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MEASURING AND ESTIMATING MATERNAL MORTALITY IN THE ERA OF HIV/AIDS *

Wendy Graham and Julia Hussein **

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** Dugald Baird Centre for Research on Women's Health, University of Aberdeen, Aberdeen, Scotland, U.K. The views expressed in the paper do not imply the expression of any opinion on the part of the United Nations Secretariat.

A. INTRODUCTION

In this 21st century, safe motherhood remains an elusive goal for many developing countries. The obstacles to progress in reducing the burden of avoidable maternal mortality and severe morbidity include both old and new challenges, and emphasise the reality of no "quick fix" nor "magic bullet". Among the older challenges are some familiar barriers to public health, such as dysfunctional health systems, poverty, and the low status of women. As regards the new challenges, foremost among these is HIV/AIDS.

Global recognition of the magnitude and implications of this modern-day plague broadly coincided with raised awareness of the neglected tragedy of maternal mortality in developing countries (Mahler, 1987; Quinn and others, 1986). Looking back over the lapsed time since then reveals several similarities in the evolution of these two major challenges to global health. The concentration of the burden in developing countries is similar, experiencing annually an estimated 99% of all maternal deaths (WHO/UNICEF/UNFPA, 2001) and a similar proportion of AIDS deaths (1999) (UNAIDS, 2003). The serious difficulties of measuring the burden, especially on a population basis, are comparable for maternal mortality and HIV/AIDS. In terms of reliable evidence of progress in reducing mortality in developing countries from either condition, there is little to celebrate, particularly in sub-Saharan Africa (AbouZahr and Wardlaw, 2001; Buve, Bishikwabo-Nsarhaza, and Mutangagura, 2002). What is perhaps most surprising however in this evolution is the comparatively limited attention given to the relationship between maternal mortality and HIV/AIDS (Graham and Newell, 1999). This has many manifestations. A search of Medline, for example, reveals just 43 papers in the last 10 years with "maternal mortality" and "HIV/AIDS" as key words, compared with over 6200 identified using "child mortality" and "HIV/AIDS".

There are a host of scientific, practical and ethical reasons for acknowledging the relationship between maternal mortality and HIV/AIDS (Berer, 1999). The focus of this paper is specifically on the challenge of measuring maternal mortality in the context of HIV/AIDS. Although there is little empirical evidence on the scale or stage of the HIV/AIDS epidemic at which effects on maternal mortality are significant, "context" here is assumed to be populations with adult prevalence rates (15-49 year olds living with HIV/AIDS) in excess of 1% and thus relates predominantly to sub-Saharan Africa with an estimated prevalence of 8.8% in late 2000 (Morrison, 2001). The first section of the paper explores possible biological or behavioural synergies. The remainder focuses on the implications of the presence of HIV/AIDS for the classification, quality, sources, and interpretation of data on maternal mortality. Finally, a brief descriptive profile of global and regional patterns in maternal mortality is given, along with recommendations on priorities for research and development.

There are two sides or facets to exploring the relationship – the effects of HIV/AIDS on the measurement of maternal mortality and the effects of HIV/AIDS on the risk of maternal mortality. In practice, these effects are totally conflated and thus hard to differentiate – the analogy being two sides to the same coin or currency, as represented in Figure 1. The latter shows that the level of maternal mortality may increase or decrease in the context of HIV/AIDS owing to changes in the numerator of deaths and/or denominator of women or births. These changes, in turn, can be due to real alterations in the risk of maternal death or of exposure. Alternatively they can be measurement artefacts, in other words, the consequences or knock-on effects of HIV/AIDS.

B. BIOLOGICAL OR BEHAVIOURAL SYNERGIES

Figure 2 presents a framework for conceptualising the measurement-risk currency. Taking first the facet representing biological or behavioural relationships, Figure 2 (right) shows this in terms of three overlapping domains. At the core are the maternal deaths among women with HIV/AIDS, grouped into three categories. AIDS can itself be regarded as the cause of maternal death when death occurs in the interval from onset of pregnancy to 42 days postpartum. Relative to a point in time before HIV/AIDS was prevalent or relative to a population without HIV/AIDS, the added effect of this cause would be an increase in the number of maternal

deaths. The innermost domain in Figure 2 also encompasses HIV/AIDS increasing the risk of other causes of maternal death – both direct obstetric, such as puerperal sepsis, or other indirect, such as malaria. Here the proven biological relationship is primarily immuno-suppression, with HIV or AIDS cases unable to withstand infections, but also other complications such as haemorrhage as well as interventions such as caesarean section (Berer, 1999; McIntyre, 1999). In the latest Confidential Enquiry into Maternal Deaths (CEMD) in South Africa, for instance, the proportion of direct obstetric deaths whose primary cause was puerperal sepsis increased from 11% in 1998 to 16% in 2001 (Pattinson and Moodley, 2002). Similarly, the proportion due to indirect infections, including AIDS, increased from 23% to 31% over the same period, and now represents the leading cause of maternal death in this country, where an estimated quarter of pregnant women attending government antenatal clinics are HIV infected.

The second domain of the risk of maternal death shown in Figure 2 relates to all pregnant and parturient women. At this level the burden of HIV/AIDS may exert an effect through the health system in terms of the availability and quality of care as well as uptake (Graham and Newell, 1999). This effect operates irrespective of the HIV or AIDS status of an individual woman. As regards, for example, the availability of care, the acute shortage of health professionals is a key factor - shortages arising both from AIDS mortality and to real and perceived risks of occupational exposure. It is self-evident that such shortages, along with other constraints to health services in the context of HIV/AIDS such as lack of safe blood for transfusions, will affect women needing care for life-threatening obstetric complications. A further consequence is seen in terms of the quality of care received, both owing to the loss of experienced professionals but also the standard of treatment where there is a high degree of HIV/AIDS suspicion, as also indicated in the South African CEMD (Pattinson and Moodley, 2002). Given that an estimated 90% of people living with HIV do not know their status (Morrison, 2001), this question of suspicion is a genuine concern, and may also affect uptake of care. Increasing poverty among families who have lost the principal earner owing to AIDS (Whiteside, 2001) may be a further reason for reduced uptake, particularly given the cost of emergency obstetric interventions.

Finally, turning to the outer domain of the risk of maternal death represented in Figure 2, HIV/AIDS exerts an influence on the universe of all women of reproductive age, both in terms of exposure to pregnancy and as a competing cause of adult female deaths. Women are only at risk of maternal death, by definition, when pregnant or recently delivered At a population level, reduced rates of conception (fecundity) owing to HIV/AIDS are well-established (Zaba and Gregson, 1998), and could therefore result in less maternal deaths. Similarly, higher spontaneous pregnancy losses, also linked with HIV/AIDS (Brocklehurst and French, 1998), would affect the number of women undergoing childbirth - the time when the probability of maternal death is greatest (AbouZahr, 1998). In terms of a competing cause (Mekonnen and others, 2002), clearly where females of reproductive age are dying of AIDS, the pool of women at risk is reduced and thus the absolute number of maternal deaths may decline. The extent to which pregnancy itself contributes to HIV disease progression and thus the risk of dying of AIDS, however, remains unclear (Ahdieh, 2001), and robust evidence from further meta-analyses is needed (French and Brocklehurst, 1998). The results from some research studies suggest that the probability of death in HIV-infected women is lower in the year after childbirth than during other periods of adulthood (Boerma, Nunn and Whitworth, 1998), possibly owing to a healthy pregnant woman effect (Ronsmans and others, 2001). Other researchers have noted this effect to persist up to two years after pregnancy or childbirth (Berer, 1999; Ng'weshemi and others, 2003).

In summary, it appears that biological and behavioural synergies can operate in negative or positive directions, thus influencing the risk of maternal death. Whereas two of the relationship domains described in Figure 2 are suggestive of an increase in the number of maternal deaths once pregnant, the outermost domain referring to all women of reproductive age highlights a possible converse effect of HIV/AIDS, namely a decrease. It is difficult however to predict the balance and magnitude of these effects on maternal mortality at the level of whole populations, as was indicated in Figure 1. Modelling may assist in this regard. Although many current models cannot project age or sex-specific patterns (UNAIDS, 2002), other forecasting tools may lend themselves to adaptation, such as the AIDS Impact Model (AIM) (Futures Group, 2003).

Opportunities to test such modelling empirically will, however, be seriously limited by the difficulties of measuring maternal mortality reliably. Some of the measurement constraints are peculiar to maternal mortality regardless of the context, but where HIV/AIDS is prevalent, further obstacles can be envisaged. This is the other facet to the measurement-risk currency and will now be discussed.

C. MEASUREMENT CHALLENGES

Maternal mortality is difficult to measure the world over. In developed countries with advanced information systems, underestimation arises primarily from misclassification of cause owing to omission from the death certificate of the pregnant or parturient status of the woman. Given the comparative rarity of maternal deaths in these settings, omission of only a few cases can have a disproportionately distorting effect on the most common indicator – the maternal mortality ratio (maternal deaths per 100,000 live births). In developing countries, problems of misclassification are combined with weak or non-existent routine information systems (AbouZahr, 1998; Berg, Danel and Mora, 1996; Graham, 2002). The barriers specifically in the context of HIV/AIDS fall again into three domains, illustrated in Figure 2 (left), namely at the level of death records, the information system, and the population. In the central domain and with the most direct relationship lies the complicating effects of HIV/AIDS on the classification of maternal deaths. At the level of the information system, HIV/AIDS may exert an influence on the quality of data captured from alternative sources. Finally in the outer domain - the population, HIV/AIDS is relevant to the use and interpretation of data on maternal mortality.

1. Classification of maternal deaths

Panel 1 sets out the definition of maternal death according to the International Classification of Diseases, Tenth edition (WHO, 1992). The extent to which this is followed in practice, especially in developing countries, largely depends on the sources and methods of data capture, as discussed later. There are however, two aspects to the classification of maternal deaths which have particular relevance for populations facing the challenge of HIV/AIDS – namely, the cause and the time of death.

a. *Cause of death*

As can be seen from Panel 1, maternal mortality has typically been defined as including direct obstetric and indirect obstetric causes but not incidental deaths. The latter category has long been the subject of debate, especially as regards deaths owing to accidents, violence or suicide. This debate questions whether there can ever be certainty that a woman's pregnancy status was not a precipitating factor, and similar uncertainty surrounds the influence of a woman's HIV/AIDS status (Berer, 1993). Given the lack of consensus, mentioned earlier, on the aggravating effects of HIV/AIDS on pregnancy and vice versa, registered deaths in pregnant or parturient women with HIV/AIDS may be presumed in some circumstances to be "incidental" and thus not regarded as maternal.

The reality in the vast majority of developing countries is that the HIV status of most maternal deaths is unknown, thus increasing the scope for misclassification. In the South African CEMD, for example, HIV status was unknown in 62% of all maternal deaths (n=3453, 1999-2001), and where it was available 78% were found to be positive (Pattinson and Moodley, 2002). These figures need to be interpreted in the light of this CEMD only capturing maternal deaths in health facilities and thus the pattern among home deaths is unknown. The situation in the poorest countries of sub-Saharan Africa is even more uncertain, since there are much lower levels of HIV Voluntary Counselling and Testing and much higher proportions of maternal deaths likely to be occurring outside the formal health sector. There is nevertheless an increasing amount of information on HIV status among pregnant women through sentinel surveillance and this perhaps represents a missed opportunity for projecting maternal mortality (Graham and Newell, 1999). Similarly, several recent community-based studies of child survival also have data on the mother, and with information on time of

death relative to pregnancy, could possibly be used to estimate maternal mortality (Crampin and others, 2003; Nakiyingi and others, 2003; Ng'weshi and others, 2003).

Variations in coding conventions for cause of death can also introduce bias, and this may be aggravated by what some authors have referred to as the "moral and symbolic aspects of AIDS" influencing the reliability of official statistics (Bonciano and Spink, 2002). Four tiers in the coding hierarchy are distinguished in ICD-10: underlying or primary cause, antecedent or precipitating factors, immediate cause, and mechanism of death. In the context of unknown HIV status and a lack of diagnostic facilities, the accuracy of attribution to these tiers must be questioned, particularly for deaths in early pregnancy. This in turn has implications for the official mortality statistics, which tend only to use the underlying or primary cause.

b. Time of death

In recognition of the problems of misclassification and uncertain diagnosis of medical causes, ICD-10 introduced a new category referred to as "pregnancy-related deaths". In some countries this has encouraged the introduction of a pregnancy status check-box onto death certificates (MacKay and others, 2000). As illustrated in Panel 1, the category of pregnancy-related deaths relies upon identification on the basis of time rather than cause, encompassing all deaths to women occurring in the interval from onset of pregnancy to 42 days postpartum. Such a time-of-death definition is utilised by estimation methods, such as the sisterhood method (Graham, Brass and Snow, 1989), in order to avoid the well-known difficulties of ascertaining specific causes of death in large-scale multi-purpose surveys (Chandromahan and others, 1998). As with any reference period for vital events there is, however, scope for reporting errors at the boundaries. In the case of deaths in early pregnancy, when the woman's state may be unknown to herself or undeclared to her relatives, this time-of-death definition offers no advantage over cause-of-death. These early pregnancy deaths are widely under-reported in most countries, but particularly where there are high levels of unsafe and illegal induced abortion (Barreto and others, 1992).

For both cause- and time-of-death definitions of maternal death, a cut-off at 42 days postpartum has long been recognised as a further source of underestimation. However, many early studies suggested that less than 1% of deaths related to pregnancy and childbirth occurred beyond the puerperium (AbouZahr, 1998). The assumption that this effect is minimal has been revisited recently, with a number of authors noting an increase in the proportion of deaths due to indirect causes for up to one year later (Etard, Kodio and Traore, 1999; McDermott and others, 1996). In recognition of this, the ICD-10 now includes the category of "late maternal deaths" for those occurring after 42 days postpartum but up to one year after the end of pregnancy or childbirth. In the recent UK CEMD, suicide emerged as the most common cause when this extended reference period was used (Drife and Lewis, 2001), so highlighting the potential for radical changes in the proportional distribution of causes with varying time-of-death definitions.

2. Quality and sources of data

There are three principal sources of data on maternal mortality: vital registration, health services, and population-based surveys (Campbell and Graham, 1990). In most developing countries, it is widely accepted that none of these alone can provide a complete and accurate picture, either at national or sub-national levels. Indeed it is for this reason that mixed methods have been developed which draw upon multiple sources, such as the Reproductive Age Mortality Studies (RAMOS) in Egypt (Ministry of Health, 1994) and Jamaica (Walker and others, 1986). Whilst some of the drawbacks to using single sources apply to all categories of mortality, as a basis for estimating maternal mortality there are also some specific difficulties. In the context of HIV/AIDS, further problems can be envisaged for each source. These problems are additional to broader threats to the information system of acute shortages of skilled personnel to maintain and use the data.

a. Vital registration

Vital registration systems which are of sufficient scope and quality for measuring levels and trends in maternal mortality only exist in a small number of countries – representing less than 7% of the estimated annual number of births globally (AbouZahr and Wardlaw, 2001). In a somewhat larger number of countries, registration is often reasonably complete for urban areas. However, this may change in the face of HIV/AIDS as urban cemeteries become full to capacity and sick individuals return to their rural place of origin to die. The issue of high mobility, both among sick adults and their surviving relatives, has emerged as a striking feature in a number of sub-Saharan countries (Urassa and others, 2001). For example, in Hai district of Tanzania, the home-coming sick constituted 19% of all adult deaths (Kintange and others, 1996). In the case of maternal deaths, this HIV-related mobility may be further aggravated by cultural norms, making it difficult to relate deaths to the true population of women at risk. For example, some women who are normally resident in a registration area may return to their relatives' home in order to deliver and, conversely, other women may move temporarily into the area in order to access health services. This greatly reduces the scope for using record linkage between vital registration and health services data for identifying maternal deaths - linkage which often forms the foundation for confidential enquiry systems in developed and transitional countries (McIlwaine, 2003).

b. *Health services*

Health services remain the main routine source of data on maternal mortality for many developing countries. The major difficulty here is gauging the scale and type of selection bias. Hospital-based estimates of maternal mortality may either be an over-estimate of the population level owing to a disproportionate representation of complicated cases or, conversely, an underestimate owing to a high percentage of deaths occurring in the community (AbouZahr, 1999). In the context of HIV/AIDS and as discussed earlier, the proportion of cases being brought to health services may decline, thus giving the false impression of falling mortality. On the other hand, these service data are frequently the most reliable source on medical cause of death. Great caution is needed, however, in using proportional distributions. Some obstetric complications can be unpredictable in onset and rapidly lead to death, such as major postpartum haemorrhage, and these are frequently underrepresented in health service sources. Moreover, underreporting in facilities may simply occur owing to the hospital ward on which death occurs. This is particularly the case for indirect causes such as tuberculosis or indeed AIDS and for puerperal obstetric cases such as sepsis, as these tend not to be admitted to the maternity wing. A further source of underreporting in facilities relates to cases of illegal induced abortion, where fear of prosecution can result in false reports from relatives or attending professionals.

c. Population-based surveys

Surveys often provide the only opportunity to establish place of maternal death on a population basis and thus to gauge the selection biases in routine health services information. However, their major disadvantage is the large sample size requirements for producing reliable current estimates (Table 1). Alternative population-based approaches are the census (Hill, Stanton and Gupta, 2001) and demographic surveillance systems (DSS) (INDEPTH, 2002), both of which have major resource implications. The census also has drawbacks in terms of timeliness, often being conducted on a decennial basis, and DSS sites can become increasingly unrepresentative of the general population as the period of surveillance lengthens. Prospective cohort studies and randomised controlled trials represent variants of continuous surveillance and are designs used in many HIV/AIDS research projects. Although maternal death has been included as an outcome of interest in some of these special studies, very few are large enough to yield robust estimates of levels, for example, in Rakai, Uganda (Sewankambo and others, 2000).

Survey-based methods utilising direct estimation are known to be adversely effected by the disintegration of the family unit which may follow a maternal death (Kwast, 1985). Such a problem may be exaggerated further in the context of HIV/AIDS where household dissolution follows loss of the head and/or

other key members (Urassa and others, 2001). Indirect estimation using the sisterhood method (Graham, Brass and Snow, 1989;) avoids this particular difficulty as the residential home of the deceased woman is not the sampling unit but rather that of their adult siblings. Similarly, by securing information on more than one woman from each sibling, this approach can rapidly accumulate women years' of risk exposure and thus has smaller sample size requirements than the direct method (WHO and UNICEF, 1997). However, the trade-off for this is the time-location of the resulting estimate, which varies according to the age-group of respondents and can be as long ago as ten years for the original sisterhood method. The Demographic and Health Surveys (DHS) have used a variant of this method for many years now (Rutenberg and Sullivan, 1991), and data are thus available at the national level for about 55 developing countries. These tend to use a reference period of 0-7 years prior to data collection, so making the interpretation of recent trends problematic. Given the average size of DHS surveys, the resulting estimates will also have very wide confidence intervals (Stanton, Abderrahim and Hill, 2000). Sibling-based methods raise a further complication given the high degree of mobility noted earlier among populations facing HIV/AIDS, since the maternal mortality data relate to the respondents' physical location rather than that of the deceased.

All survey-based approaches to maternal mortality estimation have the potential for response bias in a context with HIV/AIDS. Firstly, there is the question of the choice and availability of respondents. In populations with escalating adult mortality owing to HIV/AIDS, those interviewed in household surveys are clearly only the survivors and thus a healthy respondent effect will prevail. This is complicated by the hetero-sexual spread of HIV, which means that both women and their partners may be lost. Secondly, surviving partners may be too sick to respond, and those finally interviewed not necessarily the best informed of the circumstances surrounding a maternal death. Thirdly, several studies have found that verbal autopsy tools used to gauge the primary cause of death have low sensitivity and specificity (Sloan and others, 2001), and therefore misclassification is a common problem. Most such tools focus on identifying direct obstetric causes, and none have been adapted specifically to identify maternal deaths in populations with a high prevalence of HIV/AIDS, although some ascertain HIV-related adult mortality (Kamali and others, 1996). Finally, in such settings, there may be a greater stigma attached to reporting an adult female death from HIV/AIDS than from other causes, and this could potentially lead to over-reporting of maternal deaths (Bicego, 1997).

2. Use and interpretation of maternal mortality data

The challenges of classification and quality are concerns in the generation of primary data on maternal mortality in developing countries. The use and interpretation of these data given a context with HIV/AIDS raises further knotty problems, in terms of the choice of indicators or measures, the use of estimation models, and the interpretation of trends.

a. Indicators

Table 2 sets outs the alternative measures of maternal mortality. The most common indicator is the maternal mortality ratio, which is a measure of obstetric risk – reflecting the probability of dying once pregnant. As such this indicator does not allow for the first of the two conditional probabilities implicit in maternal mortality, namely the probability of pregnancy. In the context of HIV/AIDS, where downward trends are now being observed in some populations in live birth rates (Zaba, and Gregson, 1998), an additional useful indicator is the maternal mortality rate (maternal deaths per 100,000 women aged 15-49). The maternal mortality ratio, on the other hand, uses live births as the denominator, and is ratio rather than a rate since the numerator of maternal deaths includes some cases unrelated to live births. It has been argued that this bias is compensated for by the expected underreporting in the numerator, especially amongst deaths in early pregnancy (AbouZahr, 1998). Given an increased risk of pregnancy wastage (i.e. losses before 24 weeks gestation) and stillbirths among women with HIV/AIDS (Brocklehurst and French, 1998), a denominator based on live births is an underestimate of the population at risk. This would lead to inflation of the maternal mortality ratio, as illustrated in Figure 1, and has implications for monitoring trends.

b. Use of estimation models

In view of the limited population-based sources in many developing countries, demographic estimation models for maternal mortality have been developed by WHO, UNICEF and UNFPA. The original model was developed in 1996 and used to generate estimates of the number of maternal deaths, maternal mortality ratio and lifetime risk for the year 1990. Panel 2 describes the model parameters used for the 1995 estimates and how these differ from the original version. The latest application is shortly to be released and will provide estimates for the year 2000. As can be seen from Panel 2, the estimation process encompasses two main levels of adjustment. For the estimates produced for 1995, 16% of the developing countries listed required only minor adjustments to the figures available. For 55 countries, the national estimate of maternal mortality was derived totally from the model. These estimates and indeed the modelling process have long been the subject of controversy (AbouZahr and Wardlaw, 2001). For example, the modelled figures for the maternal mortality ratio are considerably higher than official government estimates for a large number of countries.

Many of the countries regarded as having inadequate existing data and thus with maternal mortality estimates derived solely from the WHO/UNICEF/UNFPA model, are also those with some of the highest estimates of people living with HIV/AIDS. The models used to generate the 1990, 1995 and 2000 maternal mortality figures all rely on a regression approach to predicting the proportion of maternal deaths among females of reproductive age (PMDF). The independent variables, however, have varied over the years, with allowance for the possible impact of the HIV/AIDS epidemic on levels of adult female mortality, and thus the PMDF, made in the 1995 and 2000 models. Two other predictors may also be sensitive to a context with high prevalence of HIV/AIDS, namely the General Fertility Rate (GFR) and the proportion of deliveries with skilled personnel (health professionals -PDHP). Whilst the GFR may be depressed in such contexts, the effect on the latter is harder to predict. In some countries, like Malawi, the HIV/AIDS epidemic is having a direct impact on the number of professionals practising delivery care (Government of Malawi, 1999), and thus the PDHP would be expected to decline over time. On the other hand, the denominator of the number of deliveries may also fall, and/or as the epidemic advances, women and their families may place greater importance on skilled birth attendance. For both of these latter scenarios, the effect would be an increase in the PDHP. A recent analysis of this proportion derived from DHS data, however, shows essentially no progress at the national level for many countries in sub-Saharan Africa (AbouZahr and Wardlaw, 2001).

c. Interpretation of trends

One of the most important reasons for measuring maternal mortality is undoubtedly to monitor trends. This is true in all contexts but perhaps particularly where the devastating effects of the HIV/AIDS epidemic are now being faced. Unfortunately, however, maternal mortality data as well as relevant denominator data for trend analysis remain serious information gaps, at international and national levels. The Millennium Development Goals, for example, include indicators of maternal mortality and of HIV/AIDS (United Nations, 2000). The target set for the year 2015 for the former is a 75% reduction, and for the latter static or declining HIV prevalence rates in 15-24 year old pregnant women. As noted previously, many countries are solely dependent on modelled maternal mortality estimates. These, however, are stated specifically to be unsuitable for monitoring trends in the short term and for cross-country comparisons (WHO/UNICEF/UNFPA, 2001), owing to the wide margins of "uncertainty". For example, for 1995, the lower "uncertainty bound" for the maternal mortality ratio for was 230 per 100,000 live births and the upper bound 635. Whilst these boundaries are not confidence intervals in the strict statistical or probabilistic sense, they do give an indication of the magnitude of the possible errors involved. The wide uncertainty around single point estimates means that comparisons are complicated by overlapping limits. Even if the uncertainty boundaries were narrower, changes in the model parameters used to generate the 1990 and 1995 estimates invalidate trend assesment (WHO/UNICEF/UNFPA, 2001).

An alternative source of data proposed for examining trends in maternal mortality in selected developing countries is the DHS. As mentioned previously, the DHS now provide data from the sisterhood method for 55 countries, and for many of these the information is available for more than one point in time. However, this source suffers a similar difficulty to the WHO/UNICEF/UNFPA modelling approach in terms of wide margins of error ("true" confidence intervals) around the point estimates and thus overlapping confidence intervals. A further drawback is that the estimates are retrospective and this adds considerable complexity to the interpretation of temporal patterns, especially in the context of HIV/AIDS.

This complexity is particularly well-illustrated for the case of Malawi (Bicego, Boerma and Ronsmans, 2002). The 1992 and 2000 DHS in this country showed markedly different levels for the maternal mortality ratio of 620 per 100,000 live births (95% C.I. 410-830) and 1120 (95% C.I. 950-1288) respectively. Although the confidence intervals for these averaged estimates do not overlap and so suggest a statistically significant trend, the reference periods are broad being 1986 to 1992 for the first survey and 1994 to 2000 for the second. During both these periods there were upward trends, but of different magnitudes, in HIV prevalence as estimated from national antenatal clinic surveillance systems. Much of this prevalence data comes from urban areas. Disaggregation of the estimates for rural and urban samples shows narrow but slightly overlapping confidence intervals for the former. For urban areas, on the other hand, there is no overlap but owing to the small sample size, the interval for the estimate from the 2000 survey is extremely wide, with the upper figure being more than double the size of the lower. Moreover, as these data are based on the sisterhood method, they refer to the place of residence of the sibling respondent rather than the woman who died, and this compromises rural-urban analysis. These findings undoubtedly make for both complicated and disappointing reading for safe motherhood programme managers and policy-makers in Malawi. Unfortunately further analysis at a regional level, and particularly for the Southern Region which has seen the delivery of a major safe motherhood project since 1998 (Hussein and others, 2001), is not only limited by the problem of siblings' residence but also by the sample size available from the DHS.

D. INTERNATIONAL PATTERNS OF MATERNAL MORTALITY AND HIV/AIDS

The preceding sections have highlighted a wide range of factors affecting the availability and reliability of maternal mortality data at national and international levels. Clearly, a similar degree of caution is needed regarding HIV/AIDS data, especially in sub-Saharan Africa (Buve, Bishikwabo-Nsarhaza, and Mutangagura, 2002; Morrison, 2001). What is also common to both outcomes is the difficulty of gauging the relative importance of potential biases in specific country contexts and on a population basis.

Figures 3 and 4 give a tentative snap shot of the global and regional picture for maternal mortality. It can be seen that the latest figures for reproductive health from the Global Burden of Disease (GBD) suggest that HIV/AIDS now makes the greatest contribution to the burden to females beyond the perinatal period (WHO, 2003). More than 55% of individuals living with HIV/AIDS are women (Morrison, 2001). "Maternal conditions" feature second in the GBD data, but this only includes direct obstetric problems, thus ignoring the burden of indirect obstetric conditions, including HIV/AIDS. The unpublished preliminary number of maternal deaths from modelling for the year 2000 is now estimated at 530,000 for the world (WHO, 2003), an increase on the figures estimated for 1995 of 515,000. Significantly and for the first time, the modelled number of maternal deaths for the Africa Region now exceeds that for Asia, despite the latter's considerably larger population (Figure 4). This reflects the much higher estimated maternal mortality ratio for Africa of 836 per 100, 000 live births versus 327 for Asia. Turning to the national picture, it is necessary to revert to the modelled estimates for 1995, since the 2000 figures are still unavailable. As can be seen in Table 3, globally, just six countries are estimated to account for just over half of the annual number of maternal deaths. The three African countries also report high prevalence of HIV among adults.

E. RESEARCH AND DEVELOPMENT NEEDS

Despite almost two decades of heightened awareness of the challenge to global health presented by maternal mortality and by HIV/AIDS, there remain serious gaps in knowledge regarding the nature and the significance of their interrelationship. In part this reflects the serious difficulties of measuring both outcomes, particularly on a population basis and in settings with limited information systems. This has major implications for individual developing countries seeking to monitor progress, as well as for the international community and its Millennium Development Goals. Given the geographical concentration of maternal mortality and HIV/AIDS, especially in sub-Saharan Africa, there is much to be gained from improved understanding of the synergy. Given the two distinct sides or facets to this interrelationship, it is hard to differentiate between a change in the level of maternal mortality owing to a genuine increase or decrease in risk from a change that is an artefact of measurement. Research and development must therefore proceed on both facets.

a. Effects of HIV/AIDS on the risk of maternal death

- Opportunities should be identified, such as alongside research on MTCT, for rigorously assessing the impact of pregnancy and childbirth on HIV disease progression, and of HIV/AIDS on pregnancy loss and obstetric complications
- Effects of HIV/AIDS on levels of maternal mortality under varying parameters, such as fertility decline, should be explored using adaptations of current forecasting models
- Population-based and health services data are needed to assess the direction and scale of effects of HIV/AIDS on provision, quality and uptake of maternal health services, such as skilled attendance at delivery
- Rigorous evaluation is needed of the effectiveness and cost-effectiveness of alternative safe motherhood intervention strategies in the presence of HIV/AIDS
- Studies are required to explore the relationship between the HIV/AIDS and poverty, and the consequent effects on maternal mortality
- Evidence should be gathered on shifts in the relative contribution of direct and indirect obstetric causes to maternal deaths in the presence of HIV/AIDS, and on the validity of using indirect deaths as a marker of the contribution of HIV/AIDS to maternal mortality.

b. Effects of HIV/AIDS on the measurement of maternal mortality

- Qualitative research is needed on the biases in reporting of female reproductive-age mortality in different HIV/AIDS scenarios
- Studies are needed into the consequences of HIV/AIDS-related mobility for estimating maternal mortality for defined geographical regions, especially using the sisterhood method
- Modelling methods or sensitivity analysis should be developed to assess the balance of changes in the numerator and/or denominator for maternal mortality indicators according to different HIV/AIDS scenarios
- Assessments are needed of the feasibility and utility of routine sources distinguishing between direct and indirect maternal deaths
- Opportunities should be sought for integrating the measurement of maternal mortality into programmes seeking to reduce MTCT
- Existing tools and methods for measuring maternal mortality, such as verbal autopsy techniques and RAMOS, need to be reassessed for their validity, reliability and feasibility in the context of HIV/AIDS, and appropriate enhancements sought.

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The authors are employees of the University of Aberdeen, and work on the Initiative for Maternal Mortality Programme Assessment - IMMPACT (www.abdn.ac.uk/immpact).

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TABLE 1. ILLUSTRATIVE SAMPLE SIZE REQUIREMENTS FOR ESTIMATING MATERNAL MORTALITY[1]

Measure	Expected magnitude (annual rates)	Births needed[2]	Population[3] and households[4] needed
Maternal mortality ratio: direct estimation (household-based)	500 deaths per 100, 000 live births	53,087	1, 516, 772 252, 796
Maternal mortality ratio: direct estimation (sisters-based)	500 deaths per 100, 000 live births	53, 087	235,953 117,972
Maternal mortality rate	75 deaths per 100, 000 women aged 15-49	53, 087	1, 516, 772 252, 796
Cause-specific mortality rate: e.g. haemorrhage	20 deaths per 100, 000 women aged 15-49	200, 035	5, 715, 286 444, 523

TABLE 2. PRINCIPAL MEASURES OF MATERNAL MORTALITY

Measure	Formula[5]
No. of case	No. of maternal deaths in defined population
Maternal mortality ratio	(Maternal deaths in a period) ÷ (Live births in same period)[6]
Maternal mortality rate	(Maternal deaths in a period) ÷ (Reproductive age woman-years at risk)
Lifetime risk	(Maternal deaths over the reproductive period) ÷ (Women entering reproductive period)
Proportionate mortality ratio	(Maternal deaths in a period) ÷ (Deaths to women aged 15-49 in same period)
Percentage of maternal death due to specific cause	(Maternal deaths in a period owing specific cause) ÷ (Maternal deaths in same period)

[1] Assuming desired relative precision of 12% and 95% confidence intervals
[2] Assuming General Fertility Rate of 150 per 1000 women aged 15-49
[3] Assuming Crude Birth Rate of 35 per 1000 population
[4] Assuming 6 persons per household
[5] Formulae all relate to "a defined population"
[6] Usually expressed per 100,000

TABLE 3. COUNTRIES CONTRIBUTING THE LARGEST ESTIMATED NUMBER OF MATERNAL DEATHS (1995 [1]) AND INDICATORS OF HIV/AIDS PROFILE

Country	**No. of maternal deaths**	**% of global total**	**Estimated maternal mortality ratio (deaths per 100,000 live births)**	**Prevalence (%) of HIV among adults 15-49** [2] (1999-2001)	**Prevalence of HIV among ANC attenders in major urban areas** [3] (1999-2001)
India	110,000	21	440	0.8	2.0
Ethiopia	46,000	9	1,800	6.4	14.9
Nigeria	45,000	9	1,100	5.8	4.2
Indonesia	22,000	4	470	0.1	-
Bangladesh	20,000	4	600	0.1	-
Congo (DR)	20,000	4	940	4.9	4.1
Sub-total	263,000	51	-	-	-
World	515,000	100	400	-	-
Industrialised	2,800	5	21	-	-
Developing	512,000	95	440	-	-
Least developed	230,000	-	1,000	-	-

Source:

1 WHO/UNICEF/UNFPA (2001)

2 www.milleniumindicators.org

3 www.unaids.org/barcelona/presskit/embargo.htm

PANEL 1 INTERNATIONAL CLASSIFICATION OF MATERNAL DEATHS (ICD 10)

Maternal death: the death of a woman while pregnant or within 42 days of the termination of pregnancy, irrespective of the duration or site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.

> **Direct obstetric death:** the death of a woman resulting from obstetric complications of the pregnancy state (pregnancy, labour and puerperium), from interventions, omissions, incorrect treatment, or from a chain of events resulting from any of the above.
>
> **Indirect obstetric death**: the death of a woman resulting from previous existing disease, or disease that developed during pregnancy and which were not due to direct obstetric causes, but were aggravated by the physiological effects of pregnancy.
>
> **Incidental death:** the death of a woman from unrelated causes which happen to occur in pregnancy or the puerperium

Late maternal death: death of a woman from direct or indirect obstetric causes more than 42 days but less than one year after termination of pregnancy.

Pregnancy-related death: death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the cause of death.

PANEL 2 ESTIMATES OF MATERNAL MORTALITY DEVELOPED BY WHO, UNICEF AND UNFPA

The estimation process for the 1990 and 1995 figures used a dual strategy:

- Adjusting nationally reported data using specific criteria
- Generating model-based estimates for countries with no data.

A robust regression model was developed to predict the key dependent variable – the proportion of maternal deaths among al deaths to women of reproductive age (PMDF). The model was fitted to 73 contemporary observations, including 30 from developed or transitional countries.

The parameters in the 1995 model were:

- General Fertility Rate
- Proportion of deliveries with skilled health workers
- Regional dummy variables (one for former socialist economies, and one for countries in Latin America and the Caribbean, sub-Saharan Africa and the Middle East)
- Degree of completeness of vital registration
- HIV prevalence in adults.

The 1990 model differed primarily in terms of not including an independent variable for HIV.

For each country without data, the regression model was used to predict the PMDF, and the prediction then applied to the UN population projection 1995 figure for deaths to females of reproductive age. The maternal mortality ratio was then obtained by dividing the derived number of maternal deaths bv an estimate of the number of births in 1995.

Source: WHO/UNICEF/UNFPA, 2001

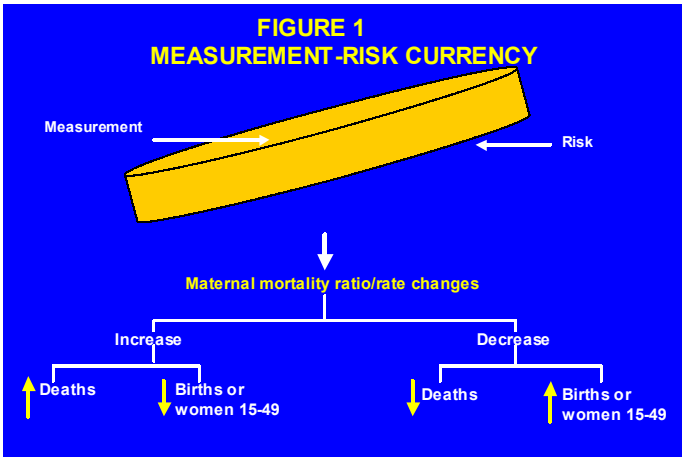
FIGURE 1
MEASUREMENT-RISK CURRENCY
Measurement
Risk
Maternal mortality ratio/rate changes
Increase
Decrease
Deaths
Births or women 15-49
Deaths
Births or women 15-49

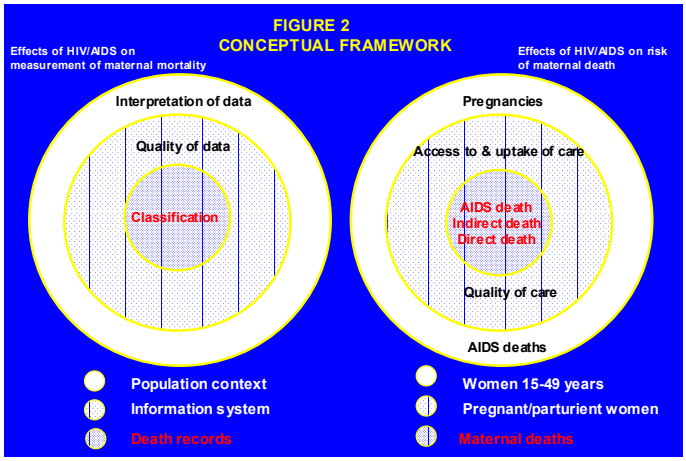
FIGURE 2
CONCEPTUAL FRAMEWORK
Effects of HIV/AIDS on measurement of maternal mortality
Effects of HIV/AIDS on risk of maternal death
Interpretation of data
Quality of data
Classification
Pregnancies
Access to & uptake of care
AIDS death
Indirect death
Direct death
Quality of care
AIDS deaths
Population context
Information system
Death records
Women 15-49 years
Pregnant/parturient women
Maternal deaths

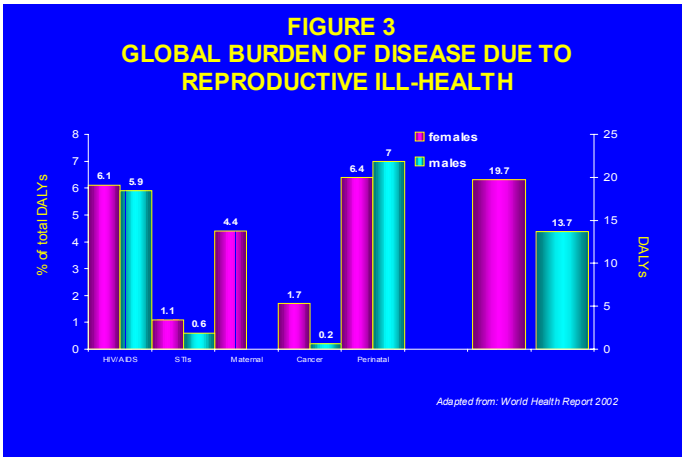
FIGURE 3
GLOBAL BURDEN OF DISEASE DUE TO REPRODUCTIVE ILL-HEALTH
females
males
% of total DALYs
DALYs
6.1
5.9
1.1
0.6
4.4
1.7
0.2
6.4
7
19.7
13.7
HIV/AIDS
STIs
Maternal
Cancer
Perinatal
Adapted from: World Health Report 2002

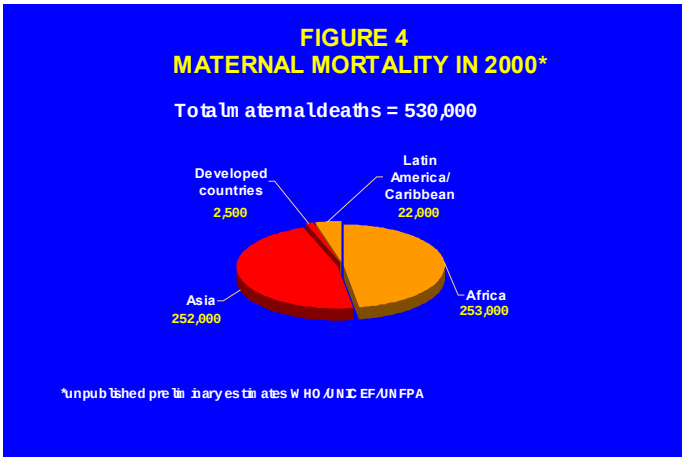
FIGURE 4
MATERNAL MORTALITY IN 2000*
Total maternal deaths = 530,000
Developed countries
2,500
Latin America/ Caribbean
22,000
Asia
252,000
Africa
253,000
*unpublished preliminary estimates WHO/UNICEF/UNFPA