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Session 50: "Determinants and trends in maternal mortality"
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Case definition of maternal mortality and estimates of MMR in Africa with special reference to the Agincourt DSS

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Abstract

Much confusion arose in the estimates of maternal mortality ratios (MMR) in developing countries because of a lack of rigor in the case definition. Most demographic surveys do not apply the WHO definition of maternal deaths, itself confusing because of the ambiguity of the concept of indirect causes of maternal death. Based on empirical evidence from South-Africa, and in particular from the Agincourt DSS, the paper shows the discrepancies between estimates based solely on 'obstetric causes', those including 'indirect causes' (WHO definition) and total 'pregnancy-related deaths' the most common definition used in demographic surveys. The paper also proposes a method to convert 'pregnancy related mortality ratio' into 'obstetric mortality ratio' taking into account the prevalence of HIV in the female adult population. Applying a consistent case definition is necessary to monitor mortality trends and to assess progresses towards Millenium Development Goal No 5.

Key Words: Maternal Mortality; Obstetric deaths; Pregnancy-related deaths; Case definition; MDG-5; Sub-Saharan Africa; South-Africa; Agincourt.

Introduction

Maternal mortality is one of the most sensitive indicators of the health transition. When life expectancy rises from low levels (say < 40 years) to high levels (say > 80 years), values of the maternal mortality ratio (MMR) decline from very high values (around 1000 maternal deaths per 100,000 live births) to below 10 per 100,000. A ratio of 1 to 100 or more is unique among the classic mortality indicators, which makes it very sensitive for assessing health problems and measuring progresses achieved by health policies and programs. For instance, in Sweden, maternal mortality was about 900 per 100,000 in 1751-1800, and was only 3 per 100,000 in 2001-2006. [Högberg & Wall, 1986; Högberg, 2004] Similar changes were observed in England and Wales, and in most developed countries for which data are available [Loudon, 1986 & 2000]. Note that during the process of the health transition, maternal mortality declines faster than mortality of women age 15-49, so that the proportion of maternal deaths among deaths of women in their reproductive ages declines, from say 15% to 25% at very high levels of mortality become less than 1% at very low levels. We will see that these values, typical of mortality changes in developed countries, are totally different in today's sub-Saharan Africa, for a number of reasons, in particular lack of clear case definition, and interference with emerging diseases, in particular HIV/AIDS.

Case definitions of maternal mortality

Several case definitions are used for defining maternal mortality, and their use is not consistent across countries and over time. [Hoyert 2007] The definitions relate either to the underlying cause of death, or to the timing of the death, or a combination of both. The timing of the death refers to the pregnancy, the delivery, and the post-partum period, that is the 42 days after delivery. This period is referred as the "maternal risk period" in this paper.

- The obstetric definition (direct causes): these include well defined causes of death, listed under the codes "O00 to O95" in the 10th revision of the International Classification of Diseases (ICD-10). Sometimes one adds the deaths from obstetric causes and their consequences occurring after the post-partum period, coded "O96" to "O97" in the ICD-10.
- The WHO definition (direct and indirect causes): these include the previous category and the so-called "indirect causes", which are infectious diseases and non-communicable diseases

assumed to be complicated by the pregnancy, coded "O98" to "O99" in the ICD-10. Including a disease such as tuberculosis, syphilis, hepatitis or other infectious and parasitic disease, or diseases such as anaemia, cardio-vascular disease or other non-communicable disease, is a matter of judgment by persons who code the cause of death, and is usually not based on epidemiological evidence of increased mortality risk. Note that some critical diseases are not included in this list of indirect causes, such as HIV/AIDS or diabetes mellitus.

- The demographic definition (pregnancy-related deaths): these include any death during the maternal risk period, irrespective of the cause, that is direct causes, indirect causes, and fortuitous causes, and include in particular external causes (accident and violence).

Other persons use also different definitions. For instance, the Health Metrics Network group proposed to include HIV deaths as well as late maternal deaths. [Hogan et al. 2010] Others have proposed to include potentially misclassified causes, such as intravascular coagulation (D65), peritonitis (K65), septicaemia (A41, A42), pulmonary embolism (I26), acute and chronic renal failure (N18 and N19), acute abdomen (R10), and hypovolaemic shock (R57.1).

In European long term time series, maternal mortality is defined primarily as obstetric deaths, which are conditions directly caused by the pregnancy, the delivery and their consequences. In fact, late maternal deaths and indirect causes were added only at time the ICD-9 was adopted, in the late 1970's. In African censuses and surveys, the last definition (pregnancy-related deaths) is the most commonly used, since most data come from demographic censuses and surveys, in particular from DHS surveys. We will show in this paper that the choice of the case definition has a considerable impact on the estimates of MMR, and on trends in MMR.

The health transition has been quite smooth in Europe and other developed countries, so that most cause specific death rates declined simultaneously outside of war periods, and with only a few exception, such as car accidents in the 1950's, breast and lung cancer at some times, and a few others, but without much consequences for the mortality of women age 15-49. Consequently, the series of the proportions of maternal deaths among deaths of women in their reproductive ages are also smooth, and declining steadily over time.

This is not the case in Africa, where numerous health problems are interfering with trends towards lower mortality. Among the leading causes of increasing mortality are HIV/AIDS, tuberculosis, malaria in countries with major resistance to antimalarial drugs, and in some cases car accidents and violence. In these cases one could face a declining obstetric

mortality while rising pregnancy-related mortality, with large consequences for the proportion of maternal deaths among deaths of women in their reproductive ages.

Maternal mortality in South Africa

To illustrate the complexity of these dynamics, and the new patterns emerging in developing countries, we will focus on maternal mortality in South Africa, a country with features of very advanced country, together with features of health problems of developing countries. In recent years, South Africa had a very with high mortality for young adults, and in particular from selected infectious diseases (HIV/AIDS and tuberculosis), from selected non-communicable disease (cancers of the female genital track), and from external causes (accidents, homicide, suicide). All these features are markedly different from any historical record in Europe and other developed countries, have their own dynamics, and deserve a thorough investigation.

Maternal mortality in the censuses of South Africa

We estimated pregnancy-related mortality from the 2001 census and the 2007 community survey conducted in South-Africa. Details of the studies are published elsewhere [Garenne et al. 2009, 2011] In brief, the pregnancy-related MMR was estimated from questions on deaths in the previous 12 months, and for women age 15-49 based on the question whether the death occurred during pregnancy, delivery or within 6 weeks after delivery. Data were found of high quality, and only the 2001 estimates needed some adjustment for missing values. Results produced very high values of the pregnancy-related MMR, with a rising trend: 542 per 100,000 in 2001, and 702 in 2007. These high values were found to be outstanding when compared with estimates based on obstetric deaths, to a point where one could question their reliability. The answer is that the two series appear consistent: the obstetric deaths account only for a small- and declining- fraction of the pregnancy related deaths, simply because the indirect and fortuitous causes are extremely high and increasing. This excess is mostly due to the high death rates from HIV/AIDS, tuberculosis, accidents and violence. We will see below that these data match well the Agincourt data set, where both types of information are available. In turn, the proportion of pregnancy related deaths among deaths of women 15-49 was abnormally low at this level of mortality, and declining while MMR was rising (6.4% in 2001 and 4.3% in 2007). Again this could be explained by the fast

rise in HIV/AIDS mortality during this period. These values are likely to change again in the future, since HIV/AIDS mortality is now declining fast, because of the massive use of Highly-Active Anti-Retroviral Therapies (HAART).

Maternal mortality in the vital registration of South Africa and in the confidential inquiry

The vital registration of South Africa is nearly complete for young adults since year 2000. Causes of death are available for the 1997-2007 period. We selected year 2006 for comparison with the 2007 Community Survey. After imputation of missing values, these data indicate that 1.1% of deaths of women age 15-49 are due to obstetric causes, and 4.3% are pregnancy-related deaths. This leads to an obstetric MMR of 183 per 100,000, and a pregnancy-related MMR of 724 per 100,000, values again roughly consistent with those of the census. Note that the uncertainty on the total number of births in 2006 is about +/- 15% if one compares registered births (0.860 million) with estimates from the 2007 community survey (1.002 million) and with official estimates obtained with the Spectrum projection model (1.131 million). This uncertainty translates into that of the MMR, obtained by dividing total maternal deaths by the number of births.

Maternal mortality in the Agincourt DSS

The Agincourt DSS is a demographic surveillance system covering a population of about 75,000 persons located in the Mpumalanga province, near the Mozambican border. The population is rural, and has been followed since 1992. [Kahn et al. 1999; 2000; 2007a; 2007b: Tollman 1994; Tollman et al. 1999; Tollman & Kahn 2007; Weiner et al. 2007] Death registration is virtually complete, and causes of death are investigated by verbal autopsies. For women who died at age 15-49 one could distinguish between those who died during the maternal risk period (pregnancy-related deaths), those who died of obstetric causes (O00-O95 in the ICD-10), those who died of selected indirect causes, and those who died of HIV/AIDS.

Preliminary findings based on the last census-round conducted in 2010 indicate a moderate level of obstetric mortality (209 per 100,000), and a high level of pregnancy-related deaths (508 per 100,000), a ratio of 1 to 2.5. (Table 2 and 3) These numbers were obtained after imputing missing values of causes of death using a hot-deck procedure stratified on age at death. Tables 2 and 3 provide the range of estimates based on the case definition, and whether or not imputation of missing values was done. Imputing missing values adds some

17% to the obstetric MMR and 30% to the pregnancy-related MMR. Including selected indirect cause adds 40%, and including HIV/AIDS an additional 20%. This gives an order of magnitude on the uncertainty of estimates of MMR only based on the case definition and completeness of the information. To these variations, one should add the statistical variations due to the small number of cases. The 95% confidence interval for the obstetric MMR is 165-265 per 100,000, and that of the pregnancy-related MMR is 435-590 per 100,000.

More important, the trends in the two extreme estimates were totally different. (Figures 1 and 2) The obstetric MMR did not show any significant trend over time during the 1992-2010 period, and fluctuated around the mean value of 209 per 100,000, with some large fluctuations which could be explained by small sample size and variations in missing values. In contrast, the pregnancy-related MMR increased markedly during the rising phase of the HIV/AIDS epidemic, from 1996 to 2006, and then declined, as did overall mortality of women aged 15-49 years. As a result, the proportion of deaths due to obstetric deaths also fluctuated, from 9.6% at baseline to 2.4% at endpoint. These fluctuations do not mimic trends in safe motherhood, but simply trends in HIV/AIDS mortality.

Relationship between obstetric mortality and pregnancy-related deaths

In a recent paper, we tried to estimate the obstetric MMR from data on pregnancy related mortality based on DHS surveys conducted in Africa. [Garenne, 2011] This follows the work conducted by Stecklov in Latin America [Stecklov, 1995] The rationale of the method is to apply the relative risk of death from causes other than obstetric death to estimate the indirect and fortuitous causes that occurred during the maternal risk period. Results of this exercise indicate that, in the current situation of Africa, obstetric deaths account for about half of the pregnancy related deaths, with major variations from 20% to 80%.

Discussion

Levels and trends in maternal mortality have raised numerous debates over the years, and became again a hot issue because the MMR is the indicator on the 5th Millenium Development Goal (MDG-5). The debates have become even more confusing in the recent years because different estimates are produced by various international agencies, which are discordant, and sometimes far away from national estimates. [Hogan et al. 2010; Garenne & McCaa 2010] Parts of the discrepancies are due to differences in case definition of maternal

mortality, parts are due to whether or not original data are corrected (for missing values, for under-count of death registration), and parts are due to random fluctuations.

The impressive declining trends documented in Sweden, in the United Kingdom, in the United States over one or two centuries, were possible because of a steady mortality decline, and because of a quasi-stable case-definition. The situation of today's sub-Saharan Africa is totally different: very large fluctuations in adult mortality, with fast ups and downs, and great variety in case definition and in data sources. Needless to say that consistent measurement tools and consistent case definition are required for assessing properly trends in maternal mortality. The wide variations of the MMR associated with case definition, missing values and random fluctuations hamper any stable estimate of maternal mortality levels and trends. Only consistent case definition, consistent source of data and quality of the data will allow one to estimate trends with some reliability.

In order to focus on safe motherhood and to monitor progress in MDG-5, demographers will have to change their paradigm, and to try estimating obstetric mortality instead of pregnancy-related deaths. [Rosenfield & Maine, 1985; Starrs, 2006] Numerous demographic techniques have been developed over the years, but they do not address properly the issue of the case definition. [Cross & Graham, 2010; Graham et al. 2008; Hill et al. 2007; Ronsmans, 2006; Stanton et al. 2001 ; Yazbeck, 2007] Solving this problem requires assessing causes of death in demographic censuses and surveys. In absence of proper death registration with medically certified causes, this implies some kind of verbal autopsy, if not full-scale verbal autopsy. This is the price to pay to properly assess progress in safe motherhood.

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Table 1: Estimates of MMR in South Africa, national level

Source, and case definition	MMR Raw data (per 100,000)	MMR After imputation	Percent of deaths among women 15-49
Censuses (pregnancy-related)			
- Census, 2001	418	542	6.4%
- Community Survey, 2007		705	4.3%
Vital registration, 2006			
- Obstetric	160	183	1.1%
- Pregnancy related	271	724	4.3%

Source: Garenne et al. 2009, 2011.

Table 2 Estimates of MMR according to case definition, Agincourt, South Africa, 1992-2010

Case definition	Number of deaths	MMR, per 100,000	95% confidence interval
Obstetric deaths	59	181	140 234
WHO definition	82	252	203 313
Including AIDS	107	328	272 397
Pregnancy-related deaths	127	358	328 464

Note: Raw data, before imputation of missing values. WHO definition includes indirect causes: infectious diseases (15) and non-communicable diseases (8). Others include external causes (3), and unknown (17).

Table 3: Estimates of MMR according to case definition and missing cases, Agincourt, South Africa, 1992-2010

	Obstetric cause		Pregnancy related death	
Period	Raw data	Imputation	Raw data	Imputation
Baseline 1992-1994	172	193	301	365
Peak 2005-2006	265	292	584	637
End-point 2009-2010	199	212	454	596

Note: Raw data defined from probable causes obtained by verbal autopsies; Imputation includes unknown causes, imputed by hot-deck procedure.

Figure 1: Trends in pregnancy-related mortality, Agincourt 1992-2010

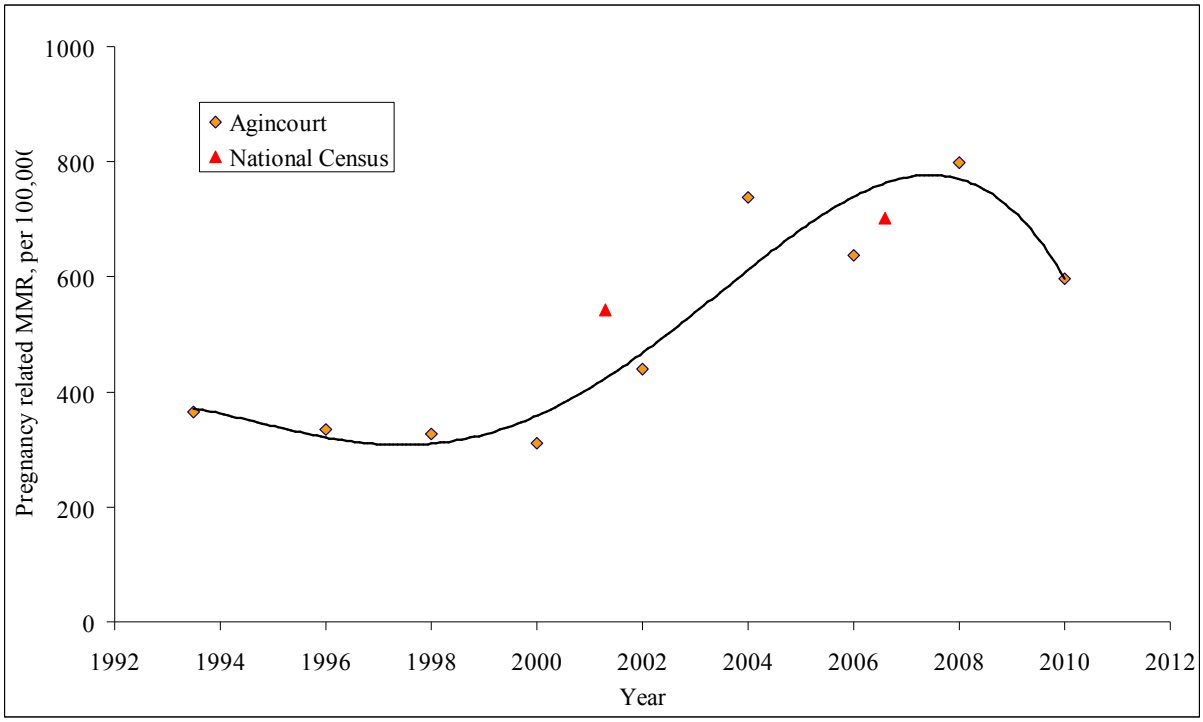
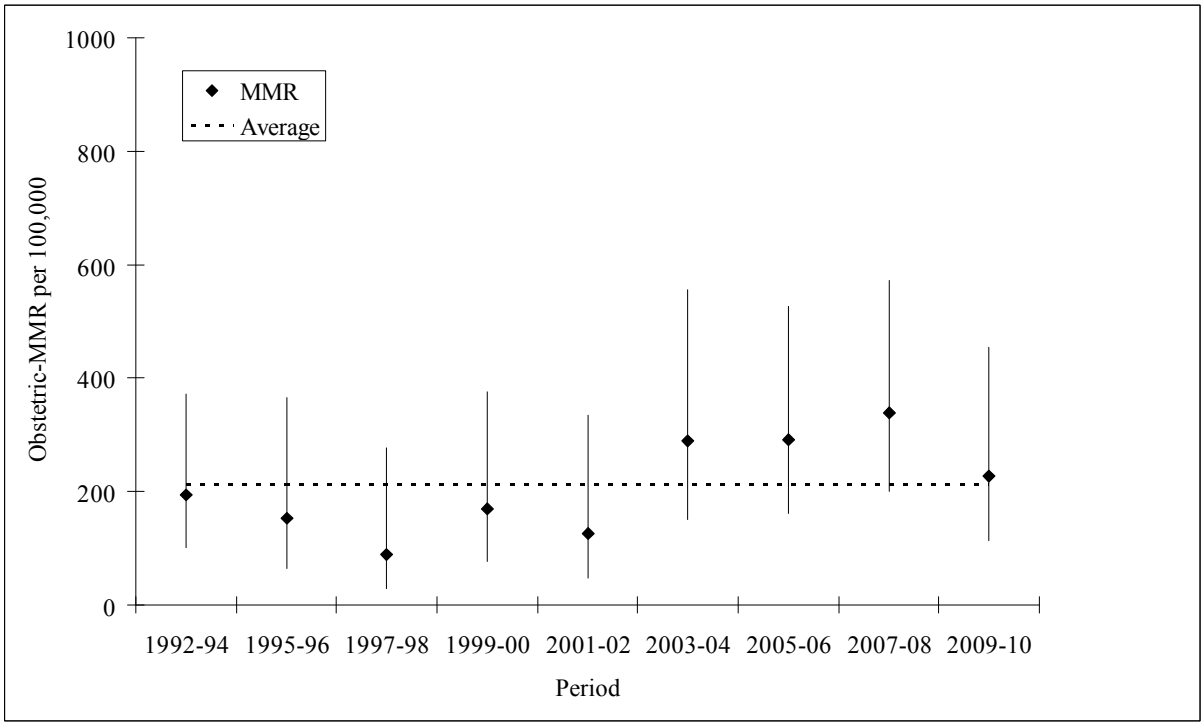


Figure 1: Trends in Obstetric mortality, Agincourt 1992-2010



Résumé en français

L'absence de définition rigoureuse cause beaucoup de confusion dans les estimations des niveaux et tendances de la mortalité maternelle dans les pays en développement. La plupart des enquêtes démographiques n'appliquent pas la définition de l'OMS, qui elle-même est confuse car elle est repose sur une ambigüité, celle du concept de cause indirecte mortalité maternelle. Cette communication part de données empiriques d'Afrique du Sud : données des recensements, de l'Etat Civil et de l'observatoire de population d'Agincourt, pour montrer les divergences entre les estimations basées sur des définitions différentes. On oppose en particulier les causes directes (obstétricales), les causes indirectes, et les décès qui se produisent au cours de la période du risque maternel (décès liés à la grossesse), qui est la définition la plus courante dans les enquêtes démographiques. La communication évoque aussi une méthode qui permet de convertir les décès maternels au sens démographique en décès obstétricaux. Cette méthode tient compte de la fécondité, de la mortalité des autres causes et de la prévalence du VIH dans la population féminine adulte. L'application stricte d'une définition spécifique sera nécessaire pour évaluer correctement les tendances de la mortalité maternelle, et pour mesurer les progrès pour la réalisation du cinquième objectif du millénaire (MDG-5).