPA *et al.* 2010).

The MMEIG approach comprises three steps. First, maternal mortality data are compiled from nationally-representative sources, such as civil registration records, surveys, censuses, and surveillance systems. Second, countries are categorised by available sources of data. Developing countries, such as southern African countries, lack complete vital registration data and so rely on other data sources. Third, for countries with good vital registration data, the Maternal Mortality Ratio (MMR) is estimated directly from data after adjusting for underreporting of maternal deaths, i.e. covering both incompleteness and misclassification (WHO, UNICEF, UNFPA *et al.* 2012). For the rest of the countries that have incomplete or no vital registration data, non-AIDS maternal mortality is estimated using a multilevel regression model fitted using national-level data recorded in censuses and surveys. Maternal mortality associated with HIV/AIDS is estimated from AIDS deaths among women of reproductive age, and proportions of these deaths occurring during the pregnancy-related period, and those that are due to maternal causes. The total maternal mortality is the sum of the non-AIDS and AIDS maternal mortality estimates.

Other institutions, such as the Institute for Health Metrics and Evaluation (IHME), have also developed global and regional estimates of maternal mortality for a comparable time span from similar data, but using different methodologies (Hogan, Foreman, Naghavi *et al.* 2010, Lozano, Wang, Foreman *et al.* 2011). In spite of overlapping time spans and data sets, estimates of maternal mortality indicators over time and across countries and regions arising from the different methodologies are significantly different, as shown in Figure 1.1. These differences in estimates of maternal

mortality arise from conceptual and practical differences in the definition of maternal deaths, and the sources and treatment of data (AbouZahr 2011).

Figure 1.1 Comparison of MMEIG and IHME estimates of the maternal mortality ratio for southern African countries for the year 2008
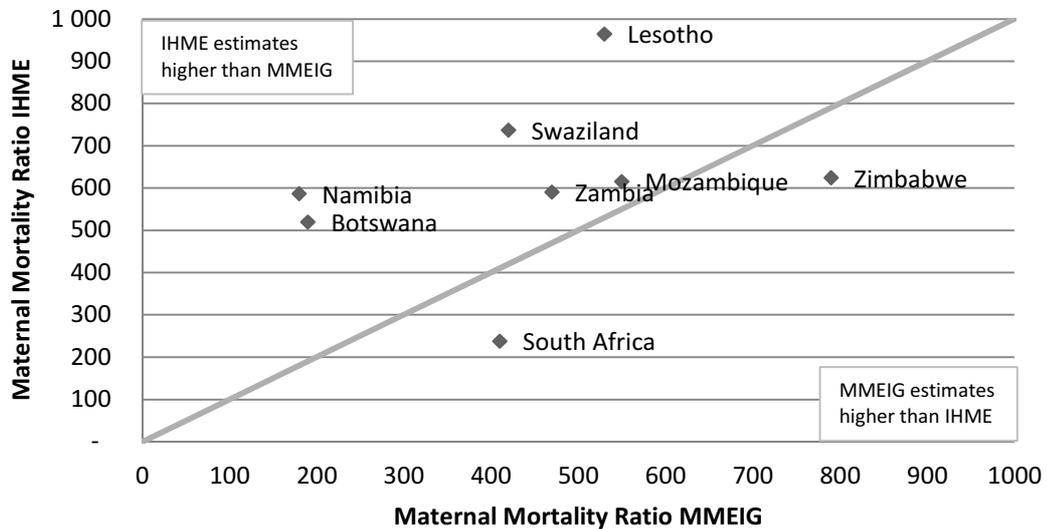
Source: Estimates of MMR extracted from IHME (Hogan, Foreman, Naghavi *et al.* 2010) and MMEIG (WHO, UNICEF, UNFPA *et al.* 2010)

The prevalence of HIV/AIDS complicates the classification of maternal deaths in situations where the attribution of cause of death is questionable because HIV status of women who die during pregnancy, childbirth, or up to the 42 days following delivery is unknown, and there is a lack of diagnostic facilities. In addition, HIV/AIDS compromises sources and quality of data through the underreporting of deaths of females of reproductive age recorded in censuses and surveys as a result of disintegration or disappearance of households following the death of a woman (United Nations 2008, Graham and Hussein 2003). Moreover, HIV/AIDS complicates the interpretation of maternal indicators and trends. For instance, increases in the number of deaths among females of reproductive age due to HIV/AIDS tend to understate estimates of the proportion maternal among deaths of females of reproductive age (PMDF) (Hakkert 2001).

This study is, therefore, intended to document clearly the methods applied by the MMEIG. This entails an interrogation of each of the assumptions (implicit and explicit) in their method of dealing with the derivation of non-AIDS and AIDS maternal mortality estimates.

1.2   Aims and objectives of the research

The main objective of this research is to analyse critically the methodology used by the MMEIG to estimate maternal mortality in countries with high HIV/AIDS prevalence. To achieve this goal, the specific objectives of this research are to:

1. document in detail the various methods for estimating maternal mortality, in addition to those used by the MMEIG;

2. examine the MMEIG's choice of model covariates for predicting non-AIDS maternal mortality, namely, gross domestic product (GDP) per capita based on purchasing power parity conversion, skilled attendant at birth (SAB) as a proportion of total live births, and general fertility rate (GFR) (Wilmoth, Zureick, Mizoguchi *et al.* 2010);

3. investigate the adjustment factor of 1.1 applied to maternal death data recorded in census and survey data to account for unreported deaths that may be due to abortion-related and other causes (Wilmoth, Zureick, Mizoguchi *et al.* 2010);

4. investigate the adjustment factor of 0.9 applied to pregnancy-related death data for sub-Saharan African countries to account for accidental/unnatural deaths that occur during pregnancy (Wilmoth, Zureick, Mizoguchi *et al.* 2010);

5. investigate the reasonableness of the WHO life tables for southern African countries;

6. investigate the grounds for the MMEIG's addition of 50% for misclassification of maternal deaths in civil registration;

7. investigate the impact of combinations of the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (*k*), and general fertility rate on the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*); and

8. investigate the reasonability of the assumption made by the MMEIG that half the number of pregnancy-related AIDS deaths is indeed due to indirect maternal causes (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

From the answers to the above, this study will draw conclusions as to the validity of the assumptions underlying the method used by the MMEIG, as well as estimate the impact of these assumptions on the estimates of maternal mortality in high HIV prevalence countries. The findings of this research will, therefore, further allow

assessment of the reliability of maternal mortality estimates in countries with high HIV prevalence where resources are spent on interventions to reduce maternal mortality. This outcome is consistent with measuring progress towards meeting Millennium Development Goal 5.

1.3   Structure of the thesis

Chapter 2 presents a review of the literature relevant to this thesis. This entails description of the MMEIG method; methods for estimating maternal mortality used by other researchers; determinants of maternal mortality; the impact of HIV/AIDS in sub-Saharan Africa; and the incidence of unsafe abortion and maternal mortality associated with it.

Chapter 3 presents the method used to produce the results that are described and analysed in Chapter 4.

Chapter 5 discusses the extent to which these results meet the objectives of this study, outlines the limitations of the method used in this research, and identifies areas for potential future research, before closing with conclusions that can be drawn from the study.

2   LITERATURE REVIEW

For the purpose of analysing critically the MMEIG methodology for estimating maternal mortality in high HIV/AIDS prevalence countries, the literature dealing with the analysis is categorised into six main areas of research. These are: a description of the MMEIG method; a description of alternative methods for estimating maternal mortality; an assessment of the impact of HIV/AIDS on the measurement of maternal mortality; and unsafe abortion and maternal mortality associated with it.

2.1   Description of the MMEIG method

2.1.1   Definition of maternal mortality

The MMEIG classifies deaths of pregnant or postpartum women as either non-AIDS-related or AIDS-related. Furthermore, within this classification deaths are categorised as either strictly maternal, pregnancy-related or pregnancy-related excluding deaths from accidents and incidental causes (Wilmoth, Zureick, Mizoguchi *et al.* 2010). For the category of deaths of women during pregnancy or up to 42 days following delivery (which this study hereafter defines as deaths occurring during the pregnancy-related period) which the MMEIG refers to as maternal, the MMEIG adopts the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, 1992 (ICD-10) definition, which 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 cause (WHO, UNICEF, UNFPA *et al.* 2010:10).

In countries that have complete civil registration systems supplemented by correct attribution of cause of death, this definition entails identification of maternal deaths as deaths of women during the pregnancy-related period occurring due to either direct or indirect (including HIV) obstetric causes (WHO, UNICEF, UNFPA *et al.* 2012). For the category of deaths of women during the pregnancy-related period to which the MMEIG refers as pregnancy-related, the MMEIG adopts the ICD-10 classification that includes a concept of "pregnancy-related death", which defines a maternal death as death of women during the pregnancy-related period regardless of the cause of death (Wilmoth, Zureick, Mizoguchi *et al.* 2010:2). For the category of deaths of women during the pregnancy-related period, which the MMEIG refers to as "pregnancy-related, no

accidents", the MMEIG includes all pregnancy-related deaths but excludes deaths identified as caused by unnatural causes or accidents (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

2.1.2   Sources of maternal death data and adjustment to the input data

Data on maternal mortality and variables relevant to the computation of the maternal mortality ratio (MMR), an indicator of maternal mortality, are acquired from individual bodies of the MMEIG and other external partners (WHO, UNICEF, UNFPA *et al.* 2012). Maternal death data are obtained from nationally-representative sources, such as civil registration, censuses, and surveys such as Demographic and Health Surveys. Deaths attributable to HIV/AIDS are obtained from the UNAIDS (2010), while data on deaths among females of reproductive age are derived from the WHO (2011b) life tables. In addition, data on the number of live births, and total female population by country are obtained from estimates developed by the United Nations Population Division (2011). Other data, such as skilled attendant at birth are obtained from the UNICEF (2010), while data on gross domestic product are obtained from The World Bank (2010) and the Penn World Tables (Heston, Summers and Aten 2011).

Prior to the estimation of the Maternal Mortality Ratio (MMR), countries are categorised into three groups based on the source and type of maternal mortality data (WHO, UNICEF, UNFPA *et al.* 2012). The first group comprises developed countries which are characterised as having complete civil registration systems (i.e. estimated completeness of death registration of at least 85%), and good attribution of cause of death (Wilmoth, Mizoguchi, Oestergaard *et al.* 2012). Even in such countries, the maternal death data, in the form of the proportion maternal among deaths of females of reproductive age (PMDF), derived from vital registration may be incomplete and/or misclassified (i.e. underreported) for a multitude of reasons. The chief drivers of underreporting of maternal deaths are misunderstanding of ICD rules, lack of record of pregnancy status on the death certificate, and the suppression of information especially relating to deaths due to abortion (WHO, UNICEF, UNFPA *et al.* 2010). To account for such underreported maternal death data, either a reported country-specific adjustment factor (if it is available), or a universal adjustment factor of 1.5, based on a literature review of published reports for select developed countries, is applied to adjust complete vital registration data. Once the observed PMDF has been adjusted for underreporting, the underlying number of maternal deaths is determined by multiplying the PMDF by the total number of females of reproductive age estimated from the

WHO (2011b) death rates and the United Nations Population Division (2011) estimates of the female population. The resulting number of maternal deaths is then divided by the number of live births estimated from United Nations Population Division (2011) data to arrive at the MMR.

The second and largest group of countries is made up of those lacking complete registration data but where other types of data are, however, available from other sources, such as censuses and surveys (Wilmoth, Mizoguchi, Oestergaard *et al.* 2012). Developing countries experiencing high HIV/AIDS prevalence, such as southern African countries, all fall in this group.

The third group of countries consists of those that do not have any source of maternal death data (WHO, UNICEF, UNFPA *et al.* 2012). These countries may have no national data on maternal mortality probably because either their populations are too small to provide reliable estimates (e.g. Cape Verde and Solomon Island) or because conflict has resulted in a breakdown of civil registration systems so that they are unable to compile maternal death data (e.g. Angola and Burundi).

Similar to developed countries, the maternal death data for countries in the second group, which are derived from censuses or surveys in the form of pregnancy-related measures of maternal mortality, such as the pregnancy-related mortality ratio, are adjusted for incompleteness and/or misclassification of maternal deaths prior to estimation of the MMR. In this case, the MMEIG applies either a reported country-specific adjustment factor (if it is available), or a universal adjustment factor of 1.1 to the observed PMDF data to account for underreporting of maternal deaths (Wilmoth, Zureick, Mizoguchi *et al.* 2010). Furthermore, to arrive at a measure of maternal mortality for sub-Saharan African countries, pregnancy-related deaths derived from census and survey data are reduced by ten per cent to account for deaths due to unnatural/accidental causes. This adjustment is based on evidence from two types of study. In one study, the ratio of maternal to pregnancy-related deaths is calculated from data sources where both types of information are available, as may be the case with Demographic and Health Surveys or Demographic Surveillance Systems. In the other type of study, the proportion of deaths that occur to pregnant women attributable to injury is estimated by assessing the risk of death due to injury among females aged 15-49 last birthday and assuming that all women, regardless of pregnancy status, experience the same risk of death from injury (Wilmoth, Zureick, Mizoguchi *et al.* 2010). However, evidence from some studies (Granja, Zacarias and Bergström 2002) suggests that

pregnant women are more at risk of dying from injury than non-pregnant women, while other studies (Ronsmans, Khlat, Kodio *et al.* 2001) are inconclusive on whether pregnancy has a protective effect on women's health.

2.1.3 Scope for misreporting and misclassification of maternal deaths by source of data

2.1.3.1 Censuses

For countries lacking complete and reliable vital registration data, a population census is one of the options for measuring maternal mortality directly. Unlike other methods, such as surveys that base estimates on a sample of the population, censuses are universal, targeting the entire population, thus reducing the uncertainty associated with measurements (WHO, UNICEF, UNFPA *et al.* 2012, Fauveau 2011).

In order to measure deaths in general, as well as pregnancy-related deaths, the United Nations (2008) recommends that the census ask questions about deaths that occurred in the household in the past 12 months. If a death is reported, follow-up questions are asked about whether the death was due to an unnatural/accidental cause, and whether the deceased was a woman aged 15-49 years last birthday, and if so, whether she died while pregnant, during childbirth, or up to 6 weeks following delivery (United Nations 2008).

In spite of the recommendations made by the United Nations (2008), there are practical challenges to measuring maternal mortality accurately. By their nature, censuses do not (and cannot) collect information on a cause-of-death basis, but instead collect information on pregnancy-related deaths. Pregnancy-related deaths comprise all deaths of women during the pregnancy-related period (i.e. pregnancy and up to 42 days following delivery) regardless of cause, excluding deaths due to unnatural causes. As such, pregnancy-related deaths tend to overestimate the proportion of deaths attributable to maternal causes because of the inclusion of deaths that may not be due to maternal causes but are only related to pregnancy in time (Hogan, Foreman, Naghavi *et al.* 2010, WHO, UNICEF, UNFPA *et al.* 2012).

The census is also susceptible to missing data on maternal deaths because of human error on the part of the enumerators. The number of pregnancy-related deaths to be used in the estimation of pregnancy-related mortality rates may be understated in a number of ways. For instance, where a household death has been identified but there is no response to the questions on the time of death relative to pregnancy. Where no specific treatment for missing responses is done, and editing of data is left to the

discretion of the analyst, it is likely that such deaths will be classified as non-maternal (Hill, Stanton and Gupta 2001). However, if missing responses are imputed using hot-deck methods, for example, it is also possible for the missing responses to be classified as either maternal or non-maternal, depending on the imputation rules.

There may be inconsistencies in responses to questions, for example, with males having responses for pregnancy status, or responses from females outside the reproductive age. Furthermore, there is scope for overstatement or understatement of the number of deaths among females of reproductive age because of recall error due to respondents extending or shrinking the reference period in response to timing of death questions (Dorrington and Bradshaw 2011).

In addition, the number of deaths of females of reproductive age recorded by the census may be underreported because of disintegration of households following the death of a woman, or in the case of single-person households, there may be no survivors to report the death (Graham and Hussein 2003, United Nations 2008, Dorrington and Bradshaw 2011). The effect of disintegrating or disappearance of households following a maternal death is more observable in developing countries where modern nuclear family structures predominate the traditional extended family system.

2.1.3.2   *Household surveys*

Household surveys designed with questions on broad causes-of-death are able to collect information on deaths that occurred in a household in the 12 months preceding the survey to enable the estimation of maternal mortality. Similar to the census, household surveys identify pregnancy-related deaths including or excluding deaths due to injury or unnatural causes, and are susceptible to similar problems of misclassification and misreporting of deaths (Dorrington and Bradshaw 2011, WHO, UNICEF, UNFPA *et al.* 2010).

Unlike censuses, household surveys are based on a sample of the total population. Household surveys may be based on samples which are not large enough to be representative of the population age, and socio-economic structure, resulting in weak analysis of maternal mortality differentials and greater uncertainty of pregnancy-related mortality estimates (Hill, Stanton and Gupta 2001, WHO, UNICEF, UNFPA *et al.* 2012).

2.1.3.3   Sibling histories from DHSs- the direct method

The DHS direct method provides a retrospective (typically five to seven years prior to the survey) estimate of maternal mortality based on the time of death relative to pregnancy, childbearing, and the postpartum period (which is generalised to two months to simplify reporting for the respondent). The respondent is asked to provide her mother's full birth history, names and ages of surviving siblings, and age at death and time of death, in years prior to survey, of deceased siblings, and to distinguish maternal deaths from non-maternal deaths, i.e. whether deceased sisters died during pregnancy, childbirth, or postpartum (Stanton, Abderrahim and Hill 1997).

Although the method requires considerable data, it has the advantage of requiring few assumptions. The chief assumptions are those of the independence of the number of siblings and their survival probability, and accurate reporting of the ages at death of deceased siblings and cause and timing of death relative to the pregnancy (Stanton, Abderrahim and Hill 1997).

Inaccurate recall among respondents may bias estimates of maternal mortality. For instance, older respondents may fail to recall accurately the deaths of siblings that occurred in the distant past. Likewise, younger respondents may fail to report distant events in their older siblings' lives, manifesting as an increasing trend in maternal mortality. It is, therefore, more likely that there will be more underreporting of dead siblings by the time of death relative to pregnancy than by the deceased sibling's age at death, preventing identification of deaths (Stanton, Abderrahim and Hill 2000, Hill, Arifeen, Koenig *et al.* 2006).

2.1.3.4   Verbal autopsy

Verbal autopsies are usually associated with Health and Demographic Surveillance System sites (HDSSs), which regularly collect birth and death data of sub-national populations in developing countries where medical certification of cause of death is unavailable (WHO, UNICEF, UNFPA *et al.* 2012). The process involves interviewing the deceased's caretakers by using a questionnaire to identify the cause of death from symptoms and events preceding death. The information acquired is then reviewed by individual physicians, physician consensus, or analysed using various probabilistic models in order to decide on the cause of death (Soleman, Chandramohan and Shibuya 2006).

In the context of southern Africa, where populations experience a generalised HIV/AIDS epidemic, HDSSs have a role to play in terms of provision of timely and

accurate cause-specific mortality estimates (Herbst, Mafojane and Newell 2011). Even though there is debate over the how generalizable the results are because of the size and isolation of HDSSs (Clark 2004), the accumulation of archives of verbal autopsy data provides opportunities that allow the study of the dynamics of the HIV/AIDS epidemic through interpretation of data by individual physicians, physician consensus, or the InterVA model (Herbst, Mafojane and Newell 2011, Byass, Kahn, Fottrell *et al.* 2011).

Verbal autopsy may, however, fail to identify correctly the cause of maternal death because of misclassification in the verbal autopsy by the diagnosing physician. According to Byass, Kahn, Fottrell *et al.* (2011), the identification and/or classification of HIV-related deaths among women of reproductive age may be influenced by the interpretation of cause of death arising from physicians' perceptions of the HIV/AIDS epidemic. They suggest that physicians tend to have inconsistent perceptions of the dynamics of the epidemic at the different stages of the epidemic. In the early stages of the epidemic, there is little knowledge about key signs and symptoms, increasing the likelihood that HIV-related deaths will be underreported and/or misclassified. Conversely, in later stages of the epidemic, physicians' perceptions of the epidemic may reflect inflated views of the impact of the epidemic on mortality (Byass, Kahn, Fottrell *et al.* 2011).

Byass, Kahn, Fottrell *et al.* (2011) further contend that nondisclosure of the deceased's HIV status due to the stigma associated with HIV-related deaths by informants may also affect the quality and detail of information on signs and symptoms of verbal autopsy data. Like physician perceptions, the extent of possible nondisclosure due to stigma is also likely to vary with development of the epidemic. In the early stages of the epidemic nondisclosure tends to be low because informants may not be widely aware of AIDS-defining signs and symptoms. However, because physician diagnosis is also not adapted to the epidemic, the likelihood of misclassification of HIV-related deaths may be higher than expected (Byass, Kahn, Fottrell *et al.* 2011). As the HIV/AIDS epidemic develops, in spite of physicians having improved diagnostic capabilities, the rise in stigma and the nondisclosure associated with it is likely to offset improved diagnoses and increase misclassification of HIV-related deaths. However, in the mature stages of the epidemic, the widespread knowledge about signs and symptoms and interventions such as testing for HIV and the provision of antiretroviral treatment are likely to reduce stigma, nondisclosure, and, hence, misclassification of HIV-related deaths (Byass, Kahn, Fottrell *et al.* 2011).

In addition to the adverse effect of HIV/AIDS, it is not uncommon for deaths due to abortion to be misclassified as non-maternal or conversely non-maternal causes of death being misclassified as abortion-related due to physician error. Further, verbal autopsy may result in misclassification of maternal deaths because of inconsistent algorithm diagnoses. On the assumption that the diagnoses by algorithm is likely to be more accurate than physician diagnoses, such errors produce a proportionately larger realisation of false positives or false negatives from the algorithm diagnoses relative to physician diagnoses of cause of death (Chandramohan, Rodrigues, Maude *et al*. 1998).

2.1.4   Estimation of maternal mortality using a multilevel regression model

After the maternal death data (recorded in vital registration for countries with complete civil registration, and accurate attribution of cause of death) and pregnancy-related death data (recorded in censuses and surveys for countries lacking complete registration data) are adjusted for underreporting and expressed as a PMDF that accounts for maternal deaths due to obstetric causes, the MMR for countries with no national-level data available for estimating maternal mortality is estimated using an indirect method. This method is based on fitting the adjusted observed maternal PMDF data to a hierarchical/multilevel regression model. This model estimates the proportion maternal among non-AIDS deaths of females of reproductive age ($PMDF^{na}$) by regressing the adjusted observed $PMDF^{na}$ on gross domestic product (GDP) per capita, skilled attendant at birth (SAB) as a proportion of total live births and general fertility rate (GFR) for each country for the years, i, centred on 1990, 1995, 2000, 2005 and 2008 as follows:

$$\ln(PMDF_i^{na}) = \beta_0 + \beta_1 \ln(GDP_i) + \beta_2 \ln(GFR_i) + \beta_3 SAB_i + offset + error$$

where the term *offset* removes AIDS deaths from the total deaths of females of reproductive age in the denominator of the PMDF.

In order for PMDF observations to be included in the model, the MMEIG applied rules for selection from the various sources of data. Maternal death data from nationally-representative sources are included in the model in preference to pregnancy-related observations or published values of PMDF or MMR, while data derived from sub-national sources, such as hospital studies, are excluded from input in the model (Wilmoth, Zureick, Mizoguchi *et al*. 2010). In addition to sub-national data, data from the indirect sisterhood method are excluded from input into the model because of the disadvantages of the method. These disadvantages, in contrast to the direct method, are the inability of the method to allow for calculation of maternal rates and ratios

pertaining to the pregnancy-related period; inability to analyse maternal mortality by parity; inability to perform data checks for completeness and plausibility; and the general requirement to make more assumptions to use the method (Stanton, Abderrahim and Hill 2000). In the event where either multiple observations of maternal mortality are derived from surveys, or where single observations are derived from censuses over the specific periods in which the model estimates maternal mortality, the MMEIG applies an equal weighting to both sets of observation (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

The choice of covariates used in the multilevel model is based on three types of indicator, namely, indicators covering social development, indicators covering process, and indicators measuring exposure to pregnancy. There is a broad range of indicators of socioeconomic development, such as, expectation of life at birth for females, under-five mortality, and female literacy (Hicks and Streeten 1979, The World Bank 2010). However, the MMEIG decided to use gross domestic product as the independent variable because of its universality "as a broader and direct measure of development" (WHO, UNICEF, UNFPA et al. 2010:6). In order to fit the model to maternal death data, the MMEIG constructs a series of GDP per capita, expressed in constant 2005 United States dollars, which are converted to international dollars using purchasing power parity conversion factors developed by The World Bank (2010) for each of the five year periods centred on 1990, 1995, 2000, 2005, and 2008 (Wilmoth, Zureick, Mizoguchi *et al.* 2010). Where no data on GDP are available from the World Bank estimates, the MMEIG uses alternative values for GDP derived either from the Penn World Tables (Heston, Summers and Aten 2011) or from country information on National Health Accounts developed by the WHO (2011a). Where GDP data do not exist for the desired year, linear interpolation of the GDP estimates encompassing the desired period is used to estimate the GDP at that point, while GDP estimates before and after the first and last GDP values are assumed to equal the respective first and last observations of GDP.

Gottlieb and Lindmark (2002) report on a wide range of indicators of process which impact on maternal mortality, the chief being the proportion of births attended by trained staff, the fatality rate due to direct obstetric complications, the number of health centres providing maternity ward services, and the proportion of all births in maternity wards. As is the case with GDP, SAB is the variable chosen by the MMEIG because of "its greater availability across time and space" (WHO, UNICEF, UNFPA *et*

al. 2010:6). Through its Multiple Indicator Cluster Survey (MICS), supplemented by DHS and other household surveys, UNICEF (2010) compiles up-to-date statistics for SAB for countries across all regions of the world. In order to fit the model to maternal death data, the MMEIG estimates GFR from data on total live births and total female population of reproductive age estimated from the United Nations Population Division (2011). As is done with GDP, the MMEIG constructs a series of live births and female population aged 15-49 last birthday directly from the UN Population Division data, and matches the series to the years centred on the five-year periods on 1990, 1995, 2000, 2005, and 2008 by applying a similar technique, as was done with GDP observations.

There are a number of indicators of fertility level from which the MMEIG could choose, namely, the total fertility rate (TFR), general fertility rate (GFR), crude birth rate (CBR), and completed fertility rate (CFR) (Bongaarts and Feeney 1998). The MMEIG uses the GFR as a covariate in its model because, unlike TFR, the former provides a direct link between the maternal mortality ratio (MMR) and maternal mortality rate (MMRate); specifically the GFR is the quotient of MMR and MMRate (Wilmoth, Zureick, Mizoguchi *et al.* 2010). The MMEIG uses SAB data maintained in the UNICEF (2010) database, which is based on the United Nations Development Group (2003) Millennium Development Goal manual for classification of skilled attendants, such as nurses and doctors, who have undergone formal training in the use of equipment and drugs appropriate for maternal care. Annual data series of SAB for each country are constructed by fitting a logit model of SAB with time as the sole covariate, and the series are time-matched to the years centred on the five year periods between 1990, 1995, 2000, 2005, and 2008 by taking a similar approach to the treatment of GDP and GFR observations.

2.1.5 Estimation of indirect AIDS maternal deaths

The proportion of AIDS deaths that qualify as indirect maternal deaths out of the total number of AIDS deaths among females aged 15-49 years last birthday is estimated as follows:

$$PMDF^{a} = uva$$

where *a* is the proportion of deaths among women aged 15-49 last birthday due to AIDS, *v* is the estimated proportion of AIDS deaths in women aged 15-49 last birthday occurring during the pregnancy-related period, and *u* is the fraction of pregnancy-related AIDS deaths due to indirect maternal causes (Wilmoth, Zureick, Mizoguchi *et al.* 2010, Wilmoth, Mizoguchi, Oestergaard *et al.* 2012, WHO, UNICEF, UNFPA *et al.* 2012).

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

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

Where the MMR is not estimated directly, it is arrived at by first multiplying the predicted PMDF by the number of deaths of women aged 15-49 last birthday (estimated from WHO (2011b) death rates and United Nations Population Division (2011) population estimates) to arrive at an estimate of the number of maternal deaths. The resulting maternal deaths are then divided by the total number of live births based on United Nations Population Division (2011) estimates to arrive at the MMR.

2.1.6 Uncertainty about maternal mortality estimates

The MMEIG's estimates of maternal mortality lie within an upper and lower limit that is designed to depict the uncertainty of these estimates. The components of uncertainty of these maternal mortality estimates arise from two sources, namely, internal and external components of uncertainty (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

Internal components of uncertainty emanate from the specification of the multilevel regression model, where estimation of a statistical model results in uncertainty in parameters of the model (Hogan, Foreman, Naghavi *et al.* 2010, Wilmoth, Zureick, Mizoguchi *et al.* 2010). Another internal source of uncertainty about estimates of maternal mortality arises from the specification of the covariates (GDP, GFR, and SAB) used in the model for non-AIDS maternal mortality. There is likely to be uncertainty in estimates of GDP, GFR and SAB for developing countries as seen in reports of such estimates by development agencies that do not report uncertainty intervals for their measurement (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

According to the MMEIG, the components of uncertainty internal to the model account for only the inferential uncertainty affecting the estimates regardless of the additional uncertainty of prediction of the individual data points (WHO, UNICEF, UNFPA *et al.* 2010). Inferential uncertainty of maternal mortality estimates for the given set of covariates (in this case GDP, SAB, and GFR) is estimated by a band of regression lines representing the plausible range of best estimates (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

Unlike the Institute for Health Metrics and Evaluation (IHME), which specifies a spatial-temporal regression model to show the correlation across countries within regions (Hogan, Foreman, Naghavi *et al.* 2010), the MMEIG states that errors associated with internal components of uncertainty are likely to be correlated across countries,

especially those that belong to the same region. The MMEIG argues that it is unlikely to have a situation in which there is either no correlation or perfect correlation across countries. As such, the MMEIG finds it more convenient to compute a sample of independent values of PMDF for each country, or to sample one PMDF value and apply it to all countries within the same region (Wilmoth, Zureick, Mizoguchi *et al.* 2010). When perfect correlation is assumed, the uncertainty of regional and global estimates of maternal mortality is large because of serial correlation of estimates at the regional level, resulting in errors in estimates reinforcing each other rather than cancelling out. Conversely, when it is assumed that no correlation exists, correlation errors at the country level tend to cancel out in aggregate, implying less uncertainty for regional and global estimates of maternal mortality (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

The MMEIG argues that it seems less likely that there is significant correlation of errors across countries for individual parameters, such as the covariates of the regression model. As motivation for the approach of sampling each parameter independently and in order to assume constant values over time for a given country, the MMEIG assume that there is probably a strong correlation over time within countries for a given covariate of the model for non-AIDS maternal mortality (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

The MMEIG identified external sources of uncertainty as those that are due to assumptions or calculations done on data before fitting the model to these data. The MMEIG chose a set of statistical distributions to model the external components of uncertainty. The MMEIG concedes that they did not have strong evidence to guide the specific choices of distribution despite discussion with experts on the subject (Wilmoth, Zureick, Mizoguchi *et al.* 2010). The residual bias in the observed PMDF values that have been adjusted for underreporting of maternal deaths is one of the external components of uncertainty in the estimates of maternal mortality. Each adjustment factor for observed PMDF was represented by a log-normal distribution with mean equal to the estimated value, and standard deviation of 0.05, resulting in errors in the adjustment factors in the range of plus or minus 10 (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

Additional data inputs, namely, births, deaths, and the proportion of deaths among women aged 15-49 last birthday due to AIDS, *a*, are another external component of uncertainty in the estimation of maternal mortality. The MMEIG assumed a bivariate

log-normal distribution to model the birth and death counts, with mean equal to the logarithm of the estimated values, a standard deviation equal to 0.05, and a coefficient of correlation of 0.7 to account for the fact that both vital events are acquired from the same set of population estimates from the United Nations Population Division (2011). Additionally, the MMEIG assumed that the log-odds of the fraction of AIDS deaths among women of reproductive age (i.e. logit(*a*)) had a normal distribution with mean equal to the log-odds of the estimated value and a standard deviation of 0.05 (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

Imprecise knowledge of parameters in the model to estimate the AIDS-related PMDF is an additional external component of uncertainty. The beta distribution over 0 and 1 was used to model the fraction of pregnancy-related AIDS deaths due to indirect maternal causes, *u*, the average exposure-to-risk to pregnancy-related mortality per live birth, *c*, and the relative risk of dying from HIV/AIDS for pregnant versus a non-pregnant women, *k* (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

After specification of probability distributions to the different external components of uncertainty, the assumed distributions were used to generate a large number (N_1=100) of model replicates. For each simulation, the model was re-estimated using the altered set of data and input parameters. Within each replicate, an additional number (N_2=10) of simulations were performed to assess the impact of the internal component of uncertainty as reflected within the model of PMDF, to yield a total of 1000 distinct outcomes (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

Simulated data were then used to compute full sets of model estimates for each time period in every country, region and the world as a whole. After simulating the combined effect of the internal and external components of the estimation process, 95% confidence intervals were derived using the 2.5[th] and 97.5[th] percentiles of the simulated distribution of estimates (WHO, UNICEF, UNFPA *et al.* 2010). To evaluate the uncertainty intervals, simulated data were used to estimate the PMDF model. Standard model outputs (such as estimated coefficients and the variance-covariance matrix) were used to simulate distributions of the model coefficients. Using these simulated results the distribution of the estimated logarithm of PMDF was approximated in order to quantify the inferential uncertainty (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

2.2 Description of alternative methods for estimating maternal mortality

2.2.1 UN Interagency methods

The earliest estimates of maternal mortality developed by WHO and UNICEF were based on a model of the maternal mortality experience for developed countries. The model used maternal death data for developed countries that have complete vital registration data and regressed maternal mortality against two independent variables, namely, the general fertility rate and the proportion of births that are assisted by a trained doctor or nurse. Prior to fitting the model, the data were adjusted for underreporting of maternal deaths. This was an improvement from an earlier model based on female life expectancy alone, which was not robust enough to estimate maternal mortality levels for individual countries (WHO and UNICEF 1996).

Following concerns expressed in international forums, namely, the failure to use available country data that were deemed to be of reasonable quality, the choice of the dependent variable in the model, and the limited range of output of the model (Hill, AbouZhar and Wardlaw 2001), WHO and UNICEF combined forces with the United Nations Population Fund (UNFPA) to review both the maternal mortality estimates for 1990 and the methodology used to derive them, and develop new estimates for 1995. The process for developing the 1995 maternal mortality estimates involved reviewing and analysing the shortcomings of the methodology for estimating maternal mortality in 1990. This was followed by compiling the most recent data on maternal mortality and key indicators deemed to have significant impact on maternal mortality by country. Thereafter, interregional and interagency consultations were held to discuss measures that ensured consistency in estimating and monitoring mortality trends. The final stage of the process involved reviewing the contemporary methodology by technical experts specifically regarding the choice of dependent variable, choice of independent variables, data inputs, and accounting for HIV/AIDS (WHO, UNICEF and UNFPA 2001).

The method itself is similar to the 1990 method as far as adjusting national data for underreporting of maternal deaths, and estimating maternal mortality for countries with no data using a model based on data for developed countries. However, in developing the method for estimating maternal mortality levels in 1995, the WHO and UNICEF use PMDF rather than the MMR as the dependent variable because the log odds-ratio of PMDF lies between 0 and 1, ensuring that the number of maternal deaths is always positive and never exceeds the total number of deaths to women aged 15-49 last birthday (Hill, AbouZhar and Wardlaw 2001). When choosing which independent variables to use in the model, the WHO and UNICEF considered variables that were

available for all countries. The underlying relationship that results in increasing maternal deaths following increases in fertility for a given risk of death during pregnancy or childbirth makes the general fertility rate (GFR) a prime candidate for inclusion in the model as an indicator of fertility (Hill, AbouZhar and Wardlaw 2001). Also included as an independent variable in the model is the percentage of deliveries assisted by a skilled attendant (TRATT) because it is widely available from DHS and household surveys and is a key determinant of maternal mortality. WHO and UNICEF reason that the appropriate management of complications of pregnancy and childbirth have the potential to reduce significantly maternal mortality (Hill, AbouZhar and Wardlaw 2001). HIV/AIDS prevalence was included, particularly as an indicator of exposure to avoid the overestimation of PMDF that would result from increases in deaths of females of reproductive age from HIV/AIDS in competition with other causes of death (Hill, AbouZhar and Wardlaw 2001). Also included in the model was an indicator of data quality, *good*VR, a dummy variable identifying a country with death registration reported as near complete (having at least ninety per cent of adult deaths reported). Finally, two other dummy variables, representing region, one identifying countries of formerly socialist Europe (FSE) and the other identifying countries of Latin America, Africa, West and South Asia (LASSAME) were included.

The final model fitted using a robust regression approach was thus as follows:

$$\ln\frac{PMDF}{(1-PMDF)} = \beta_0 + \beta_1 TRATT + \beta_2 \ln(GFR) + \beta_3 FSE + \beta_4 LASSAME + \beta_5 goodVR + \beta_6 HIV/AIDS$$

HIV/AIDS was the only variable that was not statistically significantly related to the dependent variable but was nevertheless included in the model as it was "judged the most appropriate way of avoiding possible prediction bias that might result from inflated numbers of non-maternal HIV-related deaths" (Hill, AbouZhar and Wardlaw 2001:185).

Once the model parameters were estimated by fitting the logit of PMDF against the independent variables for countries recorded to have near complete death registration, the model was used to estimate the PMDF of countries with no data or with complete death registration but questionable cause of death data. The resulting PMDF was multiplied by the number of deaths of females of reproductive age, and divided by the number of live births to give the MMR. Where data were available from Demographic and Health Surveys, Reproductive Age Mortality Studies or vital registration, the MMR was estimated directly.

2.2.2   Models used by other researchers and institutions

Stanton, Hill, AbourZahr *et al.* (1996) describe various models for estimating maternal mortality developed around the same time as the early WHO model. Boerma (1987) estimates maternal mortality from a model based on the relationship between the overall level of adult female mortality and the level of fertility as measured by the general fertility rate. The model then categorised countries into three regions, namely, countries with MMRs of less than 150 associated with proportions maternal of less than ten per cent, MMRs of 150-300 associated with proportions maternal of ten to twenty per cent, and MMRs of 300- 500 associated with proportions maternal of 20-30 per cent (Boerma 1987). Hypothetical estimates of MMR were then produced by applying model life tables of adult mortality to the proportions maternal corresponding with each of the three categories of country. The resultant estimates of MMR implied total maternal deaths of 515,000 for the period 1980-1985, consistent with the estimate of 500,000 produced by the WHO model (Stanton, Hill, AbourZahr *et al.* 1996).

Blum and Fargues (1990) subsequently proposed three methods to estimate maternal mortality from existing life tables. The first entailed direct estimation of maternal mortality using women's deaths by cause. The absolute observed number of deaths due to direct obstetric causes was expressed as a proportion of deaths due to all causes. Age-specific mortality rates of women of reproductive age were then multiplied by age-specific proportions maternal among deaths of women aged 15-49 last birthday to arrive at the age-specific maternal mortality rate. The maternal mortality ratio was then arrived at by dividing age-specific maternal mortality rates by the corresponding age-specific fertility rate. This method, however, proved to be difficult to use on developing countries where the vital registration data were subject to under-registration and misattribution of cause of death (Blum and Fargues 1990). Their second method is an indirect estimate of maternal mortality which uses a comparison of ratios of female to male age-specific mortality rates. It assumes that maternal causes are dominant among causes of death specific to women aged 15-49 last birthday, and that men within the same age group do not experience excess mortality. In this way, Blum and Fargues (1990) propose that expected ratios in the reproductive age range in the absence of maternal mortality can be estimated by interpolating between ratios prior to and after the age range 15-49 (Stanton, Hill, AbourZahr *et al.* 1996). Their third method is based on indirect estimation of maternal mortality using the slope of women's mortality rates, suggested by a Gompertz model curve. It assumes that female mortality follows a Gompertz curve in the absence of maternal mortality. Following backward

extrapolation of the logarithm of mortality rates from observed rates at ages 45 and over to ages 10-14, Blum and Fargues (1990) argue that maternal mortality manifests itself as positive deviations from the Gompertz curve (Stanton, Hill, AbourZahr *et al.* 1996).

Countries with estimates of their own criticised the WHO and UNICEF model for producing mortality estimates in excess of what they had recorded. Further, experts voiced concern over the model itself, particularly the preference for PMDF over MMR as the dependent variable, and how the use of unstandardised DHS data resulted in bias (Hakkert 2001). One of the shortcomings of using PMDF as the dependent variable in the WHO and UNICEF model of 1995 is the assumption that PMDF remains constant over time, yet in countries with high HIV/AIDS prevalence, PMDF is likely to decline because of increased deaths of females of reproductive age (Hakkert 2001).

Hakkert (2001) proposes an alternative method which, while using the same data set used by WHO and UNICEF in developing the 1995 estimates, uses MMR as the dependent variable and excludes independent variables whose inclusion in models of maternal mortality had been previously debated. The proportion of births that take place in the presence of a skilled attendant (*TRATT*) is an independent variable common to both the alternative model and the WHO/UNICEF model. New variables included are the female life expectancy at birth (e_0), the logarithm of the female life expectancy at birth (*ln e_0*), a dummy variable representing survey data (*SISTH*), and regional dummy variables, namely, *AME*, for countries in sub-Saharan Africa or North Africa or the Middle East, and *LAC*, for countries in Latin America and the Caribbean. The model is thus as follows:

$$\ln(MMR) = \beta_0 + \beta_1 e_0 + \beta_2 \ln(e_0) + \beta_3 TRATT + \beta_4 AME + \beta_5 LAC + \beta_6 SISTH$$

Hakkert (2001) argues that this alternative model provides comparable and even improved results in some instances to the WHO/UNICEF model. The model also simultaneously avoids the arbitrariness of dummy variables for data quality, and eliminates regional variables that precluded less developed countries with good social indicators from achieving mortality levels of developed regions (Hakkert 2001).

Continuing with the broad methodology of the 1990 and 1995 exercises and "for reasons of comparability, and because of a lack of clear indications that there was a better alternative" (WHO, UNICEF and UNFPA 2004:7), WHO, UNICEF and the UNFPA produced maternal mortality estimates for the year up to 2000. The 2000 model is specified below, with changes from the 1990 and 1995 model being the dummy variable *VRComplete* for countries identified by WHO as having near complete

adult death registration, and the proportion of deaths that take place in the presence of a trained attendant (*TRATT* variable renamed *SA*):

$$\log it(PMDF) = \beta_0 + \beta_1 \log it(SA) + \beta_2 \ln(GFR) + \beta_3 GDP + \beta_4 LASSAME$$
$$+ \beta_5 VRComplete$$

According to WHO, UNICEF and UNFPA (2004), the most significant difference between the 2000 estimates and the 1995 estimates is that a review of national estimates of maternal mortality was carried out, taking care to consider classification of countries according to completeness of vital registration. Further, as opposed to using deaths from the United Nations projections as was the case for the 1995 estimates, updated WHO estimates (Lopez, Salomon, Ahmad *et al.* 2002) for deaths of women aged 15-49 last birthday after adjusting to remove deaths from HIV/AIDS were used to calculate maternal deaths from the model-based PMDFs.

The WHO, UNICEF and UNFPA (2004) model of 2000 attempted to estimate uncertainty boundaries around the estimated value within which the true value would likely be found. However, because of the large margins of uncertainty around the estimates of MMR arising from estimates being derived from a variety of sources ranging from civil registration through to censuses, surveys, and community studies, the 2000 estimates were deemed more appropriate for informing policy on the magnitude of the problem of maternal mortality than for comparison of trends across countries in the short term (WHO, UNICEF and UNFPA 2004).

In response to suggestions and questions following the 2000 round of estimates, the MMEIG, a UN initiative involving WHO, UNICEF, UNFPA and The World Bank, collaborated to produce maternal mortality estimates for 2005 based on an improved methodology and new data (WHO, UNICEF, UNFPA *et al.* 2007). In this method, countries are categorised by source of maternal death data, ranging from civil registration characterised as complete with good attribution of cause of death through to those with no national mortality data. The MMR was estimated directly for countries that had maternal death data sourced from either civil registration, or from censuses, or surveys such as DHSs or DSSs, or from reproductive age mortality studies (RAMOS). For countries with no or suspect data on maternal mortality, the following statistical model was developed based on data from countries with reliable data:

$$\ln \frac{PMDF}{(1-PMDF)} = \beta_0 + \beta_1 \ln(GDP) + \beta_2 \ln(GFR) + \beta_3 VR_{complete} + \beta_4 \ln(\frac{SKA}{1-SKA})$$
$$+ \beta_5 (Eur) + \beta_6 (MENA) + \beta_7 (WP)$$

where *SKA* is the proportion of births with skilled attendants, *VRcomplete* is a dummy

equal to 1 if registration of deaths is 90% or more complete, *Eur*, *MENA* and *WP* are dummy variables for countries in Europe, the Middle East and North Africa, and Western Pacific respectively, and *GDP* and *GFR* are as defined in previous models. The 2005 method differed from the 2000 method in terms of the country categories, with the former method having eight categories compared to six in the latter model. The regional dummy variables also differed, with the 2005 model not including sub-Saharan Africa.

The 2008 model that superseded the 2005 model, estimates maternal mortality levels and trends between 1990 and 2008 (WHO, UNICEF, UNFPA *et al.* 2010). The method used for the 2010 estimates is similar to the method used for the 2008 model, both methods employing the same non-AIDS and AIDS model. However, the 2008 method included fewer countries (172 as opposed to 180) than the 2010 method because of a higher population cut-off (including countries with a population of at least 250,000 as opposed to 100,000). Consequently, the MMEIG 13% more empirical maternal, birth and population data in the 2010 method than used in the 2008 method. The most significant difference between the 2008 method and the 2010 method is the revision of estimates of the total number of deaths of women aged 15-49 last birthday to take account of more recent experience of adult mortality (WHO, UNICEF, UNFPA *et al.* 2012).

In the same year that the MMEIG produced maternal mortality estimates for the period up to 2008, the Institute for Health Metrics and Evaluation (IHME) produced a set of estimates that included nearly the same sources of country data but were based on a different methodology (Hogan, Foreman, Naghavi *et al.* 2010). The IHME adopted the ICD-10 Manual (2010) and the United Nations Development Group (2003) Millennium Development Goal Manual recommendations that require published maternal mortality rates to be based either on direct obstetric deaths or all obstetric deaths resulting from direct and indirect causes, taking care to include maternal deaths from HIV/AIDS and obstetrical tetanus. The maternal deaths derived from the application of the strict definition of direct obstetric deaths, or a combination of direct and indirect obstetric deaths, are then converted to MMRs by dividing by the number of live births from the United Nations Population Division (2009). The IHME model takes the form given below:

$$\ln(\mu_{a,i,t}) = \beta X_{a,i,t} + M_{a,i,t}$$

where μ is the maternal death rate, a is age, i represents country and t represents year, $X_{a,i,t}$ is a vector of covariates that explains variation in maternal mortality rates, and $M_{a,i,t}$ is the unexplained component of variation in maternal mortality over time. Based on analysis carried out by Hogan, Foreman, Naghavi *et al.* (2010), and on the basis of published work on previous models, the IHME concluded that the total fertility rate (TFR), gross domestic product per capita (GDP), HIV seroprevalence, neonatal mortality, age-specific female education, and indicators of five-year age groups are the most significant independent variables to model maternal mortality in their model. To validate its outcomes, four different types of predictive validity are done, namely: withholding a random sample of twenty per cent of country-years of data; withholding all data from a random sample of twenty per cent of countries; withholding the first twenty per cent of years of data for all countries; and withholding the last twenty per cent of years for all countries. The output of the model is then compared with the twenty per cent of the sample withheld to verify how well the model predicted the actual data outcomes.

This study has, however, been superseded by another study by the IHME, the major differences between the two studies being an updated data set and the use of an ensemble modelling strategy (Lozano, Wang, Foreman *et al.* 2011). Unlike the modelling strategy in the preceding model Lozano, Wang, Foreman *et al.* (2011) argue that ensemble models, which are weighted averages of individual component models, have the advantage of yielding more accurate predictions bound by more accurate uncertainty intervals. This change in the modelling approach by Lozano, Wang, Foreman *et al.* (2011) has resulted in significantly lower estimates of maternal mortality after the year 2000 compared to the estimates produced by Hogan, Foreman, Naghavi *et al.* (2010) for the same period.

2.2.3   Other approaches to estimating maternal mortality

Confidential enquiries into maternal deaths (CEMD) are routine investigations of all or a representative sample of deaths due to maternal causes occurring in an area/country. Multidisciplinary teams of health professionals carry out investigations into the numbers, causes, and avoidable factors associated with each woman's death (Hussein 2007, Lewis 2004).

The primary function of a CEMD is an audit to identify the preventable factors in the health facilities. Where the data used are nationally representative, the maternal mortality ratios (MMR) can be determined for the period of enquiry (Lewis 2004). A

CEMD uses multiple sources of data to ensure that coverage is as complete as possible. The main source of maternal death data are healthcare facilities, such as hospitals, supplemented by accounts of cause of death acquired from communities through the verbal autopsies (Lewis 2004).

South Africa is the only country in southern Africa that has a confidential enquiry into maternal deaths, and has published reports of its findings (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012). In its first CEMD report for maternal deaths as at 1998, the National Committee on Confidential Enquiry into Maternal Deaths (NCCEMD) did not attempt to calculate a MMR because they considered the maternal death data to be too incomplete to yield robust estimates of MMR. However, the study did make some important findings, namely, that AIDS was the second largest cause of maternal deaths, and that maternal deaths in which AIDS was an indirect cause were probably underestimated because of low HIV testing among pregnant and parturient women, and that deaths due to complications of abortion and early pregnancy terminations were underreported (National Committee on Confidential Enquiries into Maternal Deaths 1999), possibly because of the stigma attached to abortion and/or HIV/AIDS death.

Significantly more maternal death data, in addition to live birth data based on the census of 1996, were available in the second CEMD, which enabled the calculation of the MMR using maternal death data for the period 1999 to 2001. In spite of the increase in maternal deaths following improved reporting from health facilities in aggregate, there was still underreporting of maternal deaths at the sub-national level. Rural areas in particular, where only a small proportion of maternal deaths occur in healthcare facilities, were responsible for most underreporting of maternal deaths. In addition, reports of low numbers of maternal death were also received from private hospitals. However, the leading cause of death was non-pregnancy related infection, such as sepsis and septic abortion resulting from AIDS (National Committee on Confidential Enquiries into Maternal Deaths 2003).

The third CEMD improved reporting of HIV status among maternal deaths because of improved access to HIV testing services at antenatal clinics following the Prevention of Mother-to-Child-Transmission (PMTCT) programme. Over the period of the enquiry (2002-2004), HIV/AIDS was the leading cause of maternal deaths (National Committee on Confidential Enquiries into Maternal Deaths 2006).

The fourth CEMD report concurs with the third report that AIDS, through non-pregnancy related infections, remains the leading cause of maternal death in South Africa. For women who die in healthcare facilities, the MMR of HIV positive women is as much as ten times that of HIV negative women (National Committee on Confidential Enquiries into Maternal Deaths 2011).

The fifth confidential enquiry (National Committee on Confidential Enquiries into Maternal Deaths 2012) reports an increase in maternal deaths that occurred in healthcare facilities in 2008-2010 compared to the preceding period of assessment. The majority (70%) of maternal deaths were due to non-pregnancy-related infections, obstetric haemorrhage, and hypertension. Non-pregnancy related infections, primarily due to HIV (possibly also manifested as tuberculosis or pneumonia) accounted for about half (40.5%) of maternal deaths due to the abovementioned leading causes of death. In South Africa, HIV is therefore observed to consistently increase the incidence of maternal mortality among women who die in healthcare facilities.

A table which summarises and compares the various methods of estimating maternal mortality described above appears in **Appendix 1**.

2.3   The impact of HIV/AIDS on the measurement of maternal mortality

The measurement of accurate maternal mortality levels is adversely affected by high prevalence of HIV/AIDS among women of reproductive age. One of the obstacles to the accurate classification of AIDS deaths among pregnant or parturient women is knowledge of their HIV status. Antenatal care coverage varies in sub-Saharan Africa, being as high as 74% of women making at least one antenatal visit and as low as 43% of women making at least four antenatal care visits for the period 2005-2011 (WHO 2012b). However, attendance of antenatal care does not necessarily translate into universal knowledge of HIV status among pregnant women. It is, therefore, prudent to interpret HIV status obtained from antenatal clinic data with caution as such data may be select for pregnant women who attend public health facilities, thereby excluding pregnant women who attend private health facilities who are deemed to have a relatively low prevalence of HIV (Wilkinson 1999).

Estimates of maternal mortality derived from health facility data are susceptible to upward bias, where a large number of maternal deaths occur in facilities because of a disproportionate representation of complicated cases referred to specialist hospitals (Graham and Hussein 2003). Conversely, data based on health facilities may underestimate maternal mortality where maternal deaths occur outside health facilities,

such as may be the case in rural areas where it is not unusual for maternal deaths to occur at home, largely because of women's inability to travel long distances to seek emergency maternal care where transportation is not available or poor quality of care associated with health care facilities deters women from seeking such care (Thaddeus and Maine 1994, National Committee on Confidential Enquiries into Maternal Deaths 2011). Similarly, it is also possible for maternal deaths to be underreported within health facilities where the death of women of reproductive age occurs in non-maternal wards and pregnancy status is unknown (Graham and Hussein 2003).

HIV/AIDS also adversely affects the use and interpretation of indicators of maternal mortality such as PMDF and MMR. By definition, PMDF is the proportion of deaths classified as maternal among deaths of women of reproductive age due to all causes, including deaths due to HIV/AIDS. Thus, on the one hand, in countries where HIV/AIDS prevalence is high, PMDF tends to be understated because of the increasing number of total deaths attributable to HIV/AIDS among women of reproductive age (Hakkert 2001). On the other hand, high HIV/AIDS prevalence among pregnant women may adversely affect live-birth data, the denominator of the MMR. HIV/AIDS is known to cause ectopic pregnancies and stillbirths among infected pregnant women, resulting in overstatement of the MMR from mismatch of maternal births and live-birth data because of fewer records of live-birth data (Graham and Hussein 2003).

High HIV/AIDS prevalence may also indirectly affect the estimation of maternal mortality where maternal mortality indicators such as PMDF or MMR are estimated using statistical models (Graham and Hussein 2003). Where the coefficients were estimated using populations in which GFR was not depressed by HIV/AIDS, models that include the general fertility rate (GFR) as an independent variable in the regression of PMDF or MMR (WHO, UNICEF and UNFPA 2004; 2007; 2010) may underestimate maternal mortality in scenarios where HIV/AIDS depresses GFR through its adverse effect on fertility (Chen and Walker 2010).

HIV/AIDS may create upward and/or downward bias in models that model PMDF or MMR against skilled attendance at birth (SAB) (WHO, UNICEF and UNFPA 2001; 2004; 2007; 2010) if the coefficients were estimated using populations where SAB was not depressed by HIV/AIDS. Although, there may be a positive bias on SAB when families place greater importance on SAB, resulting in more births being recorded as occurring under the supervision of a skilled attendant, such as a nurse or doctor. On the other hand, HIV/AIDS may result in a negative bias on SAB when

skilled attendants are reluctant to attend to maternal emergencies because of the risk of infection (Graham and Hussein 2003) provided that the coefficients are estimated from populations which do not account for this bias.

Even in the absence of HIV/AIDS, southern African countries face challenges in identifying an accurate cause of maternal deaths primarily because of a lack of diagnostic facilities, which results in misclassification of deaths among females of reproductive age. The lack of knowledge of HIV status in countries with high prevalence of HIV/AIDS, owing to poor access to HIV testing facilities, exacerbates misclassification of cause of death among pregnant or parturient women because of the introduction of multiple causes of death (such as pneumonia and tuberculosis) associated with HIV/AIDS (Khan, Wojdyla, Say *et al.* 2006, Ronsmans and Graham 2006).

A further obstacle to attributing an accurate cause of death in pregnant or parturient women in southern Africa is the lack of clear understanding of ICD rules and variations in coding conventions that make it difficult to distinguish between the primary cause of death, precipitating factors, the immediate cause of death, and the mechanism of death (Graham and Hussein 2003) in cases where HIV/AIDS manifests itself as an indirect cause of death in pregnant or parturient women when it is in its advanced stages (Rosen, de Zoysa, Dehne *et al.* 2012).

2.4   Unsafe Abortion and associated maternal mortality

The WHO (1992) defines unsafe abortion as the termination of unwanted pregnancy either by people who are not qualified to carry out such procedures with appropriate equipment or in an unsanitary environment that does not conform to the minimum standards considered appropriate to handle emergencies or post-abortion care. Safe abortions, on the other hand, are defined as those that meet the legal requirements in countries with liberal laws. Such liberties exist when abortion is legal on request with or without limits on the gestation period or to protect women's mental or physical health on socioeconomic grounds following rape or incest (Sedgh, Singh, Shah *et al.* 2012).

Even though legalising abortion is expected to make the procedure safer, there are barriers that still limit access of pregnant women to safe abortion services. Such barriers include public education of the legal status of abortion; refusal by health care personnel to offer services because of conscientious objection; shortages of skilled personnel; and administrative requirements, such as gestational limits or spousal/parental consent or mandatory waiting periods (Singh, Wulf, Hussain *et al.* 2009). Comparisons between countries in which abortion is legal and those where it is prohibited or between

developed and developing countries have shown that the incidence of abortion does not vary by much, suggesting that illegality does not necessarily translate to low incidence of abortion (Singh, Wulf, Hussain *et al.* 2009, Shah and Åhman 2009).

Unsafe abortions, however, contribute significantly to maternal deaths worldwide (Sedgh, Singh, Shah *et al.* 2012), with most maternal deaths due to unsafe abortion occurring in sub-Saharan Africa (Lancet 2009). Maternal deaths due to unsafe abortion often occur among women with unwanted pregnancies who self-induce abortion or who obtain clandestine abortion services from medical practitioners or backstreet traditional providers (Grimes, Benson, Singh *et al.* 2006, Bateman 2007, Bateman 2011). Consequently, unsafe abortions and the maternal mortality associated with them often go undocumented (Haddad and Nour 2009). For cases with complications of abortion that do get referred to health care facilities, these abortions and their consequent maternal deaths represent only a fraction of the unknown number of women who seek and die from unsafe termination of pregnancy (Shah and Åhman 2009, WHO 1996).

South Africa is still in transition from more to less restrictive abortion laws (Sedgh, Singh, Shah *et al.* 2012). Evidence of the gap between enactment of legislation and its effective implementation in health care facilities lies in the significant proportion (3.4%) of maternal deaths due to unsafe abortion recorded in the CEMD over the period 2005 to 2007 (National Committee on Confidential Enquiries into Maternal Deaths 2011). Bateman (2007) comments that analyses of the second and third CEMD provide an optimistic appraisal of the trends in safe termination of pregnancy as the number of maternal deaths due to septic abortion declined over the two triennia between 1999 and 2004. This suggests that the increase in maternal deaths due to septic abortion was probably because of HIV/AIDS (Bateman 2007).

Of abortion-related maternal deaths in the fourth CEMD, early pregnancy terminations constitute the majority of such deaths. Even though the extent of underreporting of maternal deaths due to early pregnancy termination is unknown, it is likely that underreporting is higher in rural populations and, consequently, lower numbers of deaths recorded for rural populations compared to urban populations (National Committee on Confidential Enquiries into Maternal Deaths 2011). Incidentally, the incidence of abortion is higher in the urban population, and subsequent estimates of maternal death due to unsafe abortion are more likely to be representative of the proportion of pregnancy-related deaths due to all causes. However, because the

incidence of abortion is lower in rural populations, maternal death from causes other than unsafe abortion is more likely to be more prevalent (WHO 2011c).

Some underreporting of maternal deaths due to unsafe abortion may occur because of the varying terms used to refer to abortion in health care facilities, for instance, "miscarriage", "menstrual regulation", or "mini-abortion" (Grimes, Benson, Singh *et al.* 2006). This inconsistency further causes misreporting of deaths where a death due to an abortion is registered as a death due to an obstetric cause other than abortion (Walker, Campero, Espinoza *et al.* 2004).

There is also scope for misclassification of maternal deaths among women with an underlying HIV/AIDS condition who die from septic infection where there is a history of an unsafe abortion. The existence of multiple comorbidities may complicate the attribution of abortion as a primary cause, a contributing factor, or an incidental event in the death (National Committee on Confidential Enquiries into Maternal Deaths 2011).

In conclusion, this literature review has shown that there is no shortage of approaches to estimating maternal mortality. In spite of the various approaches to estimating maternal mortality, a recurring theme is that of sparse data for women of reproductive age, whether general or maternal death data, abortion-related death data, or data on HIV status. The sparseness of these data has, in part, contributed to various assumptions (often made without strong evidentiary basis) (Wilmoth, Mizoguchi, Oestergaard *et al.* 2012) being applied to data in order to account for the underreporting inherent in these data. The various modelling approaches themselves have also contributed to differences in estimates of maternal mortality as manifested in the wide uncertainty intervals about the estimates of maternal mortality. It is on this background that this research seeks to investigate each of the assumptions (implicit and explicit) in the MMEIG method of dealing with the derivation of non-AIDS and AIDS maternal mortality estimates.

The MMEIG estimates for maternal mortality for the period 1990 to 2010 for countries with high HIV prevalence (WHO, UNICEF, UNFPA *et al.* 2012) are assessed by considering three aspects of their method. First the choice of covariates included in the model of non-AIDS maternal mortality is investigated by collecting and reviewing literature that identifies factors which significantly influence maternal mortality most often. Next, the reasonability of the various adjustment factors is investigated by reviewing published studies that estimate these adjustment factors, or provide data from which these factors can be estimated for southern African countries. These adjustment factors are those that account for the misclassification of maternal deaths in civil registration; the misreporting of deaths due to abortion-related and other causes; those that account for deaths due to accidental/unnatural causes among pregnancy-related deaths. This is followed by an investigation into the reasonability of the WHO life tables for countries in southern Africa, and assumptions which account for AIDS deaths that occur during the pregnancy-related period, and pregnancy-related AIDS deaths due to indirect maternal causes in the AIDS-related model for estimating indirect maternal deaths due to HIV/AIDS.

3.1   Estimation of non-AIDS maternal mortality

3.1.1   Choice of covariates

The model used by the MMEIG to estimate non-AIDS related maternal mortality (due to direct or indirect causes) is based on a multilevel regression model of non-AIDS PMDF data against three independent variables, namely, gross domestic product (GDP) per capita, skilled attendant at birth (SAB) as a proportion of total live births, and the general fertility rate (GFR) (WHO, UNICEF, UNFPA *et al.* 2012, Wilmoth, Zureick, Mizoguchi *et al.* 2010). In order to investigate the validity of the choice of covariates made by the MMEIG, published work that investigated the determinants of maternal mortality in developing countries is reviewed.

In order to justify the inclusion of a covariate in the model of maternal mortality, the relationship between the covariate and maternal mortality must have been found to have been statistically significant by at least one study. The internal validity of the meta-analysis is assessed by evaluating the soundness of the methodologies of the primary studies and whether the meta-analysis contains enough studies to provide power for its

test (ideally at least 30 studies). Even though the analysis is limited to the number of studies collected, the diversity of the methods used in each study in arriving at the same conclusion moderates this limitation, with the harmony of results carrying more weight than the number of studies found.

3.2   Adjustment factors

3.2.1   Adjusting for misclassification of maternal deaths in civil registration

In order to assess the reasonability of the adjustment factor (1.5) by the MMEIG for misclassification of maternal deaths in civil registration, an assessment of the applicability to southern African countries of the findings of published literature that identified studies of the misclassification of maternal deaths in civil registration by the MMEIG is carried out.

3.2.2   Adjusting for misreporting of deaths due to abortion-related and other causes

In order to investigate the validity of the adjustment factor (1.1) by the MMEIG (WHO, UNICEF, UNFPA *et al.* 2012, Wilmoth, Zureick, Mizoguchi *et al.* 2010) to pregnancy-related death data recorded in censuses, Demographic and Health Surveys and household surveys to account for unreported deaths due to abortion-related and other causes, such as early pregnancy loss, a review of the literature in which estimates of the proportion of deaths due to unsafe abortion are published is carried out. In order to do this it is assumed that mortality due to abortion-related and other causes occurs mainly as a result of unsafe abortion, as evidenced by studies that have shown that where reported as a cause of death, spontaneous abortion (miscarriage) is rarely responsible for maternal death (Grimes, Benson, Singh *et al.* 2006, Åhman, Dolea and Shah 2000). Much of the literature used to investigate the validity of the adjustment factor is based on work done by the WHO (2004; 2007; 2011), which has published several reports describing the methodology behind the development of global and regional estimates of unsafe abortion and the mortality levels associated with it.

Regional estimates (which are assumed to be relatively more robust than country-specific estimates) of the incidence of unsafe abortion and the mortality associated with it are aggregated from country estimates. Countries for which the proportion of maternal deaths due to unsafe abortion is investigated collectively belong to southern Africa (comprising South Africa, Botswana, Swaziland, Lesotho and Namibia) and selected countries from eastern Africa (comprising among others, Zimbabwe, Malawi, Zambia and Mozambique) based on the classification of countries by regions of the

world by the United Nations Population Division (2009). The respective estimates of the incidence of deaths due to unsafe abortion for the southern African and eastern African region inclusive of the period (1990-2008) over which the MMEIG estimated levels of maternal mortality published by the WHO (2004; 2007; 2011) and other related research (Ahman and Shah 2011, Shah and Åhman 2009, Thonneau 2001) are then compared for reasonability with the fixed adjustment factor of 1.1 assumed by the MMEIG. In addition to the regional estimates of the proportion of maternal deaths due to unsafe abortion, national estimates for South Africa acquired from its confidential enquiries into maternal deaths (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012) are included in the comparison with the fixed adjustment factor of 1.1 assumed by the MMEIG.

In order to generalise country experiences to the region it is, however, worth noting that countries in the same region have differing fertility experiences and laws on abortion that affect the incidence of unsafe abortion and mortality associated with it. For instance, while some southern African countries legally allow abortion to save the life or to preserve the health of a woman, only South Africa, among countries in the southern African region, legally allows early-stage abortion on request without restriction (Guttmacher Institute 2012). It is, therefore, necessary to document the grounds on which types of abortion are legal for each region in order to investigate whether there is an association between the incidence of unsafe abortion (and associated mortality) and the legal status of abortion, and whether there is a significant difference by region or legal status of abortion (Sedgh, Singh, Shah *et al.* 2012, Shah and Åhman 2009, Singh, Wulf, Hussain *et al.* 2009).

3.2.3 Accounting for deaths due to accidental/unnatural causes among pregnancy-related deaths

In order to investigate the validity of the assumption made by the MMEIG that the fraction of deaths due to accidental/unnatural causes that occur during pregnancy is 10% of non-AIDS deaths for countries in sub-Saharan Africa (approximately equivalent to multiplying non-AIDS deaths by 0.9) (Wilmoth, Zureick, Mizoguchi *et al.* 2010), relevant literature on the cause of death of pregnancy-related deaths will be consulted. South Africa's vital registration data are a key source of data and will, in addition, be used as a proxy for the region as its vital registration system comprises the largest continuous data set for cause of death in southern Africa (Birnbaum, Murray and Lozano 2011).

Vital registration data on deaths of by pregnancy status and deaths by cause of death (i.e. natural or unnatural) classification among women aged 15-49 last birthday for South Africa (Stats SA 2002; 2005; 2006; 2007; 2008; 2009; 2010) for the period 1997 to 2009 will be used to estimate the proportion of pregnancy-related deaths due to unnatural causes. To allow comparison of estimates of the proportion of deaths due to unnatural causes occurring during pregnancy for South Africa, the results of a studies (Dorrington and Bradshaw 2011, Garenne, McCaa and Nacro 2011, Garenne 2011) investigating the proportion of deaths due to unnatural causes among pregnancy-related deaths for the 2001 Census and 2007 Community Survey for South Africa will be assessed and compared with the assumption of 10% made by the MMEIG in its model.

3.3 Estimation of indirect maternal deaths due to AIDS

3.3.1 Assumptions for accounting for HIV/AIDS in pregnancy-related deaths

The MMEIG assumes that the proportion of AIDS deaths in women aged 15-49 last birthday occurring during the pregnancy-related period is given by the following formula:

$$v = \frac{kcGFR}{1+(k-1)cGFR}$$

In this formula, *GFR* represents the general fertility rate, which is the average number of births per women aged 15-49 last birthday; *k* is the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women; and *c* is the average time exposed-to-risk (in years) to pregnancy-related death per live birth. In order to assess the applicability of this formula to estimating the proportion of AIDS deaths in women aged 15-49 last birthday occurring during the pregnancy-related period, *v*, the DemProj module of the Spectrum population projection software will be used to produce estimates of the number of births and the number of women aged 15-49 last birthday required to estimate the general fertility rate, *GFR*, for countries in southern Africa for each year between 1990 and 2010. The investigation will assume that *k* is equal to 0.4 and that *c* is equal to 1 as assumed by the MMEIG in its method (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

In order to assess the reasonability of the aforementioned estimates of *v* derived from the application of *GFR* in the MMEIG formula, alternative estimates of *v* for each of the southern African countries for the period 1990 to 2010 will be produced using data from the AIDS Impact Model (AIM) integrated in the Spectrum population projection software. AIM provides estimates of the number of AIDS deaths among

pregnant women and the total number of AIDS deaths among females aged 15-49 years last birthday. Dividing the number of AIDS deaths among pregnant women by the total number of AIDS deaths among females aged 15-49 years last birthday produces estimates of the proportion of AIDS deaths in women aged 15-49 years last birthday occurring during pregnancy. It will be assumed that the definition of pregnancy used by AIM for deaths among pregnant women captures both pregnancies that do not result in live birth (due to early loss of pregnancy) and those up to and including child delivery, but excludes the period of exposure to pregnancy-related mortality after delivery. In order to arrive at a pregnancy-related estimate that accounts for exposure-to-risk to pregnancy-related mortality during the 42 days after childbirth, the proportion of AIDS deaths occurring during pregnancy will be adjusted upwards to include an additional 6/52 of a year of exposure-to-risk to pregnancy-related mortality.

Next, the validity of the value assumed for v is further investigated by reviewing literature on sub-national estimates of v produced using direct information from the verbal autopsy questionnaires on pregnancies and AIDS deaths from published Health and Demographic Surveillance Site (HDSS) studies (Zaba, Ronsmans, Momodou *et al.* 2011). In these studies, direct information on pregnancies, births and deaths is used to identify deaths that occurred to women during pregnancy or up to the 42 days following delivery. In order to assess the reasonableness of these site-specific estimates, the relative risk of death from HIV/AIDS of pregnant versus non-pregnant women, k, implied by the site-specific estimates of v will be determined for each HDSS. Values of k implied by site-specific estimates of v for each DSS will be determined by assuming that the average exposure-to-risk to pregnancy-related mortality per live birth, c, is 1 year and that the general fertility rate takes values characteristic of countries in which the HDSSs are located. The resultant values of k will be compared and assessed for reasonability with corresponding site-specific estimates from other studies (Garenne 2011).

The final step in the investigation of v is to test the sensitivity of v to different values of k. In order to test the sensitivity of v to k, the value of v is calculated for a range of general fertility rates characteristic of countries in southern Africa and a range of k.

3.3.2 Assumptions for accounting for HIV/AIDS in maternal deaths
Following this, the validity of the MMEIG assumption for the fraction of pregnancy-related AIDS deaths due to indirect maternal causes, (i.e. u=0.5) (Wilmoth, Zureick,

Mizoguchi *et al.* 2010, WHO, UNICEF, UNFPA *et al.* 2012), is investigated by reviewing literature on site-specific estimates of *u* from published HDSS studies (Zaba, Ronsmans, Momodou *et al.* 2011). Unlike pregnancy-related deaths which can be identified directly from information on pregnancies, births and deaths, maternal deaths can only be identified through the signs and symptoms recorded in the VA questionnaire (Zaba, Ronsmans, Momodou *et al.* 2011).

The fraction of pregnancy-related AIDS deaths due to indirect maternal causes in the literature being reviewed is estimated in two ways; by likelihood of AIDS death or HIV status. The HIV status of women who died during the pregnancy-related period, where available, is acquired from serological surveys, or when unavailable, from the InterVA model for interpreting verbal autopsy data. For robustness of results, the studies being reviewed compared estimates from the observed data with likely AIDS deaths in pregnant women generated from InterVA classification of deaths from the verbal autopsy questionnaires.

3.4   WHO life tables for southern African countries

The reasonability of the level of death rates for females aged 15-49 years last birthday will be investigated by assessing the methodology for estimating the WHO (2011b) life tables for countries in the southern African region (WHO 2012a). This is followed by a comparison of the WHO life table country estimates with corresponding mortality rates derived from Spectrum population projection software (including AIM projections for the effect of HIV/AIDS) for the respective countries for the ten-year intervals 1990, 2000, and 2009. This analysis allows an assessment of the impact of death rates on the estimates of the number of deaths of women aged 15-49 last birthday (estimated by multiplying the WHO (2011b) death rates by the United Nations Population Division (2011) population estimates) and subsequent estimates of the number of maternal deaths implied by the PMDF.

4   DATA ANALYSIS AND RESULTS

This chapter presents the results of the methods applied in the preceding chapter. The results for each method are presented and discussed.

4.1   Choice of covariates: Factors influencing maternal mortality

The literature searched for was research on 'determinants' and 'predictors' of and 'factors associated with' maternal mortality to examine the MMEIG's choice of model covariates for predicting non-AIDS maternal mortality. In order to provide power for its test and justify inclusion in this research, a study had to include at least 30 countries from sub-Saharan Africa. Table 4.1 summarises the main characteristics of a review of literature identified using the above criteria that investigate the various factors which influence maternal mortality.

Table 4.1 Summary of studies investigating the factors that influence maternal mortality

Study	Period/ year of study	No. of countries studied	No. of covariates of maternal mortality studied	Significant predictors of maternal mortality
Lee *et al* (1997)	1987-1990	78	5	5
Shen and Williamson (1999)	1990	79	12	10
Shiffman (2000)	1998	64	6	6
Robinson and Wharrad (2001)	1988-1997	155	5	5
Sloan *et al* (2001)	1999	84	7	2
Buor and Bream (2004)	1990-1998	28	8	5
Betran *et al* (2005)	2004	141	8	3
McAlister and Baskett (2006)	1985-2001	148	12	5
Alvarez *et al* (2009)	1997-2006	45	18	13

The period/year of study refers to either the period over which data used in the study were collected or to the year for which maternal mortality was estimated. For instance, data used in the study by Shen and Williamson (1999) estimate maternal

mortality as at 1990 but regresses the estimates against socioeconomic data collected from as far back as the 1960s or 1970s. Of the literature reviewed, six (Lee, Park, Khoshnood *et al.* 1997, Robinson and Wharrad 2001, McAlister and Baskett 2006, Shiffman 2000, Sloan, Winikoff and Fikree 2001, Betran, Wojdyla, Posner *et al.* 2005) are worldwide studies, two (Buor and Bream 2004, Alvarez, Gil, Hernandez *et al.* 2009) focus on sub-Saharan African countries, while one (Shen and Williamson 1999) focuses on less developed countries including several from sub-Saharan Africa. All of the studies comprise enough countries (at least 30) to provide sufficient power for each test, with the exception of one study (Buor and Bream 2004) comprising 28 countries.

The studies reviewed investigate the strength of association of various factors with maternal mortality, ranging from economic (out-of-pocket expenditure on health, government expenditure on health and education), health-related (antenatal care coverage, infant mortality, access to sanitation and water), educational (contraceptive prevalence) through to measures of gender empowerment (female seats in parliament, female economic activity, and female professional and technical workers). The definition of maternal mortality used in the studies varies maternal mortality ratio (Buor and Bream 2004, Alvarez, Gil, Hernandez *et al.* 2009, McAlister and Baskett 2006), to maternal mortality rates (Lee, Park, Khoshnood *et al.* 1997, Robinson and Wharrad 2001) through to pregnancy-related mortality ratio (Shen and Williamson 1999). After each of the studies investigated the strength and direction of association of maternal mortality with the various factors that influence it, the results of the multivariate analyses of each variable's ability to predict maternal mortality are reported. Table 4.2 summarises the factors identified as influencing maternal mortality most often.

Table 4.2 Factors identified as significantly influencing maternal mortality most often

Factor	Frequency of a significant p-value
Skilled attendants at birth	7
Gross national income per capita	6
Female literacy rate	5
School enrolment ratio	5
Government expenditure on health	4
Female life expectancy at birth	3
Total fertility rate	3

Indicators of social development are the most frequently reported factor that influence maternal mortality. In the six studies (Lee, Park, Khoshnood *et al.* 1997, Shen and Williamson 1999, Buor and Bream 2004, Alvarez, Gil, Hernandez *et al.* 2009,

Shiffman 2000, Robinson and Wharrad 2001) in which it is reported as significantly influencing maternal mortality, the correlation of gross national income per capita with maternal mortality is large and negative (-0.91, -0.887, -0.78, -0.770, -0.543, -0.456). This result suggests that increases in gross national income per capita result in substantial decreases in maternal mortality.

Another indicator of social development that the studies have investigated and is indicated as significantly influencing maternal mortality is the female literacy rate. Female literacy rate is defined as the percentage of females aged 15 and above who can read and write (Alvarez, Gil, Hernandez *et al.* 2009, Lee, Park, Khoshnood *et al.* 1997). In two studies (Lee, Park, Khoshnood *et al.* 1997, Robinson and Wharrad 2001), female literacy and, in another study (Alvarez, Gil, Hernandez *et al.* 2009), adult literacy are negatively correlated (-0.82, -0.757, -0.517) with maternal mortality. This result suggests that increases in female literacy work to reduce maternal mortality. In another study by McAlister and Baskett (2006), the association of female literacy with maternal mortality is expressed in terms of the extent of variation in maternal mortality explained by female literacy in the multivariate model estimating maternal mortality. Directly, female literacy was found to explain slightly under 50% ($R^2=48.6\%$) of the variation in maternal mortality while the human development index which includes female literacy (controlling for the effect of life expectancy at birth and school enrolment) was found to explain over 80% ($R^2=81.2\%$) of the variation in maternal mortality.

Another indicator of social development that is reported as significantly influencing maternal mortality is school enrolment (whether female or combined enrolment, or whether separated into primary and secondary). Where the association of school enrolment with maternal mortality is reported as a coefficient of correlation, the relationship is negative (ranging from -0.386 to -0.86), suggesting that an increase in school enrolment reduces maternal mortality. The study by McAlister and Baskett (2006) found school enrolment to explain about half ($R^2=48.0\%$) of the variation in maternal mortality while the study by Lee, Park, Khoshnood *et al.* (1997) found that the human development index which includes school enrolment (controlling for the effect of life expectancy at birth and female literacy) had a large negative correlation (-0.86) with maternal mortality.

The indicator of process that is reported to significantly influence maternal mortality is skilled attendants at birth. The association of skilled attendants at birth with maternal mortality is reported as a negative coefficient of correlation (ranging from

−0.572 to −0.895), suggesting that an increase in skilled attendants at birth reduces the incidence of maternal mortality.

Two other indicators of social development that are reported, although relatively less frequently, as significantly influencing maternal mortality are female life expectancy at birth and government expenditure on health. Where the association of female life expectancy at birth with maternal mortality is reported as a coefficient of correlation (Lee, Park, Khoshnood *et al.* 1997, Buor and Bream 2004), the relationship is negative (−0.489, −0.9) suggesting that increases in life expectancy at birth are associated with decreases in maternal mortality. In the study by McAlister and Baskett (2006), the human development index which includes female life expectancy at birth (controlling for school enrolment and female literacy) was found to explain over 80% (R^2=81.2%) of the variation in maternal mortality, reinforcing its significance as a factor that influences maternal mortality. Likewise, the study by Lee, Park, Khoshnood *et al.* (1997) shows that life expectancy at birth has a large negative (−0.82) correlation with maternal mortality.

Government expenditure on health (whether total or per capita) is also reported as having a significant impact on maternal mortality. The association of government expenditure on health with maternal mortality is negative (−0.452, −0.714, −0.742) (Alvarez, Gil, Hernandez *et al.* 2009, Shiffman 2000, Buor and Bream 2004) suggesting that increases in government expenditure on health reduce maternal mortality. The study by Betran, Wojdyla, Posner *et al.* (2005) reports government health expenditure as significantly influencing maternal mortality but does not provide the extent of correlation.

The only indicator of exposure to pregnancy that is reported as significantly influencing maternal mortality is the total fertility rate. Where the association of total fertility rate with maternal mortality is reported as a coefficient of correlation (Shen and Williamson 1999, Buor and Bream 2004) the relationship is positive (0.192, 0.74), suggesting that an increase in total fertility rate increases incidence of maternal mortality. The study by McAlister and Baskett (2006) reports that the total fertility rate explains about 65% (R^2=65.4%) of the variation in maternal mortality, further reinforcing the positive association of total fertility rate with maternal mortality. Appendix 2 summarises the studies investigating the factors that were consulted.

In a model for estimating maternal mortality developed by Hakkert (2001), female life expectancy at birth and the percentage of births attended by trained health personnel (which Hakkert (2001) refers to as TRATT) are deemed to be covariates that

significantly influence maternal mortality. In another model for estimating maternal mortality developed by the Institute for Health Metrics and Evaluation (IHME), covariates considered as candidates for its maternal mortality model are categorised into three groups based on the strength of epidemiological evidence. The first group of covariate exhibits strong evidence and biologically plausible pathways (age-specific fertility rates, proportion of births taking place in health facilities, total fertility rate, and proportion of births attended by a skilled professional). The second group of covariates exhibit weaker evidence than the first group and a less direct causal pathway (proportion of women with four or more antenatal care visits, female education by age, HIV prevalence adjusted for antiretroviral treatment, health system access, neonatal death rate, and a measure of malnutrition). The third group of covariates exhibit general evidence of association with maternal mortality (per capita income expressed as United States Dollars) (Lozano, Wang, Foreman *et al.* 2011).

In spite of these associations with maternal mortality, there is multi-collinearity among factors that measure the same effect on maternal mortality, such as female literacy and female school enrolment ratio. Including such factors that measure the same effect being investigated in the model for estimating non-AIDS maternal mortality will probably not change the result much but because of multi-collinearity the model will not reveal much information about redundant, independent variables among those that influence maternal mortality most often. Perhaps to remedy this problem it would be prudent to drop the variable that contributes least to the model when tested separately with other independent variables. It would be wise to also exclude independent variables that are subsets of the dependent variable, such as female life expectancy at birth, as it becomes unclear which factor is influencing the other.

In its model, the MMEIG has used covariates that have a strong biological pathway (i.e. SAB and GFR), and one with a general but strong association with maternal mortality (i.e GDP). While increases in GDP and SAB, and decreases in GFR, may be associated with predictions of lower levels of maternal mortality, the statistical model used by the MMEIG describes only the relationship between the underlying maternal mortality data against changes in the covariates of the model. The model does not readily explain changes in maternal mortality due entirely to interventions to reduce maternal mortality which may be unrelated to changes in the covariates (AbouZahr 2011), and there is greater need to investigate adjustments to the underlying maternal mortality data.

4.2   Adjustment factors

4.2.1   Adjusting for misclassification of maternal deaths in civil registration

The MMEIG reviewed the experience of 39 studies of countries with good vital registration (WHO, UNICEF, UNFPA *et al.* 2012). None of the countries from which these studies were done is from sub-Saharan Africa, therefore not allowing generalisation of experiences across countries. Bradshaw and Dorrington (2012) have applied the 50% adjustment to 2009 estimates of MMR for South Africa on the basis that over 90% of adult deaths are registered in South Africa's vital registration system (and therefore comparable with developed countries). It is likely that applying an adjustment factor of 50% to other southern African countries that do not have civil registration systems as complete as that of South Africa will understate deaths classified as maternal. It is therefore likely that an adjustment factor greater than 50% is required for other southern African countries that do not have civil registration systems as complete as those whose experience is used to inform the adjustment factor in order to adequately account for the misclassification of maternal deaths in civil registration.

4.2.2   Accounting for the misreporting of maternal deaths due to abortion-related and other causes

Figure 4.1 displays the results of a review of the literature that investigated the proportion of maternal deaths due to unsafe abortion in eastern Africa and southern Africa as well as South Africa, as summarised in Appendix 3. The proportions of maternal deaths due to unsafe abortion are plotted at the midpoint of the period to which they refer. Other causes (such as infections associated with early pregnancy loss) are assumed to contribute an insignificant proportion of deaths, and accounting for deaths due to abortion-related causes, therefore, sufficiently incorporates deaths due to other causes. As such, this investigation focuses solely on misreporting of maternal deaths due to abortion-related causes.

The regions of eastern Africa (comprising among others, Zimbabwe, Malawi, Zambia and Mozambique) and southern Africa (comprising South Africa, Botswana, Swaziland, Lesotho and Namibia) as classified by the United Nations Population Division (2009) collectively contain countries in which the proportion of maternal deaths due to unsafe abortion is investigated by this study. South Africa, through its confidential enquiries into maternal deaths (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012) compiles national estimates of the incidence of maternal mortality due to unsafe abortion and is accordingly included in the review of studies. In addition, the assumption made by the

MMEIG throughout the period of investigation, i.e. that 10% of maternal deaths due to abortion-related and other causes are not reported (which is equivalent to an upward adjustment of 1.1 to maternal death data), is also displayed in Figure 4.1 for comparison with national (i.e. South Africa) and regional estimates of the proportion of maternal deaths due to unsafe abortion.

Figure 4.1 Estimates of the proportion of maternal deaths due to unsafe abortion, 1998-2009
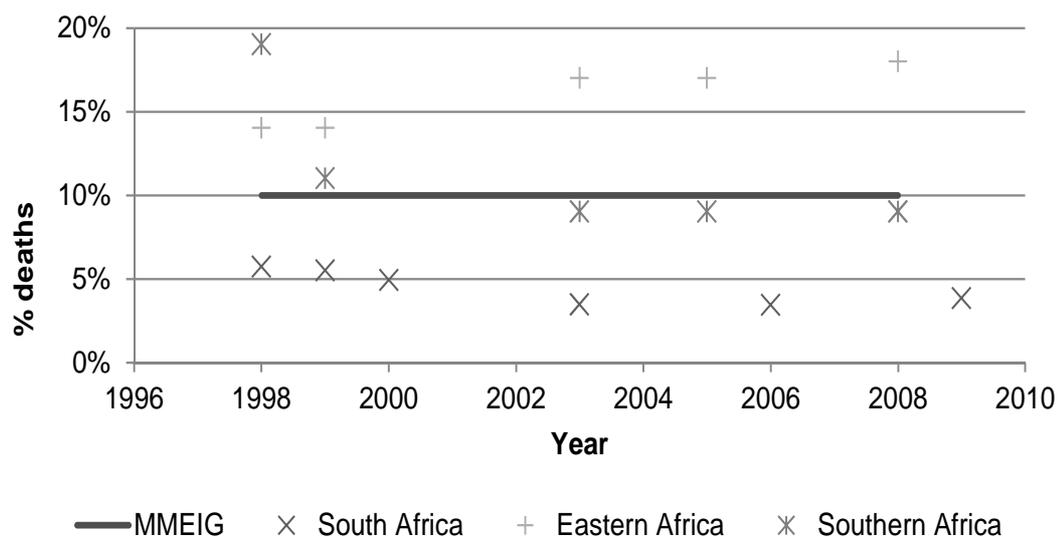
Source: Estimates of maternal deaths due to unsafe abortion for the various years extracted from Thonneau (2001), Shah and Åhman (2009), Ahman and Shah (2011), WHO (2004; 2007; 2011), National Committee on Confidential Enquiries into Maternal Deaths (1999; 2011; 2012)

Figure 4.1 shows that the proportion of maternal mortality due to unsafe abortion for southern Africa lies between 9% and 11% but is weighted more towards 9% because of more studies (Ahman and Shah 2011, Shah and Åhman 2009, WHO 2007, WHO 2011c) estimating it around that point. The proportion of maternal deaths due to unsafe abortion for southern Africa lies below but close to the assumption made by the MMEIG for countries where no specific adjustment for completeness is available. The proportion of maternal deaths due to unsafe abortion for eastern Africa is estimated to be moderately higher than that assumed by the MMEIG and on an upward trend over the period 1998 to 2008. During the same period the estimates of the proportion of maternal deaths due to unsafe abortion for South Africa as estimated from the confidential enquiries into maternal deaths (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012) show a relatively constant

level in the incidence of maternal mortality due to unsafe abortion though lower than both the assumption made by the MMEIG and estimates for southern Africa.

Figure 4.2 Proportion of countries by legal grounds on which abortion is permitted as at 2007
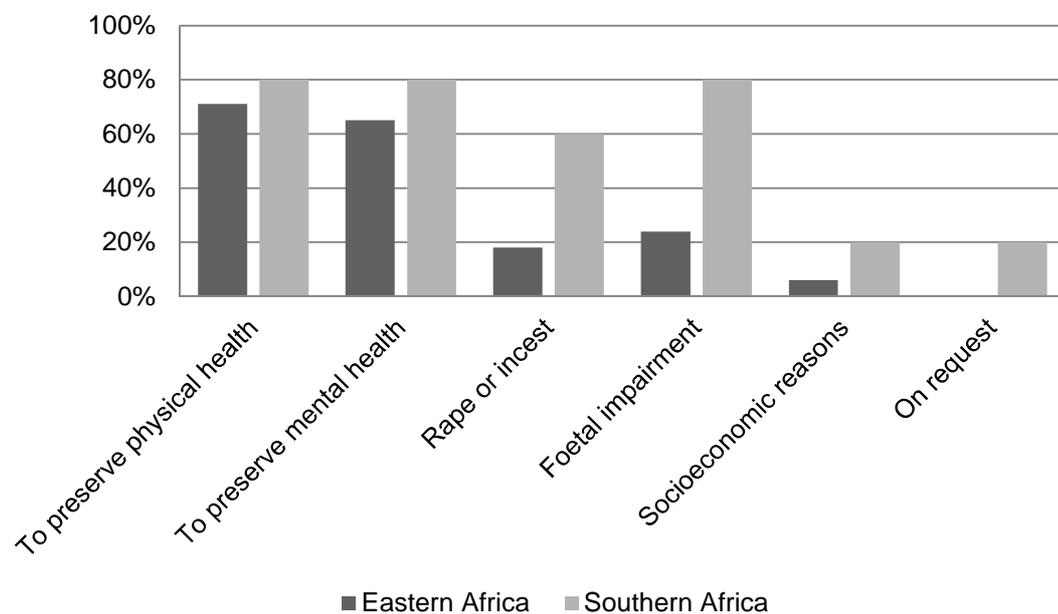
Source: Data extracted from WHO (2011c)

Figure 4.2 shows the proportion of eastern and southern African countries by legal grounds on which abortion is permitted for the year 2007 as compiled by the WHO (2011c). Overall, southern Africa has higher proportions of countries for the range of legal grounds on which abortion is allowed. In light of this, it is important to note that data for mortality associated with unsafe abortion are uncertain and are at best estimates and therefore more indicative than precise estimates of country and regional experiences (WHO 2004; 2007; 2011). However, in spite of this limitation, it is possible to draw tentative conclusions from these estimates. While the level of maternal deaths due to unsafe abortion for South Africa as estimated by confidential enquiry (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012) is shown to have decreased over the period 1998 to 2008, and therefore also likely to influence that of the southern African region downwards, eastern Africa appears to be experiencing increases in the level of maternal deaths. Hence, based on current data and estimation methods, applying a universal adjustment factor of 1.1 to eastern Africa would be unreasonable and likely to result in under-correction for deaths due to unsafe abortion. Conversely, applying the MMEIG assumption to South Africa (whose

national-level estimates of the proportion of maternal deaths due to unsafe abortion may also influence regional estimates) results in over-correcting for deaths due to unsafe abortion. However, given the proximity of the MMEIG assumption to estimates of the proportion of mortality from unsafe abortion for southern Africa, it would be reasonable to apply the MMEIG assumption to maternal deaths data for southern Africa.

There is, however, scope for bias given the uncertainty in the estimation of the incidence of unsafe abortion and the mortality associated with it, and it is not certain in which direction this bias may act. Bias emanates from adjustments to account for overreporting of unsafe abortions as spontaneous. Further bias comes from the assumptions made by the WHO (2004; 2007; 2011) that sub-national experience of unsafe abortion can be generalised to national, and that countries with no data can have data substituted from countries with similar abortion laws, fertility experiences, contraceptive coverage and urban/rural differences. The availability of national data for South Africa, however, may make its estimates more robust than for the regions where there are sparse country data. Therefore, given the sparse data on the incidence of abortion and the mortality associated with it, the extrapolation of unsafe abortions and associated mortality is likely to result in these estimates exceeding observed evidence by unreasonable factors, thereby compounding uncertainty associated with these estimates.

4.2.3 Accounting for deaths due to accidental/unnatural causes among pregnancy-related deaths

4.2.3.1 Vital registration

Table 4.3 shows the proportion of pregnancy-related deaths due to unnatural causes among deaths of women aged 15-49 last birthday recorded through vital registration from South Africa. There is no classification of pregnancy-related deaths by cause of death prior to 2006, as only total counts of pregnancy-related deaths by ICD-10 classification of cause of death and global counts of total numbers of deaths due to natural and unnatural cause are provided in Stats SA (2002; 2005; 2006; 2007; 2008; 2009; 2010) reports.

Assuming that cause of death for unnatural deaths is verified through autopsy and, therefore, that deaths due to unnatural causes are correctly documented in vital registration (Dorrington and Bradshaw 2011), an adjustment factor of 90% would have to be applied to data for all deaths to account for incompleteness of reporting in vital registration of deaths due to natural causes. This estimate of completeness of death

reporting is based on estimates derived by Dorrington and Bradshaw (2011) using death distribution methods on vital registration data from South Africa for the period 1997 to 2007. However, in this case, there is no need to adjust for completeness of death registration.

Table 4.3 The proportion of pregnancy-related deaths due to unnatural causes recorded in South African vital registration, 2006-2009

Year	Non-natural underlying cause
2006	0.3
2007	0.2
2008	0.2
2009	0.2

Source: Extracted from Statistics South Africa (2007)

Over the period 2007 to 2009, the proportion of pregnancy-related deaths due to unnatural causes among women aged 15-49 last birthday for South Africa is 100% higher (and 200% higher in 2006) than the 10% level assumed by the MMEIG. The results suggest that the fraction of accidental/unnatural deaths occurring during pregnancy for South Africa is greater than assumed by the MMEIG, and hence the application of the MMEIG adjustment under-corrects for unnatural deaths occurring during pregnancy based on evidence recorded in vital registration.

4.2.3.2 *Deaths in the household reported in the census and community survey*

The investigation done by Dorrington and Bradshaw (2011) using data for deaths in the household reported in the 2001 Census and 2007 Community Survey in South Africa was consulted to examine the contribution of unnatural causes to deaths of pregnant women. The 2001 Census asked respondents about the occurrence of deaths in the household in the preceding 12 months, and if there was a death, whether the deceased was a woman under 50 years of age. In addition, the 2007 Community Survey asked households the date of death (i.e. month and year), the sex of the deceased, and the age of the deceased.

The results of the investigation of the 2001 Census and 2007 Community Survey data show that the percentage of deaths of women aged 15-49 last birthday that are due to unnatural causes occurring during the pregnancy-related period is around 16-17% (Dorrington and Bradshaw 2011). These results suggest that the assumption made by the MMEIG - that the fraction of accidental/unnatural deaths occurring during pregnancy is around 10% of non-AIDS deaths for sub-Saharan African countries

(Wilmoth, Zureick, Mizoguchi *et al.* 2010) - probably under-corrects for the proportion of unnatural deaths occurring during pregnancy. However, in considering these results it is prudent to note that household death data reported in the census and survey are likely to exaggerate the proportion of deaths due to unnatural causes because of reliance on the respondent's response to questions on cause of death instead of verification of cause of death through autopsy. Dorrington and Bradshaw (2011) suggest that data captured by the census exaggerate the proportion of deaths caused by unnatural causes by an absolute magnitude of at least 10%.

In conclusion, this analysis has shown that the MMEIG's adjustment to non-AIDS deaths of 10% under-corrects for the expected fraction of pregnancy-related deaths due to unnatural causes. This will overstate subsequent estimates of the maternal deaths following under-adjustment of pregnancy-related deaths for unnatural deaths. It is likely that the under-correction for the proportion of pregnancy-related deaths due to unnatural causes in other southern African countries with less complete vital registration data will be higher than for South Africa, and maternal mortality estimates may be higher than expected.

4.3 Assumption for accounting for the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*)

4.3.1 Modelling estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*)

It is possible to estimate national-level values of the proportion of AIDS deaths occurring during the pregnancy-related period from the MMEIG method. The MMEIG assumes that the proportion of AIDS deaths in women aged 15-49 last birthday occurring during the pregnancy-related period is given by the following formula:

$$v = \frac{kcGFR}{1 + (k-1)cGFR}$$

In this formula, *GFR* represents the general fertility rate, which is the average number of births among women aged 15-49 last birthday; *k* is the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women; and *c* is the average exposure-to-risk (in years) to pregnancy-related death per live birth.

The MMEIG makes two assumptions for estimating the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, *v*, for countries with high HIV prevalence (Wilmoth, Zureick, Mizoguchi *et al.* 2010). The first assumption is that the relative risk of death from HIV/AIDS for

pregnant versus a non-pregnant women, *k*, is 0.4 (suggesting that the mortality rate of pregnant women infected with HIV is 40% of that of non-pregnant women aged 15-49 last birthday infected with HIV). The second assumption is that the average exposure-to-risk to pregnancy-related death per live birth, *c*, is 1 year (accounting for exposure to the risk of mortality within the 39 weeks of gestation, plus an allowance for pregnancies not resulting in a live birth, and for pregnancies that result in birth, an additional 6 weeks of exposure to mortality after delivery) (Wilmoth, Zureick, Mizoguchi *et al.* 2010).

In order to derive the general fertility rate to apply in the MMEIG formula for estimating *v*, the DemProj module of Spectrum population projection software is used to acquire estimates of the number of births and the number of women aged 15-49 last birthday for countries in southern Africa for each year between 1990 and 2010. Equivalently, the general fertility rate may also be derived from United Nations Population Division (2011) projections of the number of births and the number of women aged 15-49 last birthday. DemProj uses data from the United Nations World Population Prospects to make projections (Stover and Kirmeyer 2008). As such, the general fertility rates estimated separately from DemProj projections are a close approximation to that of the United Nations Population Division projections. The data from DemProj projections are available as an unbroken annual time series, whereas data from the United Nations Population Division (2011) projections are available in five year intervals, and thus the preference for data from DemProj projections in this investigation.

A summary of the estimates of *v* derived by applying the MMEIG formula to the GFR from DemProj (represented by v_G) for the same period over which the MMEIG carries out its estimates is shown in Table 4.4. The level of *v* ranges from around 0.03 to 0.09 for southern African countries. All countries show a decreasing trend in *v* except for Zambia and Malawi, which have a relatively constant trend, reflecting the trend in *GFR* over time in the respective countries. Appendix 4 provides a complete time series of estimates of *v* derived by applying the MMEIG formula to the GFR from DemProj for each of the southern African countries for the period 1990 to 2010.

Table 4.4 A comparison of estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (v) derived by applying the MMEIG formula to the GFR from DemProj (v_G) and estimates derived from AIM projections of the number of AIDS deaths (v_A)

Country	1990	1995		2000		2005		2010	
	v_G	v_G	v_A	v_G	v_A	v_G	v_A	v_G	v_A
South Africa	0.051	0.042	0.070	0.038	0.078	0.036	0.078	0.033	0.068
Zimbabwe	0.075	0.061	0.117	0.054	0.115	0.050	0.105	0.047	0.086
Swaziland	0.083	0.068	0.111	0.058	0.116	0.052	0.111	0.048	0.094
Namibia	0.072	0.061	0.096	0.054	0.099	0.048	0.099	0.042	0.084
Botswana	0.066	0.053	0.077	0.045	0.088	0.040	0.084	0.037	0.071
Lesotho	0.067	0.061	0.097	0.056	0.117	0.051	0.104	0.046	0.087
Malawi	0.082	0.076	0.147	0.074	0.159	0.073	0.159	0.074	0.152
Zambia	0.089	0.087	0.139	0.088	0.153	0.088	0.154	0.090	0.153
Mozambique	0.083	0.079	0.101	0.079	0.116	0.076	0.125	0.069	0.120

In order to assess the reasonability of the estimates of v derived from the application of *GFR* to the MMEIG formula, estimates of v for each of the southern African countries for the period 1990 to 2010 were produced using data from the AIDS Impact Model (AIM) module of the Spectrum population projection software. In order to project the number of AIDS deaths among pregnant women, AIM first estimates the number of pregnant women infected with HIV. To do this calculation AIM assumes that about 15 per cent of pregnancies do not result in birth because of miscarriage, spontaneous abortion or stillbirths. As such, the estimated number of pregnant women infected with HIV is the number of births to pregnant women infected with HIV divided by 0.85 (Stover 2009). The number of these pregnant women infected with HIV who die during pregnancy and at child birth is then divided by the projected total annual number of AIDS deaths among women aged 15-49 last birthday to estimate the proportion of AIDS deaths among women that occur during pregnancy.

It is not clear whether the definition of pregnancy used by the AIM projection includes the period 42 days after delivery but it is assumed that it does not. Pregnant women infected with HIV are exposed to the risk of mortality during pregnancy for the gestation period of 39 weeks. However, not all pregnancies result in birth. For instance, women whose pregnancies spontaneously terminate, and, therefore, do not result in birth, are assumed to be exposed to the risk of pregnancy-related death for 13 to 22

weeks of pregnancy (WHO 2011c). It is therefore prudent to assume that the AIM projections of the total number of AIDS deaths occurring during pregnancy imply an exposure-to-risk to pregnancy-related mortality of 39 out of 52 weeks for pregnant women infected with HIV, including pregnancies that do not result in birth. In order to account for the 42 days of exposure to pregnancy-related mortality after child birth for the approximately 85 per cent of pregnancies that result in birth, the proportion of AIDS deaths in women that occur during pregnancy is therefore adjusted upwards by a factor of 6/52. This procedure results in an estimate of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, v, that is logically consistent with that produced by the MMEIG formula. These values of v derived from AIM projections of the number of AIDS deaths (i.e. v_A) are presented in Table 4.4.

The level of v derived from AIM projections of the number of AIDS deaths (i.e. v_A) for southern African countries ranges from around 0.07 to 0.16. The estimates of v derived from the application of general fertility rate to the MMEIG formula differ from estimates of v derived from the number of AIDS deaths (acquired from AIM projections). The results of the latter method, which estimates v from the number of AIDS deaths (v_A), are at least 1.2 times larger than the results of the former method, which estimates v from the general fertility rate (v_G). A summary of the complete annual time series of estimates of v derived from AIM projections of the number of AIDS deaths is shown in Appendix 5.

In order to investigate the differences between the results of v estimated from the application of general fertility rate to the MMEIG formula and those derived from the number of AIDS deaths, the value of the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k, which equates the estimates of v for each method is determined for each year. The results of this investigation are shown in Figure 4.3. The results suggest that the value of k varies from 0.41 (Lesotho) to 0.93 (Zimbabwe). The level of k exhibited by southern African countries is consistently higher than 0.4, and thus it is likely that applying the MMEIG assumption (i.e. that $k=0.4$) to southern African countries will under-correct the mortality rate of pregnant women infected with HIV relative to the mortality rate of non-pregnant women aged 15-49 infected with HIV. A summary of the complete annual time series of results is shown in Appendix 6.

Over time, the relative risk of death of pregnant women infected with HIV is lower than that of non-pregnant women aged 15-49 last birthday infected with HIV. Prior to 2000, the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k, for all countries except Mozambique, increased with time to a point where mortality from HIV among pregnant and non-pregnant women was almost equal. After the year 2000 (2005 for South Africa), the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women for these countries, decreased. It is likely that increases in access to antiretroviral therapy for pregnant women infected with HIV (UNAIDS 2008) explain this decreasing, albeit, high relative risk of death from HIV/AIDS for pregnant versus non-pregnant women.

Figure 4.3 The relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (k) that equates the estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (v)
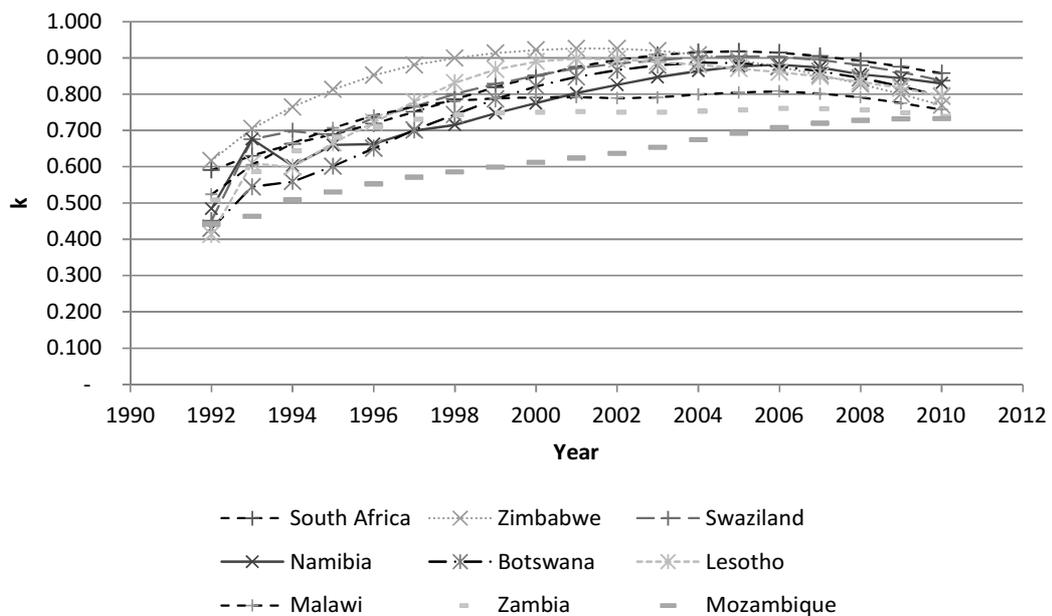
4.3.2 Sub-national estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (v)

Figure 4.4 shows estimates of v for the period 1993 to 2010 for the ALPHA-Network health and demographic surveillance system sites (HDSSs) (Zaba, Ronsmans, Momodou et al. 2011). This proportion is derived in two ways; directly and indirectly. The direct method uses serological data in which HIV status is recorded and attributed to deaths of women during pregnancy and up to 42 days following delivery. The indirect method uses responses from the verbal autopsy (VA) to identify signs and symptoms suggesting HIV/AIDS (Zaba, Ronsmans, Momodou et al. 2011). Four sites (Karonga, Manicaland,

Kisesa, and Masaka) use both verbal autopsy and serological surveillance (SS) data to identify HIV status, while two sites (Agincourt and Nairobi) exclusively use verbal autopsy classification to identify HIV status.

Figure 4.4 Estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*) for the period 1993 to 2010; ALPHA-Network HDSSs

HDSS site

■ Serological Surveillance (SS)   ■ Verbal Autopsy (VA)

Source: Adapted from Zaba, Ronsmans, Momodou *et al.* (2011)

It is possible to assess the reasonableness of these estimates by determining the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k, implied by the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, v, specific to each site. Values of k implied by estimates of v for each HDSS site, assuming that the average exposure-to-risk of pregnancy-related mortality per live birth, c, is 1 and that the general fertility rate takes on values between 0.1 and 0.2, are shown in Table 4.5. The results show that the k implied by a given estimate of v decreases with increases in general fertility rate. Doubling the general fertility rate approximately halves the values of k implied by the estimate of v for each HDSS site. It is therefore likely that, given the site-specific general fertility rate, the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k, will be higher (but less than 1) than is implied by the national-level GFR for each estimate of v.

Table 4.5 The relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (*k*) implied by estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*) for the period 1993 to 2010; ALPHA-Network HDSSs

Study	Estimate of *v*	Implied *k* when GFR is		
		0.1	0.15	0.2
ALPHA sites SS	0.02	0.17	0.11	0.08
ALPHA sites VA	0.04	0.34	0.22	0.15
Kisesa VA	0.04	0.42	0.27	0.19
Karonga SS	0.09	0.86	0.54	0.38
Karonga VA	0.04	0.35	0.22	0.15
Masaka SS	0.01	0.09	0.06	0.04
Manicaland SS	0.04	0.33	0.21	0.15
Manicaland VA	0.04	0.42	0.26	0.19
Nairobi VA	0.06	0.62	0.39	0.28
Agincourt VA	0.02	0.22	0.14	0.10

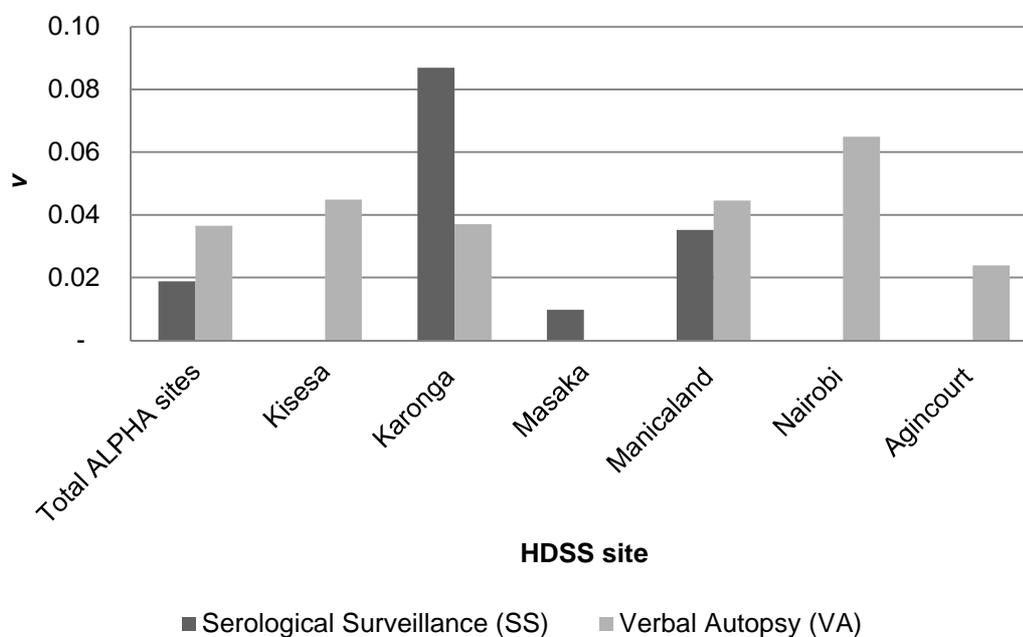**Source**: Calculated using estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, *v*, from Zaba, Ronsmans, Momodou *et al.* (2011)

4.3.3 Impact of combinations of the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (*k*) and general fertility rate on the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*)

According to the results of an analysis of model output carried out by the MMEIG, in practice *k* ranges from 0.3 to 0.6 for all countries with high HIV prevalence. In order to minimise the potential error in its model the MMEIG therefore assumes that *k* has a value of 0.4 (Wilmoth, Zureick, Mizoguchi *et al.* 2010, Wilmoth, Mizoguchi, Oestergaard *et al.* 2012). In order to test the sensitivity of *v* to *k*, the value of *v* is calculated for a range of general fertility rates characteristic of countries in southern Africa and a range of *k*. For most countries in southern Africa the *GFR* lies between 0.1 and 0.2. The value of *c* is kept at 1 as the average exposure-to-risk to pregnancy-related mortality per live birth, *c*, after delivery (i.e. $39/0.85 + 6$) closely approximates 1. The results of this investigation are shown in Table 4.6.

Table 4.6 The proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (v) for combinations of general fertility rate (*GFR*) and relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (k)

	GFR		
k	**0.10**	**0.15**	**0.20**
0.10	0.01	0.02	0.02
0.40	0.04	0.07	0.09
0.60	0.06	0.10	0.13
0.80	0.08	0.12	0.17

The results show that the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, v, increases linearly with the general fertility rate, *GFR*, and the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k. Increasing *GFR* from 0.1 to 0.2 for the same k approximately doubles v. At low levels of k the change in v among all levels of *GFR* is negligible. At higher levels of k, the change in v among all levels of *GFR* is more significant. Applying the assumption made by the MMEIG for countries with high HIV prevalence (i.e. that k=0.4) will, therefore, tend to under-correct the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, v.

4.4 Assumption for accounting for the fraction of pregnancy-related AIDS deaths due to indirect maternal causes (u)

Depending on whether data observations have been classified as pregnancy-related (including or excluding unnatural causes) or maternal (direct and indirect obstetric causes), the MMEIG assumes that either all pregnancy-related AIDS deaths are due to maternal causes (i.e. u=1), or that half the number of AIDS deaths that occur during pregnancy is due to maternal causes (i.e. u=0.5) (Wilmoth, Zureick, Mizoguchi *et al.* 2010, Wilmoth, Mizoguchi, Oestergaard *et al.* 2012). Maternal death data that separate deaths directly due to maternal causes from those that are incidental among pregnant women are, however, scarce (Ronsmans, Khlat, Kodio *et al.* 2001). The challenge becomes one of accurately identifying deaths among HIV-positive women where either

pregnancy is an aggravating factor resulting in death or in which HIV/AIDS aggravates obstetric conditions that may result in death (Rosen, de Zoysa, Dehne *et al.* 2012).

It is, however, possible to determine estimates of the fraction of pregnancy-related AIDS deaths due to indirect maternal causes from demographic surveillance system sites that record serological data, or from cause of death output of the InterVA model for interpreting verbal autopsy data. The only study that could be found that investigates the fraction of pregnancy-related AIDS deaths due to indirect maternal causes is an as yet unpublished study by the ALPHA network (Prof. Basia Zaba, personal communication[1]). In this study, about 58% of women among ALPHA network HDSS sites who died from HIV/AIDS during the pregnancy-related period were deemed to have died from indirect maternal causes. Although this estimate of u is consistent with the assumption made by the MMEIG (i.e. u=50%), there is uncertainty associated about this estimate of u. The sample size is too small (n=26) to yield a statistically significant result. In spite of the uncertainty associated with estimating u, applying the assumption that half the estimated number of AIDS deaths that occur during the pregnancy-related period is due to maternal causes does not appear to be unreasonable, thus cannot be said to lead to over- or under-statement of the contribution of indirect maternal mortality due to HIV/AIDS to overall maternal mortality.

4.5   WHO life tables for southern African countries

The World Health Organization has produced life table estimates for all member States (including southern African countries) for the years 1990, 2000, and 2009. The estimation process entails a review of observed adult mortality levels and trends recorded in surveys, censuses, and vital registration. Adult mortality rates fitted from the logit model life table system using the global standard do not incorporate high HIV/AIDS epidemic patterns because the observed underlying life tables are not derived from countries experiencing the HIV/AIDS epidemic. Separate estimates of deaths due to HIV/AIDS are added separately to account for mortality due to AIDS (WHO 2012a).

Figure 4.5 compares estimates of mortality rates for females aged 15-49 years last birthday for South Africa for the ten-year interval 1990, 2000, and 2009 from the WHO (2011b) life tables, Spectrum population projection model, and the ASSA 2008 AIDS

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[1] 5 July 2012

and Demographic model. The mortality estimates for Spectrum are similar to (albeit slightly higher than) the WHO life table estimates, and show an increasing trend over the period 1990-2010. The mortality estimates for the ASSA model show an increasing trend between 1990 and 2000, after which they increase at a decreasing rate, and at a significantly lower level than both the WHO (2011b) life table and Spectrum population projection model estimates. It is likely that the separate addition of mortality due to AIDS to WHO life table estimates overstates deaths due to AIDS, whereas the ASSA model estimates incorporate the impact of interventions such as highly active antiretroviral therapy, which reduce mortality due to HIV/AIDS. It is therefore likely that death rates from WHO life tables will overstate the number of deaths of women aged 15-49 last birthday (estimated from multiplying the WHO (2011b) death rates by the United Nations Population Division (2011) population estimates). This consequently results in a higher number of maternal deaths arising from multiplying PMDF by the number of deaths of women aged 15-49 years last birthday. Conversely, using estimates of mortality from the ASSA model results in lower estimates of the number of deaths of women aged 15-49 years last birthday, and consequently lower numbers of maternal deaths. In spite of these estimates, there is considerable uncertainty about levels of mortality in populations experiencing high HIV/AIDS prevalence (Murray, Ahmed, Lopez *et al.* 2000).

Figure 4.5 Comparison of estimates of mortality rates for females aged 15-49 years last birthday in South Africa, 1990-2010
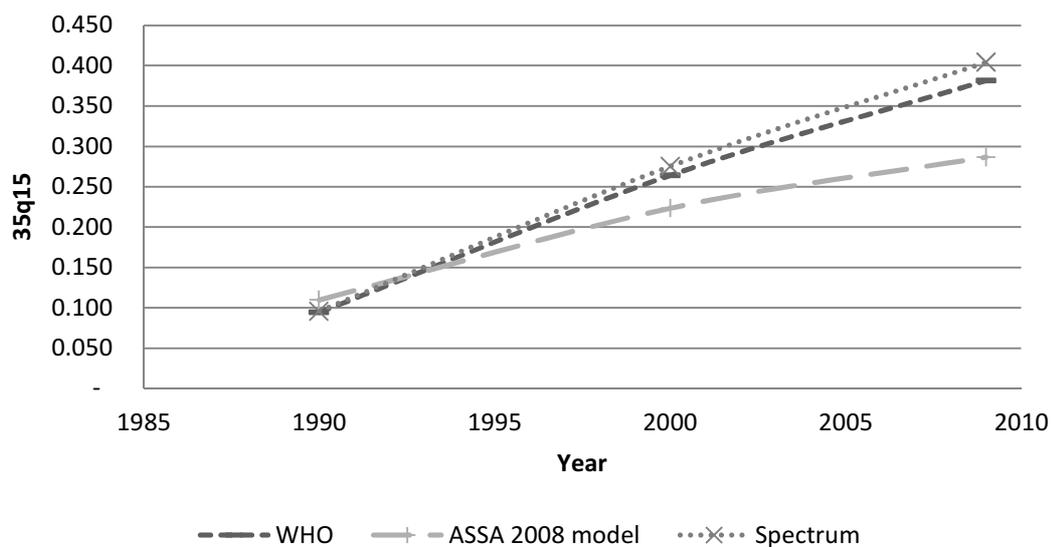
In conclusion, it is more likely that not all pregnancy-related AIDS deaths are due to maternal causes (i.e. $u=1$), but rather that some proportion will be due to maternal

causes and some part due to HIV/AIDS (approximated by the assumption that u=0.5). This assumption will understate the number of AIDS deaths due to maternal causes estimated as occurring among pregnant women infected with HIV/AIDS. Evidence from this research suggests that the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period, v, and the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, k, both increase linearly with the general fertility rate. It is therefore likely that the number of AIDS deaths that occur during pregnancy due to maternal causes will be lower than the number of AIDS deaths due to indirect maternal causes, requiring the assumption that u be greater than 0.5. It is therefore likely that in countries experiencing high HIV/AIDS prevalence, AIDS will be a significant cause of death among pregnant women infected with HIV/AIDS.

5   DISCUSSION

The chief objective of this study was to analyse critically the methodology used by the MMEIG to estimate maternal mortality in countries with high HIV/AIDS prevalence. The study set out to document clearly the methods applied by the MMEIG and then interrogate each of the assumptions (explicit and implicit) in their method. This chapter examines the extent to which the results obtained from a review of the literature meet the set objectives, and outlines the limitations of the method employed. In accordance with explaining the importance and relevance of the results of this study, this chapter identifies areas for potential future research before closing with conclusions that can be drawn from the study.

5.1   Discussion on findings of assumptions in the MMEIG method

At first glance, the estimates of maternal mortality published by the MMEIG (WHO, UNICEF, UNFPA *et al.* 2012) do not make it immediately clear to what extent changes in the maternal mortality rate (MMR) can be attributed to the respective contribution of the non-AIDS model and the AIDS model. However, investigation of the assumptions underlying each component of the model, which is the objective of this research, sheds some light on this puzzle. The covariates of the non-AIDS model are responsible for trends exhibited by maternal mortality estimates, while the underlying empirical data used in both the non-AIDS and AIDS models are responsible for the level of maternal mortality (AbouZahr 2011).

The gross domestic product contributes directly through government expenditure on healthcare, which translates into provision of training for skilled healthcare professionals and more and better-equipped facilities that avert maternal deaths. Other factors associated with the gross domestic product, such as female literacy and school enrolment, are indirectly responsible for a reduction in maternal mortality through improved knowledge of and use of antenatal and postnatal care services, and ability to negotiate better care with respect to place of delivery and skill level of health professional. Likewise, increase in skilled attendance at birth (SAB) and decreases in the general fertility rate (GFR) are associated with decreases in maternal mortality. Consequently, this trend is predicted by the MMEIG's model of non-AIDS maternal mortality. As much as other studies have identified gross domestic product as the most significant driver of trends in the MMEIG estimates (AbouZahr 2011), the factor

influencing maternal mortality in studies that have been consulted is skilled attendance at birth as a proportion of total live births.

Figure 5.1 Maternal Mortality trends for southern African countries, 1990-2010
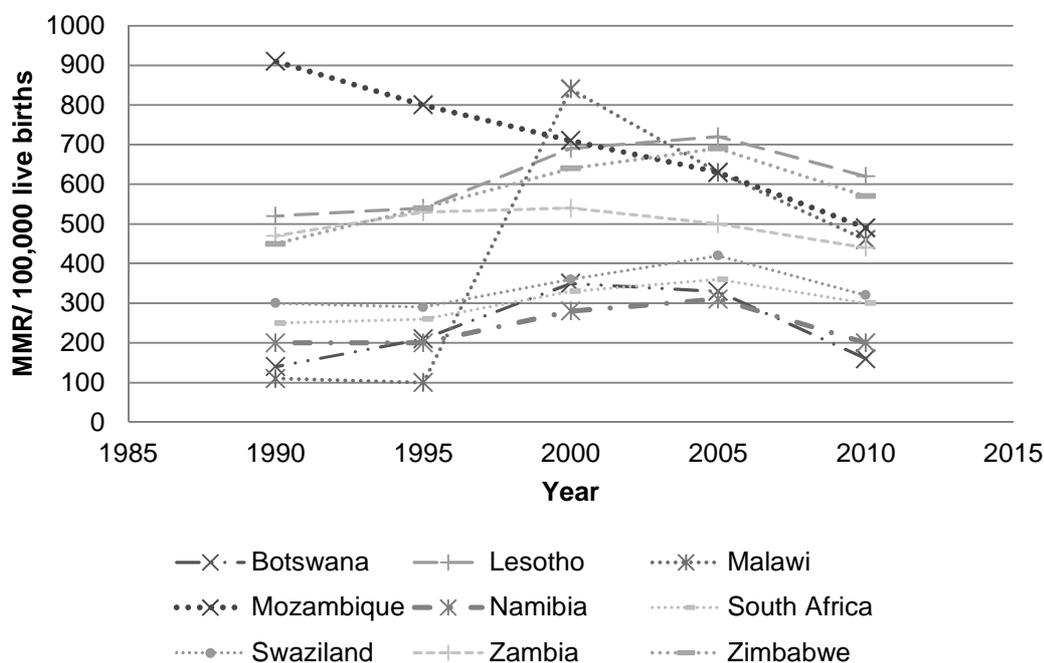
Source: Data extracted from estimates of MMR published by the MMEIG (WHO, UNICEF, UNFPA *et al.* 2012)

Inspection of the MMEIG estimates of maternal mortality illustrated in Figure 5.1 shows three distinct patterns. One pattern comprises countries exhibiting a trend that first increases and then decreases over time, both at a lower level (Botswana, South Africa, Namibia, and Swaziland) and at a higher level (Zimbabwe and Lesotho), with Zambia lying in between these extremes. The second pattern exhibits a rapidly decreasing trend in maternal mortality that is approximately linear (Mozambique). The final pattern is erratic (Malawi). Overall, after the year 2005, the trend shown by the MMEIG's estimates of maternal mortality is decreasing.

As shown in Figure 5.1, the level of maternal mortality varies significantly among countries and also within countries. At the extreme, the maternal mortality estimates for Malawi for the early years (relative to the estimates for later years) are anomalous and unlikely to be correct. There is no evidence to assert this but these early estimates are too low to be plausible. The results of this study show that the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, *k*, for Malawi exhibited an upward trend from 1990 to 2000, remaining relatively constant afterwards. This trend in

k estimated for Malawi by this study suggests that the contribution of deaths due to HIV/AIDS during the pregnancy-related period towards overall maternal mortality increases with time, consistent with the rapid increase in overall maternal mortality between 1995 and 2000. On the other hand, the trend shown for Malawi after the year 2000 is likely to be the result of lower contribution of non-AIDS maternal mortality to overall maternal mortality, possibly because after the year 2000, *k* is estimated to be constant, suggesting that the contribution of deaths due to AIDS during the pregnancy-related period to overall mortality is also constant. This implies that the decrease in overall maternal mortality must be due to decreases in non-AIDS maternal mortality.

The levels and trends for Botswana, South Africa, Namibia, and Swaziland are so similar that it is reasonable to use South Africa as a proxy because it has data from vital registration and surveys, which may help to explain the level and trend of maternal mortality estimates. According to estimates published by the MMEIG, shown in Figure 5.1, maternal mortality for South Africa increases gradually in the 1990s and increases markedly between 1995 and 2000, before peaking in 2005 and then gradually decreasing afterwards. This trend of the MMR is different from the trend estimated for South Africa by Bradshaw and Dorrington (2012). They argue that, based on vital registration data from 2009, the MMR for South Africa was still on an upward trend. In order to assess the reasonableness of the MMIEG estimates of the level and trend of MMR, it is, therefore, worthwhile investigating the contribution of non-AIDS deaths and AIDS deaths to overall maternal mortality.

As regards the contribution of HIV/AIDS to maternal mortality, the results of this research show that a *k* ranging from 40% to 93% across southern African countries equates the estimates of *v* derived from application of *GFR* in the MMEIG formula and the *v* derived from the number of AIDS deaths. The results suggest that pregnant women infected with HIV experience mortality rates that are between 40% and 93% that of non-pregnant-women infected with HIV depending on the point in time. The only time at which the implied *k* for southern African countries matches the range within which the MMEIG assumes there will be insignificant variation in results (i.e. 30%-60%) is the early 1990s, when the AIDS epidemic was in its infancy. This result is counterintuitive as it would be expected that the mortality rate of pregnant women infected with HIV and the mortality rate of non-pregnant women infected with HIV would be similar in the early years of the epidemic. This is because there has probably not been enough time for the infection to build up in the body and have an adverse

impact on the mortality of those infected. This odd result is probably explained by errors in AIM projections of the number of AIDS deaths, possibly emanating from the non-representative nature of data especially for rural populations, which tend to be underrepresented (Ghys, Brown, Grassly *et al.* 2004). The trend for *k* after the year 2000 is as expected, and decreases. Possibly, this is due to selection against pregnancy for women infected with HIV (Le Coeur, Khlat, Halembokaka *et al.* 2005), and also decreased mortality among infected pregnant women following increased coverage of antiretroviral treatment (UNAIDS 2008, McIntyre 2005).

This study shows further that the results for HDSS estimates of *v*, and the *k* implied by these estimates, are each approximately over 250% higher than the *v* estimated either from application of *GFR* in the MMEIG formula or estimated from the number of AIDS deaths and the *k* associated with these estimates. For a given estimate of *v*, the implied *k* decreases with increases in *GFR*. HDSS sites often comprise relatively small, geographically isolated populations that do not fully represent the fertility, mortality and migration experiences of the general national population (Clark 2004). It is therefore possible that it is this unrepresentativeness of HDSS sites that explains the large difference in magnitude of estimates of *v*.

The fraction of AIDS deaths occurring during pregnancy that is due to indirect maternal causes (i.e. *u*=58%) from the only study (Prof. Basia Zaba, personal communication[2]) that could be found by this research is not inconsistent with the 50% assumed by the MMEIG. Although the estimate for *u* is slightly larger than the 50% assumed by the MMEIG, it is likely that application of the MMEIG assumption will significantly understate AIDS deaths due to indirect maternal causes. This is because the rarity of maternal deaths (i.e. few observations relative to deaths of females of reproductive age) increases the variability of the small numbers of AIDS deaths due to maternal causes estimated following small changes in *u*.

Nevertheless, it is difficult to conceive whether it is practically possible to distinguish AIDS deaths which occur "as a result of" being pregnant from other AIDS deaths occurring during the pregnancy-related period (Prof. Basia Zaba, personal communication[3]). This inability to distinguish between AIDS deaths due to direct or indirect maternal causes ultimately estimates of the AIDS-related PMDF. Assuming that all pregnancy-related AIDS deaths are due to maternal causes (i.e. *u*=1) will overstate the

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[2] 5 July 2012
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expected level of maternal mortality. Conversely, assuming that half the number of AIDS deaths that occur during pregnancy is due to maternal causes (i.e. u=0.5) will understate the expected level of maternal mortality. Therefore, as there is no robust evidence to suggest that u is different from 50 per cent (except in the yet unpublished estimate of u=58%), the MMEIG assumption provides a best estimate that neither overstates nor understates AIDS deaths due to indirect maternal causes.

With regard to non-AIDs deaths, the results of this research show that the proportion of pregnancy-related deaths due to unnatural causes estimated from vital registration is approximately 100% to 200% higher than the ten per cent assumed by the MMEIG. The MMEIG (WHO, UNICEF, UNFPA *et al.* 2012), however, do not make use of vital registration for countries in southern Africa, which they characterise as lacking good complete vital registration data but where other types of data are available. South Africa does have vital registration data which have been analysed by researchers (Bradshaw, Laubscher, Dorrington *et al.* 2004) to identify and correct deficiencies to render such data reasonable for use in order to estimate maternal mortality (Bradshaw and Dorrington 2012). Even though other southern African countries have incomplete vital registration data, similar research to correct for incompleteness of death registration would allow incorporation of country-specific vital registration data into maternal mortality models. Therefore, based on the evidence from South African vital registration, it is likely that the exclusion of vital registration data (of whatever state) from southern African countries, arguably, also excludes maternal death observations that would otherwise inform levels and trends of maternal mortality consistent with experience in the population.

Investigation of the research objective using the findings from Dorrington and Bradshaw (2011) based on the 2001 Census and 2007 Community Survey shows that an additional 16-17% of non-AIDS deaths are due to unnatural causes occurring during the pregnancy-related period. This result comes with a caveat that the use of census and surveys to estimate maternal mortality based on the question on household deaths tends to overstate the number of deaths due to unnatural causes occurring during the pregnancy-related period for reasons of poor data handling by fieldworkers and analysts (Dorrington and Bradshaw 2011). Therefore, based on evidence from vital registration and household reports of deaths in censuses and surveys, the MMEIG's adjustment to account for pregnancy-related deaths due to unnatural causes understate the expected proportion of pregnancy-deaths due to unnatural causes. This under-correction for

pregnancy-related deaths due to unnatural causes consequently results in overstatement of pregnancy-related deaths due to maternal causes, and subsequently higher estimates of maternal deaths than expected.

This study shows further that, based on current data and estimation methods, about ten per cent of maternal deaths are due to unsafe abortion in southern Africa, which is approximately double the estimate for South Africa over the period 1998 to 2000. The estimate for countries surrounding South Africa but classified by the United Nations Population Division as belonging to eastern Africa is approximately 3 times larger than the estimate for South Africa. Notably, there are differences between regional estimates and also between countries (South Africa being the proxy) and regions. Data on the incidence of unsafe abortion are so sparse that it is not reasonable to assume that countries belonging to the same region or with similar abortion laws, fertility experiences or contraceptive usage have similar experiences of unsafe abortion and mortality associated with it. The results of this study, therefore, demonstrate that there is much uncertainty associated with estimating the proportion of maternal deaths due to abortion-related and other causes. It is therefore not clear whether the adjustment for abortion-related causes and other causes by the MMEIG will overstate or understate the expected level of maternal mortality in southern African countries.

The applicability of the WHO life tables to southern African countries is questionable. In the case of South Africa, the results of this study have shown that the WHO life tables overstate mortality of females aged 15-49 years last birthday compared to estimates of mortality from the ASSA model. It is likely that the WHO life tables do not accurately account for interventions such as prevention-of-mother-to-child (PMTCT) and highly active antiretroviral therapy (HAART) to reduce mortality in women infected with HIV. Application of the death rates from the WHO life tables, therefore, overstates the estimated number of deaths of women aged 15-49 last birthday from all causes. This subsequently overstates estimates of the number of maternal deaths implied by the observed PMDF, resulting in an overstatement of the MMR.

In conclusion, this research acknowledges that there is need to generalise assumptions regarding experiences of countries with high HIV prevalence. However, there are country-specific experiences that, without being included in the modelling exercise, will reflect accurately mortality levels and trends. Chief is vital registration. In southern Africa, apart from South Africa, coverage of death registration is low (Rao, Bradshaw and Mathers 2004). In spite of this, it is possible to adjust for this

incompleteness in order to incorporate these vital country-specific data into models. The universal availability from vital registration of data on cause of death of pregnancy-related deaths is one such form of data that would aid the adjustment to pregnancy-related death data to improve estimates of maternal mortality. This research has also shown that there are differences in HIV/AIDS experiences among southern African countries, and that estimates of v, k, and u are higher than assumed by the MMEIG. Even though the construction of the model for non-AIDS mortality tends to predict lower levels of maternal mortality, the underlying data and adjustments to these data suggest maternal mortality estimated by the MMEIG model is higher than expected.

5.2   Limitations of the research

Due to sparse data (and consequently limited research) on maternal mortality, this study was forced at times, to rely too heavily on single pieces of literature to tackle certain aspects of the research question. The question on unsafe abortion was over-reliant on work done by the WHO (2004; 2007; 2011), which, at times, has been criticised widely for the spurious accuracy of its estimates for developing countries in sub-Saharan Africa, questionable assumptions and adjustments for extrapolating sub-national experience to national experience, and piling errors upon each other by not revising its methodology (Antkowiak and O'Bannon 2003d, Antkowiak and O'Bannon 2003c, Antkowiak and O'Bannon 2003a, Antkowiak and O'Bannon 2003b). Other studies (Shah and Åhman 2009, Shah and Åhman 2010, Sedgh, Singh, Shah *et al.* 2012, Ahman and Shah 2011) that were used to tackle the research question were based on the same work done by the WHO, which created circularity in the results produced or at least repeated the estimates produced by the WHO.

At other times there was no other choice but to use individual studies as these would be the only authority with findings that could address the research objective. This was the case with work by Zaba, Ronsmans, Momodou *et al.* (2011) (including yet unpublished work) which investigated the assumptions for u and v specific to southern African sub-populations affected by high HIV prevalence.

5.3   Suggestions for further research

Given the scarcity of maternal mortality data, further research into sources of data offers scope for further development in the field of maternal mortality. Confidential enquiry into maternal deaths offers national-level estimates of maternal deaths by cause of death, but only captures deaths that occur in health care facilities which exclude

maternal deaths that occur in facilities but are outside maternal wards and deaths outside health care facilities (Dorrington and Bradshaw 2011). In order to derive estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period from CEMD data it would be ideal to also develop corresponding national-level estimates of maternal deaths occurring outside health care facilities. The fraction of maternal deaths occurring outside health facilities may possibly be inferred from the nearly fifty per cent (58%) of deliveries occurring outside healthcare facilities in sub-Saharan Africa (Rogo, Oucho and Mwalali 2006). Once national-level estimates of maternal deaths occurring within and outside health facilities have been derived, it would be ideal also to account for deaths due to unnatural/accidental causes occurring during pregnancy that would have occurred in hospital wards other than maternity wards. These missing deaths would then be added to unnatural/accidental deaths occurring during pregnancy derived from vital registration or censuses/surveys. A final adjustment to the complete set of maternal deaths would be to account for the differential AIDS mortality rates among pregnant women, which can be inferred from antenatal clinic data, which would itself need to be adjusted upwards to represent the national-level of HIV experience. It is anticipated that such treatment of confidential enquiry data would render it more useful to investigating maternal mortality in high HIV prevalence settings.

Even though data for estimating the general fertility rate are readily available, there is a wide margin of error in estimating the impact of HIV/AIDS on maternal mortality because of challenges of estimating the relative risk of death from HIV/AIDS of infected pregnant and non-pregnant women. The use of projections of AIDS deaths has proved to provide estimates with lower margins of error, and offer a direct way of investigating the impact of HIV/AIDS on maternal mortality. These projections can be further improved by modelling the effect of antiretroviral treatment on the survival of both pregnant women infected with HIV/AIDS in order to estimate death rates that reflect the experiences of women in countries affected by high HIV/AIDs prevalence.

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Appendix 1 A summary of the different methods of estimating maternal mortality

Boerma (1987) model of levels of maternal mortality in developing countries, 1980-1985	The model is based on the relationship between the overall level of adult female mortality and the level of fertility as measured by the general fertility rate. The resultant estimates of MMR imply total maternal deaths of 515,000, consistent with the frequently quoted estimate of 500,000 maternal deaths. • Estimates from the model are purely hypothetical as the categorisation of countries by MMRs is acknowledged to be subjective and spurious.
Blum and Fargues (1990) models of estimates of maternal mortality in countries with defective data, Bamako (1974-1985) and other developing countries	The first method entails direct estimation of maternal mortality by multiplication of age-specific mortality rates of women of reproductive age by corresponding age-specific proportions maternal among deaths of women aged 15-49 years. • The method proved difficult to use on developing countries where the vital registration data are subject to under-registration and misattribution of cause of death. The second method is an indirect estimate of maternal mortality which uses a comparison of ratios of female to male age-specific mortality rates, and assumes that maternal causes are dominant among causes of death specific to women of reproductive age, and that men within the same age group do not experience excess mortality. The third method is based on indirect estimation of maternal mortality that assumes that female mortality follows a Gompertz curve in the absence of maternal mortality.

A summary of the different methods of estimating maternal mortality, cont'd

WHO and UNICEF (1996) model of estimates of maternal mortality in 1990 developing countries	This method estimates maternal mortality for countries lacking complete vital registration data by regressing maternal mortality data from developed countries on general fertility rate and the proportion of births that are assisted by a skilled health professional. • The method arguably improves robustness of individual country estimates of maternal mortality compared to an earlier model based on life expectancy alone. • However, the model fails to use available country data that are deemed to be of reasonable quality; debatable choice of the dependent variable (MMR?) in the model; and the limited range of output of the model.
WHO, UNICEF and UNFPA (2001) model of estimates of maternal mortality in 1995 in UN MDG regions and countries	Conceptually similar to the 1996 method, this model used PMDF instead of MMR as the dependent variable, and included additional independent variables to account for completion of vital registration by region, and exposure to HIV. • The use of PMDF as a dependent variable was, however, the subject of debate among researchers who argued that the assumption that PMDF remains constant is violated in populations experiencing a high HIV epidemic.
Hakkert (2001) model of country estimates of maternal mortality	This model is an alternative to the WHO, UNICEF and UNFPA (2001) model of estimates of maternal mortality in 1995. Unlike the UN model, this model uses MMR as the dependent variable. • The use of MMR as a dependent variable is argued to have the benefit of being robust to high HIV prevalence, unlike PMDF.
WHO, UNICEF and UNFPA (2004) model of estimates of maternal mortality in 2000 in UN MDG regions and countries	The 2004 model is conceptually similar to the 2001 model, but includes GDP and excludes HIV as an independent variable. • The model estimates uncertainty boundaries around the estimated value within which the true value would likely be found. However, estimates from the method were associated with large margins of uncertainty, rendering them unsuitable for trend analysis. • The most significant difference with the 2001 model is that the 2004 model calculated PMDF from deaths adjusted to remove HIV-related deaths.

A summary of the different methods of estimating maternal mortality, cont'd

WHO, UNICEF, UNFPA et al. (2007) model of estimates of maternal mortality in 2005 in UN MDG regions and countries	The 2007 model represents a change in methodology by the MMEIG that entailed grouping countries by available data source, and specifying a statistical model to estimate maternal mortality for countries lacking complete vital registration data. • The MMEIG 2007 model allowed trend analysis of MMR estimates interpretable within (wide) limits of uncertainty.
WHO, UNICEF, UNFPA et al. (2010) model of estimates of maternal mortality in 2008 in UN MDG regions and countries	The 2010 model uses multilevel regression to generate non-AIDS PMDFs at multiple time points between 1990 and 2008, as well as a separate statistical model to estimate HIV-related maternal deaths, unlike the 2005 model that uses a regression model to generate single-period PMDFs. Moreover, the 2010 model is based on a larger data set than that used in the 2005 model. • The MMEIG 2008 model also makes explicit adjustment to account for maternal deaths due to unnatural causes, abortion-related and other causes, and deaths indirectly related to HIV/AIDS. • Compared to the IHME estimates, the MMEIG 2008 estimates are higher and are associated with larger uncertainty bounds.
IHME (Hogan, Foreman, Naghavi et al. 2010) model of estimates of maternal mortality (1980-2008) in UN MDG regions and countries	The IHME model is based on regression of maternal mortality on GDP, TFR, HIV seroprevalence, neonatal mortality and female education to estimate maternal mortality for countries and/or time periods lacking empirical data. • The IHME model differs with the MMEIG 2010 model in its estimation of HIV-related mortality: the IHME uses a counterfactual method that compares maternal mortality estimates with and without HIV, whereas the MMEIG 2008 model assumes that indirect maternal deaths due to HIV are a function of k and u4.

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[4] Where *k* is the relative risk of death from HIV/AIDS for pregnant versus non-pregnant women, and *u* is the fraction of pregnancy-related AIDS deaths due to indirect maternal causes.

A summary of the different methods of estimating maternal mortality, cont'd

IHME (Lozano, Wang, Foreman et al. 2011) model of estimates of maternal mortality in UN MDG regions and countries	This model by the IHME is an updated version of the previous IHME model that uses a larger data set. • The modelling strategy is based on ensemble models which are argued to have the advantage of yielding more accurate predictions bound by more accurate uncertainty intervals.
South African CEMD (National Committee on Confidential Enquiries into Maternal Deaths 1999; 2003; 2006; 2011; 2012)	South Africa has conducted confidential enquiries into maternal deaths almost two decades after formal approaches to estimating maternal mortality were started by different interest groups. The primary function of a CEMD is an audit to identify the preventable factors in the health facilities. • CEMDs have the advantage of providing a more comprehensive picture of maternal mortality than generally available from maternal health records. Also CEMDs are flexible enough to allow focus on specific leading causes of maternal death. • Maternal death data recorded by CEMDs are select for women who have access to health care facilities, and may not be representative of the general population of females of reproductive age.
WHO, UNICEF, UNFPA et al. (2012) model of estimates of maternal mortality in 2010 in UN MDG regions and countries	The 2012 model is similar to the 2010 model, both methods employing the same non-AIDS and AIDS model. • The most significant difference from the previous model is the revision of estimates of the total number of deaths of reproductive age women to take account of more recent experience of adult mortality.

Appendix 2 Studies investigating the factors that influence maternal mortality

Study	Period/year of study	no. of countries in study	Factors associated with maternal mortality	Correlation coefficient	Significance (p<0.05) as a predictor of maternal mortality
Alvarez et al (2009)	1997-2006	45	Infant mortality rate	0.815	<0.001
			Antenatal care coverage	-0.413	0.006
			Skilled attendants at birth	-0.572	<0.001
			Access to improved water source	-0.399	<0.001
			Access to improved sanitation	-0.261	0.091
			Adult literacy rate	-0.517	<0.001
			Contraceptive prevalence	-0.622	<0.001
			Ratio of female to male literacy rate	-0.485	0.002
			Primary school enrolment rate	-0.386	0.018
			Female primary school enrolment rate	-0.435	0.012
			Education index	-0.543	<0.001
			%GNP expenditure on health	-0.109	0.488
			%GNP expenditure on education	-0.242	0.138
			Gross national income per capita	-0.456	0.002
			External resources for health	0.266	0.085
			Government expenditure on health	-0.12	0.442
			Out-of-pocket expenditure on health	0.365	0.016
			Per-capita government expenditure on health	-0.452	0.002

Studies investigating the factors that influence maternal mortality, cont'd

Study	Period/year of study	no. of countries in study	Factors associated with maternal mortality	Correlation coefficient	Significance (p<0.05) as a predictor of maternal mortality
Buor and Bream (2004)	1990-1998	28	Gross National Product per capita	-0.543	≤0.05
			Health expenditure	-0.742	≤ 0.01
			Female literacy	0.487	≤0.05
			Skilled attendants at birth	-0.592	≤0.01
			HIV/AIDS prevalence	-0.364	>0.05
			Total fertility rate	0.192	>0.05
			Political stability	-0.344	>0.05
			Life expectancy at birth	-0.489	≤0.05
McAlister and Baskett (2006)	1985-2001	148	Infant mortality rate	77.2***	0.002
			Total fertility rate	65.4***	0.424
			Female literacy rate	48.6***	0.039
			Combined enrolment ratio	48.0***	0.004
			Year of suffrage	18.1***	0.574
			Seats in parliament held by women	0.20***	0.75
			Female professional and technical workers	16.5***	0.111
			Ratio of estimated female to male earned income	7.6***	0.075
			Female economic activity	4.6***	0.634
			Human development index	81.2***	<0.0001
			Gender-related development index	82.9***	<0.0001
			Gender empowerment measure	25.0***	0.187

*** represents R^2 values for the component of variation of maternal mortality explained by the factor

Studies investigating the factors that influence maternal mortality, cont'd

Study	Period/year of study	no. of countries in study	Factors associated with maternal mortality	Correlation coefficient	Significance (p<0.05) as a predictor of maternal mortality
Lee et al (1997)	1987-1990	78	Female life expectancy at birth	-0.9	<0.001
			Female literacy	-0.82	<0.001
			Primary school enrolment ratio	-0.64	<0.001
			Secondary school enrolment ratio	-0.86	<0.001
			Real GDP per capita	-0.91	<0.001
Shen and Williamson (1999)	1990	79	Real GDP per capita	-0.78	-0.83**
			Economic growth	-0.36	-0.30**
			Population per doctor	0.81	0.30**
			Calories per capita	-0.68	-0.05
			Total fertility rate	0.74	0.29**
			Contraceptive prevalence	-0.81	-0.35**
			Skilled attendants at birth	-0.74	-0.28**
			Secondary school enrolment ratio	-0.7	-0.19**
			Age at first marriage	-0.72	-0.16**
			Foreign investment	-0.35	0.12
			Foreign debt increase	0.34	0.14*
			Commodity concentration	0.15	0.17**
Robinson and Wharrad (2001)	1988-1997	155	Gross National Product	-0.887	<0.001
			Female literacy	-0.757	<0.001
			Physicians per 1000 population	-0.921	<0.001
			Nurses per 1000 population	-0.87	<0.001
			Skilled attendants at birth	-1.371[5]	<0.001

* and ** represent the correlation coefficient for predictors of maternal mortality where coefficients are considered significant if the coefficient is at least 1.5 times and 2 times the size of its standard error respectively.

[5] The correlation coefficient is reported as having an absolute value greater than 1.0 throughout the study by Robinson and Wharrad (2001), and as such has been disregarded in the analyses.

Studies investigating the factors that influence maternal mortality, cont'd

Study	Period/year of study	no. of countries in study	Factors associated with maternal mortality	Correlation coefficient	Significance (p<0.05) as a predictor of maternal mortality
Betran et al (2005)	2004	141	Skilled attendants at birth (%)		<0.0001
			Infant mortality rate		0.0003
			Health expenditure per capita		0.0004
			Population growth rate		>0.05
			Male Probability of death between 15 and 59		>0.05
			Female net primary school enrolment		>0.05
			Urban population (%)		>0.05
			Contraceptive-use prevalence rate		>0.05
Sloan et al (2001)	1999	84	Literacy	-0.79	>0.05
			Tetanus toxoid immunisation	-0.29	>0.05
			Antenatal care	-0.59	>0.05
			Contraceptive prevalence	-0.77	<0.001
			Skilled attendance at delivery	-0.86	<0.001
			Institutional delivery	-0.78	>0.05
			Gross national product	-0.46	>0.05
Shiffman (2000)	1998	64	Female gross secondary-school enrolment	-0.897	<0.01
			Skilled attendance at delivery	-0.895	<0.01
			Income per capita	-0.77	<0.01
			Health expenditure as %GDP	-0.714	<0.01
			Antenatal care	-0.628	<0.01
			Female gross secondary-school enrolment	-0.623	<0.01

Appendix 3 Summary of the proportion of maternal deaths due to unsafe abortion, 1998-2010

| Year | Proportion of maternal deaths due to unsafe abortion | | |
	South Africa	Eastern Africa	Southern Africa
1998	5.7%	14%	19%
1999	5.5%	14%	11%
2000			
2001			
2002			
2003	3.5%	17%	9%
2004	5.2%[6]		
2005		17%	9%
2006	3.4%		
2007	3.3%[7]		
2008		18%	9%
2009	3.8%		

Source: Estimates of maternal deaths due to unsafe abortion for the various years extracted from Thonneau (2001), Shah and Åhman (2009), Ahman and Shah (2011), WHO (2004; 2007; 2011), National Committee on Confidential Enquiries into Maternal Deaths (1999; 2011; 2012)

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[6] This estimate is reported in the fourth confidential enquiry for the period 2005-2007 and is superseded by the estimate reported in the fifth for the period 2008-2010. It is plotted against 2004 (instead of 2003) for comparison with the estimate for 2003.

[7] Similarly, this estimate is reported in the fourth confidential enquiry for the period 2005-2007 and is superseded by the estimate reported in the fifth for the period 2008-2010. It is plotted against 2007 (instead of 2006) for comparison with the estimate for 2006.

Appendix 4 Estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*) derived by applying the MMEIG formula to the GFR from DemProj

Year/Country	South Africa	Zimbabwe	Swaziland	Namibia	Botswana	Lesotho	Malawi	Zambia	Mozambique
1990	0.051	0.075	0.083	0.072	0.066	0.067	0.082	0.089	0.083
1991	0.048	0.071	0.079	0.068	0.062	0.065	0.080	0.087	0.081
1992	0.046	0.069	0.077	0.067	0.060	0.064	0.078	0.086	0.080
1993	0.044	0.065	0.073	0.064	0.056	0.062	0.077	0.086	0.079
1994	0.043	0.063	0.071	0.063	0.055	0.061	0.076	0.086	0.079
1995	0.042	0.061	0.068	0.061	0.053	0.061	0.076	0.087	0.079
1996	0.041	0.059	0.065	0.059	0.051	0.060	0.075	0.087	0.078
1997	0.040	0.057	0.063	0.057	0.049	0.060	0.075	0.088	0.078
1998	0.039	0.056	0.061	0.056	0.047	0.059	0.075	0.088	0.078
1999	0.039	0.055	0.059	0.055	0.046	0.058	0.075	0.088	0.079
2000	0.038	0.054	0.058	0.054	0.045	0.056	0.074	0.088	0.079
2001	0.038	0.053	0.057	0.053	0.043	0.055	0.074	0.088	0.079
2002	0.037	0.052	0.056	0.051	0.042	0.054	0.073	0.088	0.080
2003	0.037	0.051	0.055	0.050	0.041	0.053	0.073	0.088	0.079
2004	0.036	0.051	0.053	0.049	0.041	0.052	0.073	0.088	0.078
2005	0.036	0.050	0.052	0.048	0.040	0.051	0.073	0.088	0.076
2006	0.035	0.050	0.051	0.047	0.039	0.050	0.074	0.088	0.075
2007	0.034	0.049	0.050	0.046	0.039	0.049	0.074	0.088	0.074
2008	0.034	0.049	0.049	0.044	0.038	0.048	0.074	0.088	0.072
2009	0.033	0.048	0.048	0.043	0.038	0.047	0.074	0.089	0.071
2010	0.033	0.047	0.048	0.042	0.037	0.046	0.074	0.090	0.069

Appendix 5 Estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*) derived from AIM projections of the number of AIDS deaths

Year/Country	South Africa	Zimbabwe	Swaziland	Namibia	Botswana	Lesotho	Malawi	Zambia	Mozambique
1992	0.046	0.069	0.077	0.067	0.060	0.064	0.078	0.086	0.080
1993	0.044	0.065	0.073	0.064	0.056	0.062	0.077	0.086	0.079
1994	0.043	0.063	0.071	0.063	0.055	0.061	0.076	0.086	0.079
1995	0.042	0.061	0.068	0.061	0.053	0.061	0.076	0.087	0.079
1996	0.041	0.059	0.065	0.059	0.051	0.060	0.075	0.087	0.078
1997	0.040	0.057	0.063	0.057	0.049	0.060	0.075	0.088	0.078
1998	0.039	0.056	0.061	0.056	0.047	0.059	0.075	0.088	0.078
1999	0.039	0.055	0.059	0.055	0.046	0.058	0.075	0.088	0.079
2000	0.038	0.054	0.058	0.054	0.045	0.056	0.074	0.088	0.079
2001	0.038	0.053	0.057	0.053	0.043	0.055	0.074	0.088	0.079
2002	0.037	0.052	0.056	0.051	0.042	0.054	0.073	0.088	0.080
2003	0.037	0.051	0.055	0.050	0.041	0.053	0.073	0.088	0.079
2004	0.036	0.051	0.053	0.049	0.041	0.052	0.073	0.088	0.078
2005	0.036	0.050	0.052	0.048	0.040	0.051	0.073	0.088	0.076
2006	0.035	0.050	0.051	0.047	0.039	0.050	0.074	0.088	0.075
2007	0.034	0.049	0.050	0.046	0.039	0.049	0.074	0.088	0.074
2008	0.034	0.049	0.049	0.044	0.038	0.048	0.074	0.088	0.072
2009	0.033	0.048	0.048	0.043	0.038	0.047	0.074	0.089	0.071
2010	0.033	0.047	0.048	0.042	0.037	0.046	0.074	0.090	0.069

Appendix 6 The relative risk of death from HIV/AIDS for pregnant versus non-pregnant women (*k*) that equates the estimates of the proportion of AIDS deaths in women aged 15-49 last birthday that occur during the pregnancy-related period (*v*)

Year/Country	South Africa	Zimbabwe	Swaziland	Namibia	Botswana	Lesotho	Malawi	Zambia	Mozambique
1992	0.59	0.62	0.45	0.48	0.43	0.41	0.52	0.51	0.44
1993	0.63	0.71	0.68	0.68	0.54	0.61	0.60	0.59	0.46
1994	0.66	0.76	0.70	0.60	0.56	0.60	0.66	0.64	0.51
1995	0.69	0.81	0.69	0.66	0.60	0.67	0.71	0.68	0.53
1996	0.72	0.85	0.73	0.66	0.65	0.72	0.74	0.71	0.55
1997	0.75	0.88	0.77	0.70	0.70	0.78	0.77	0.73	0.57
1998	0.79	0.90	0.80	0.72	0.74	0.83	0.78	0.74	0.59
1999	0.82	0.91	0.83	0.75	0.79	0.87	0.79	0.75	0.60
2000	0.85	0.92	0.85	0.78	0.82	0.89	0.79	0.75	0.61
2001	0.88	0.93	0.87	0.80	0.85	0.90	0.79	0.75	0.62
2002	0.89	0.93	0.88	0.83	0.87	0.90	0.79	0.75	0.64
2003	0.91	0.92	0.89	0.85	0.88	0.89	0.79	0.75	0.65
2004	0.92	0.91	0.90	0.86	0.89	0.88	0.80	0.75	0.67
2005	0.92	0.89	0.90	0.88	0.89	0.87	0.80	0.76	0.69
2006	0.91	0.88	0.90	0.88	0.88	0.86	0.81	0.76	0.71
2007	0.90	0.85	0.89	0.87	0.86	0.85	0.80	0.76	0.72
2008	0.89	0.83	0.88	0.85	0.84	0.83	0.79	0.76	0.73
2009	0.88	0.80	0.86	0.84	0.82	0.82	0.77	0.75	0.73
2010	0.86	0.77	0.84	0.83	0.79	0.80	0.76	0.74	0.73
Country average over period	**0.81**	**0.85**	**0.81**	**0.76**	**0.76**	**0.79**	**0.75**	**0.72**	**0.62**