

# Global burden of maternal sepsis in the year 2000

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World Health Organization,  
Geneva, July 2003

## 1. Introduction

Historically, puerperal sepsis has been a common pregnancy-related condition, which could eventually lead to obstetric shock or even death. During the 19<sup>th</sup> century, it took on epidemic proportions, particularly when home delivery practice changed to delivery in lying-in hospitals, as there still was a total ignorance of asepsis. In 1843 Oliver Holmes in Boston, USA, was the first to establish that puerperal fever was contagious and was carried by the unwashed hands of the physician from bed to bed. In 1847 Semmelweis in Vienna, Austria also concluded that examiners might transmit infection from live patients as well as from the dead and ordered his students to scrub with the chlorine solution before every physical examination. This led to a striking decrease of mortality due to puerperal sepsis from 11% in 1846 to 3% in 1847<sup>1</sup>.

With the introduction of antibiotics puerperal fever declined further in developed countries. Today though, nosocomial infections, particularly for operative deliveries, and increasing antibiotics resistance is regularly noted<sup>2</sup>. Puerperal sepsis is still prevalent in developing countries and continues to present a significant risk of obstetric morbidity and mortality to women in these regions<sup>2</sup>.

Puerperal infection is a general term used to describe any infection of the genital tract after delivery. Because most temperature elevation in the puerperium is caused by pelvic infections, the incidence of fever after childbirth may be a reliable index of their incidence and several definitions have been based on the degree of pyrexia. The major consequences of puerperal infections are chronic or acute pelvic inflammatory disease, bilateral tubal occlusion and infertility.

Maternal sepsis ranked 46<sup>th</sup> in terms of DALYs in GBD 1990 and its burden accounted for 18% of total burden for maternal conditions. Estimated deaths due to puerperal sepsis accounted for 15% of all maternal deaths in GBD 1990. This draft paper summarizes the data and methods used to produce the Version 2 estimates of maternal sepsis burden for the year 2000.

## 2. Case and sequelae definitions

A WHO technical working group on The Prevention and Management of Puerperal (1995) infections proposed in 1992 the following definition of **puerperal sepsis**<sup>3</sup>:

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<sup>1</sup> Epidemiology and Burden of Disease WHO Geneva (EBD/GPE)

- Infection of the genital tract occurring at any time between the rupture of membranes or labour, and the 42nd day postpartum in which 2 or more of the following are present:
  - Pelvic pain
  - Fever i.e. oral temperature 38.5°C or higher on any occasion
  - Abnormal vaginal discharge, e.g. presence of pus
  - Abnormal smell/foul odour of discharge
  - Delay in the rate of reduction of the size of the uterus (<2cm/day during the first 8 days)

On the same occasion, the WHO Technical Working group considered that **puerperal infections** is a more general term than puerperal sepsis and includes not only infections due to sepsis, but also all extra-genital infections and incidental infections:

1. Infections of the genito-urinary system related to labour, delivery and the puerperium:
  - Infections related to the uterus and its associated structures (endometritis)
  - Infections related to the urinary tract
2. Infections specifically related to the births process but not of the genito-urinary system, e.g. breast abscess
3. Incidental infections, e.g. malaria, respiratory tract infections

Table 2.2 lists the definitions used by GBD 2000.

**Table 2.2 GBD 2000 case and sequelae definitions for maternal sepsis**

Cause category	GBD 2000 Code	ICD 9 codes	ICD 10 codes
Maternal sepsis	U044	670, 672, 675	O85, O86
Sequela	Definition		
Episodes	Major puerperal infection, <b>excluding</b> infection following abortion, minor genital and urinary tract infection following delivery and mastitis.		
Infertility	Failure to conceive again following puerperal sepsis		

### 3. Population prevalence and incidence studies

Appropriate epidemiological studies were identified by a MEDLINE and PubMed search, using the key words 'sepsis', 'pregnancy complications', 'incidence', and 'epidemiology' and by tracking references from the papers identified in this way; in addition, we examined regional offices literature databases and statistics, performed a key word search of major obstetric and gynaecology journals and consulted with experts for unpublished work.

#### 3.1 Incidence

As with other obstetric morbidities, the definitions of puerperal sepsis vary from one study to another, which makes their comparability difficult. Moreover, hospital-based studies are not a reliable source of data for developing countries, because many women do not have access to health facilities, for many reasons: geographical distance, financial constraints, cultural beliefs – sometimes

they have to ask permission from their husbands to go to hospital, thus the population delivering in hospitals may not be representative for the general obstetric population.

Self-reported maternal morbidity tends to over-estimate the incidence of conditions under study, and the results very much depend on the sensitivity and specificity of the instrument. Several attempts have been made to validate the results of self-reported maternal morbidity, and some of them compared the results from interviewing women shortly after hospital-delivery with hospital-case notes. Table 3.1 presents the sensitivity and specificity of post-partum infection as recalled and reported to interviewers in these studies. Comparisons are difficult, as studies may have used different definitions and study design, and their results may not be generalised to the population who does not deliver in hospital. Thus, self-reported maternal morbidity cannot be used to provide accurate estimates of prevalence and incidence. However, until a more comprehensive data collection on all deliveries, especially in developing world, will become feasible, self-reports in response to well designed and well-worded interviews may be the only way to collect information about maternal morbidity<sup>4</sup>.

**Table 3.1. Sensitivity and specificity of puerperal sepsis as recalled and reported to interviewers**

	Philippines 1995 <sup>5</sup>	Bolivia 1998 <sup>6</sup>	Ghana 1996 <sup>7</sup>	Indonesia 1997 <sup>8</sup>
Questions	“very high fever postpartum”	“presence of infection”		“high fever postpartum”
Sensitivity	0.56	not calculated (too few cases)	0.25	NA
Specificity	0.93	0.99	0.99	0.86

*Adapted from ref4*

Another problem may be that most postpartum infections take place after hospital discharge, which is usually 24 hours after delivery. Therefore, in the absence of postnatal follow-up, as is the case in many developing countries, many cases of puerperal infections can go undiagnosed and unreported<sup>2</sup>. Table 3.2 summarizes the results from studies on puerperal sepsis, emphasizing the variability of puerperal sepsis incidence according to the definition used.

**Table 3.2. Incidence studies for maternal sepsis**

Region	Study population	Type of study	Years	Sample size	Diagnostic criteria	Incidence per 100 live births	Ref.
<b>AFRO D</b>							
Nigeria	Ife State hospital, <i>Ile-Ife</i>	retrospective hospital based	1986-1995	8428 deliveries	Fever >38°C, persistent abdominal pain, sub-involution of the uterus, foul-smelling vaginal discharge, and septic wounds of genital tract	1.7	9
Senegal	2 urban areas (Saint Louis and Kaolack)	population-based study on a cohort of pregnant women	1996	3476 live births	peritonitis, septicaemia or foul-vaginal discharge, leading to hospitalisation, hysterectomy or death	0.23	10
Niger	Niamey, 6 maternity wards	maternity wards-based, longitudinal	1997	3625 deliveries	Puerperal infection	0.22	11
Burkina Faso, Mali, Mauritania, Niger, Senegal, Cote d'Ivoire*	Ouagadougou, Bamako, Nouakchott, Niamey, Kaolack region, Abidjan*	population-based, multicentre; door-to-door census of all pregnant women	Dec 1994-June 1996	20326 women; 19694 lb	septicaemia, peritonitis, odorous vaginal discharge, leading to hospitalisation in the interest of the mother's safety, or to hysterectomy or death	0.09 (0.05-0.14)	12
<b>AFRO E</b>							
South Africa	Kalafong and Pretoria Academic hospitals	prospective descriptive multicentre study: audit of maternal near miss (daily case notes review)	Sept 1996 - Aug 1997	13429 deliveries	near miss: a woman with severe organ dysfunction or organ failure during pregnancy or within 6 weeks after delivery	0.07	13
Uganda	Mulago hospital	cross-sectional hospital based	Mar-Aug 1997	9043 deliveries	puerperal infection	1.14	14
<b>AMRO A</b>							
USA	Parkland Hospital, Texas	RCT to evaluate the influence of heparin on septic thrombophlebitis	1996-1998	44922 pregnant women	prolonged infection: fever and pelvic infection that persisted 5 days despite antibiotic treatment; pelvic thrombophlebitis:	0.15	15

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**Table 3.2 (continued). Incidence studies for maternal sepsis**

Region	Study population	Type of study	Years	Sample size	Diagnostic criteria	Incidence per 100 live births	Ref.
USA	Boston MA, 2826 HMOs, Harvard Pilgrim Health Care	retrospective analysis of ambulatory records, pharmacy dispensing data and admin claims for hospitals, ERs and other care outside the health centre	1993-1995	2746 pregnant women (2301 VD, 525 CS)	32 diagnostic, testing or pharmacy dispensing codes indicative of postpartum infection, reviewed for 30 days postpartum	6 (7.4 in CS and 5.5 in VD)	<sup>16</sup>
<b>AMRO B</b>							
El Salvador	Cuscatlan department (a rural area)	community based survey	1994-1996	636 pregnancies	self-reported 2 or more of the following within 42 days of delivery: fever, abdominal pain, purulent discharge, or medical diagnosis of postpartum endometritis	9.3	<sup>17</sup>
<b>EURO A</b>							
UK	North Thames region	retrospective analysis of singleton pregnancies - St Mary's information system database	1988-1997	385120 singleton pregnancies	genital tract infection, pyrexia of unknown origin	2.98	<sup>18</sup>
UK	South East Thames Region; 19 maternity units	prospective hospital based case-control study	March 1997-February 1998	48865 deliveries	infection associated with 2 or more of the following: temp <38° C or <36° C, heart rate >100/min, resp. rate >20/min or PaCO <sub>2</sub> <32mmHg, WBC >17 or <4 or >10% immature plus bacteraemia	0.03	<sup>19</sup>
Austria, Belgium, Finland, France, Ireland, Italy, UK	Upper Austria, Brussels, Part of Finland, Lorraine, Champ/Arden. Centre, Cork, Puglie,	prospective hospital based	1995-1997	161956 pregnant women	severe sepsis at the time of pregnancy outcome (birth, abortion etc): co-existence of infection plus one or more of the following: temp.>38° C or <36° C, heart rate >90,	0.09	<sup>20</sup>

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resp. rate >20 or  
 PaCo<sub>2</sub><32,  
 WBC>12000 or  
 <4000 or >10%  
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For the current version of the GBD, the incidence of maternal sepsis by WHO sub-region was calculated as a function of:

- incidence of sepsis following vaginal birth with a skilled birth attendant;
- incidence of sepsis following vaginal birth without a skilled birth attendant;
- incidence of sepsis following caesarean section birth with/without antibiotic prophylaxis.

We assumed that skilled birth attendance was a proxy for clean delivery practices. These estimates include urinary tract infection and endometritis but an important difference compared to GBD 1990 is that the current definition excludes mastitis and surgical site infections. They have both short duration, with no long-term consequences and essentially no mortality.

The incidence of sepsis following vaginal birth in facilities was estimated from a study by Yokoe and others [16] of post-partum infections in the USA as it used comprehensive post-discharge surveillance methods to identify all cases of puerperal sepsis. In their study, the authors screened automated ambulatory medical records, hospital and emergency room claims, and pharmacy records of 2,826 members of a health maintenance organization who gave birth in a 30-month period. Because puerperal sepsis often develop after discharge and women are reluctant to go to the hospital, using only hospital data will underestimate the real incidence. By cross-checking ambulatory with pharmacy dispensing data and hospital data, the authors attempted to identify all cases of puerperal infections. The rate of puerperal infections was 2.5% in women who had a vaginal delivery.

Differentials in the incidence of sepsis between home and facility births is likely to be the result of a number of different factors. Incidence is likely to be higher in facilities as a result of nosocomial factors, while unclean delivery practices or traditional practices such as insertion of substances into the vagina are likely to foster the development of sepsis in home deliveries. A study from Zaria, Nigeria reported a rate of post-partum genital sepsis of 14.8% among women who delivered at home compared to 7.9% in those who delivered in facility [17]. A study from Senegal demonstrated an incidence of sepsis of 8.7% for home deliveries compared to 1.9% for deliveries in health facilities [18]. In terms of clean delivery practices, Semmelweis in 1847 documented reductions in mortality due to puerperal sepsis from 11% to 3% as a result of the introduction of scrubbing protocols with chlorine solution before every physical examination [19].

While recognising the complex interplay of factors which result in differentials between in sepsis incidence between home deliveries and facility deliveries, we arbitrarily assumed births in facility

would reduce the incidence of sepsis by 50%. Vaginal births out of facilities were therefore assumed to have an incidence of 5.0%.

From the USA study by Yokoe and others [16] the rate of puerperal infections following C-section deliveries was 5.3% (relative risk 2.1). A Cochrane review of antibiotic prophylaxis for caesarean section demonstrated a RR of 0.29 for prophylaxis compared to no prophylaxis [20]. As no information was given on the use of antibiotic prophylaxis in the Yokoe study, we assumed the regional coverage of 80%. Back-calculating antibiotic prophylaxis results in an incidence of sepsis of 10.1% following caesarean section with no antibiotic prophylaxis. This figure is similar to the rates found in the Cochrane review [20], where the average rate of endometritis in the control groups in those women undergoing elective CS of 9.2% (0-24%), and for the women undergoing non-elective CS the average incidence of endometritis in the control groups was 28.6% (3-61%).

Caesarean section and antibiotic prophylaxis coverage rates by region are shown in Table 3.3. The majority of information on antibiotic coverage is from teaching hospitals which is not likely to be representative of the country or region. These are therefore best guess estimates. Using the incidence rates by type of birth and coverage rates detailed above, the overall incidence of maternal sepsis was calculated by region (Table 3.3).

**Table 3.3. Data and assumptions used to estimate regional incidence rates for puerperal sepsis**

WHO region	Proportion of deliveries with skilled birth attendance (per 100 live births)	Estimated C-section rate per 100 live births	Antibiotic prophylaxis coverage per 100 C-section births	Estimated incidence rate per 100 live births
AFRO D	46	4.2	20	4.1
AFRO E	45	4.2	20	4.1
AMRO A	99	10.2	80	2.7
AMRO B	89	26.1	50	3.7
AMRO D	52	26.1	20	5.2
EMRO B	87	10.0	50	3.2
EMRO D	47	8.5	20	4.3
EURO A	99	10.2	80	2.7
EURO B1	87	10.2	50	3.2
EURO B2	93	10.2	50	3.1
EURO C	99	10.2	50	2.9
SEARO B	64	7.3	50	3.7
SEARO D	34	5.8	20	4.5
WPRO A	100	10.2	80	2.7
WPRO B1	72	7.3	50	3.5
WPRO B2	57	7.3	50	3.8
WPRO B3	64	7.3%	50	3.7

**Sequelae of puerperal sepsis**

In the absence of antibiotic treatment or in the more severe cases, puerperal infection may be complicated by pelvic chronic pain, pelvic inflammatory disease and secondary infertility<sup>2</sup>. Also, the more severe cases are responsible for the high rates of mortality from sepsis in developing countries. The methodology developed by AbouZahr et al in estimating the burden of infertility due to puerperal sepsis and unsafe abortion for GBD 1990, was used again for the GBD 2000 estimates<sup>2</sup>.

### 3.3 Risk factors for the development of maternal sepsis

It is generally considered that pelvic infections are more common among women of poor socioeconomic status compared with middle- or upper-class patients, but the precise reason for that is unclear. Some other factors have been considered also to predispose to puerperal infections: anaemia, poor nutrition and prolonged labour particularly occurring in young primipara are the most frequently cited<sup>2</sup>. In a study at the Ife State Hospital in Nigeria the predisposing factors associated with sepsis were: anaemia in 69.2% of cases, prolonged labour (labour lasting more than 12h) in 65.7%, frequent vaginal examinations in labour (more than five) in 50.7%, and premature ruptured membranes in 31.5%<sup>9</sup>.

During the last few years, a growing body of evidence suggests that the single most important risk factor for postpartum infection is caesarean section (CS)<sup>21, 22, 16</sup>. A Cochrane systematic review conducted by Smaill and Hofmeyer, identified 66 randomized controlled trials comparing antibiotic prophylaxis or no treatment for both elective and non-elective CS<sup>21</sup>. They found an average rate of endometritis in the control groups in those women undergoing elective CS of 9.2% (0-24%), and for the women undergoing non-elective CS the average incidence of endometritis in the control groups was 28.6% (3-61%). The use of antibiotic prophylaxis reduced by two thirds to three quarters the incidence of endometritis, for all studies combined. Yokoe et al in USA, using comprehensive post-discharge surveillance methods to identify all cases of puerperal infections that occurred in women who delivered at Brigham and Women's Hospital, Boston from January 1993 to June 1995, found a rate of puerperal infections following CS of 7.4%, compared to 5.5% in women who had vaginal delivery<sup>16</sup>.

There are also community factors which increase the women's risk of developing puerperal infections, such as delivery by an untrained birth attendant, lack of transportation and long distance from a woman's house to the health facility, cultural factors which may delay care-seeking behaviour, low status of women which contributes to their poor health in general, lack of knowledge of symptoms and signs of puerperal sepsis, and availability of postnatal care<sup>2</sup>.

Considering the increasing trend of rates of caesarean section all over the world, it is likely that puerperal infection incidence will see a similar trend in future years. The rising incidence of nosocomial infections and of antibiotic resistance may also contribute to this.

## 4. Mortality and case fatality

Few studies report on the case fatality of puerperal sepsis (tables 4.1 and 4.2). These studies show that sepsis is still a highly lethal condition, even if its incidence is not so high. However, it is difficult to extrapolate their results to all the regions, as studies may have used different definitions and they report only on hospital populations, which may have higher risks and thus higher case fatality rates.

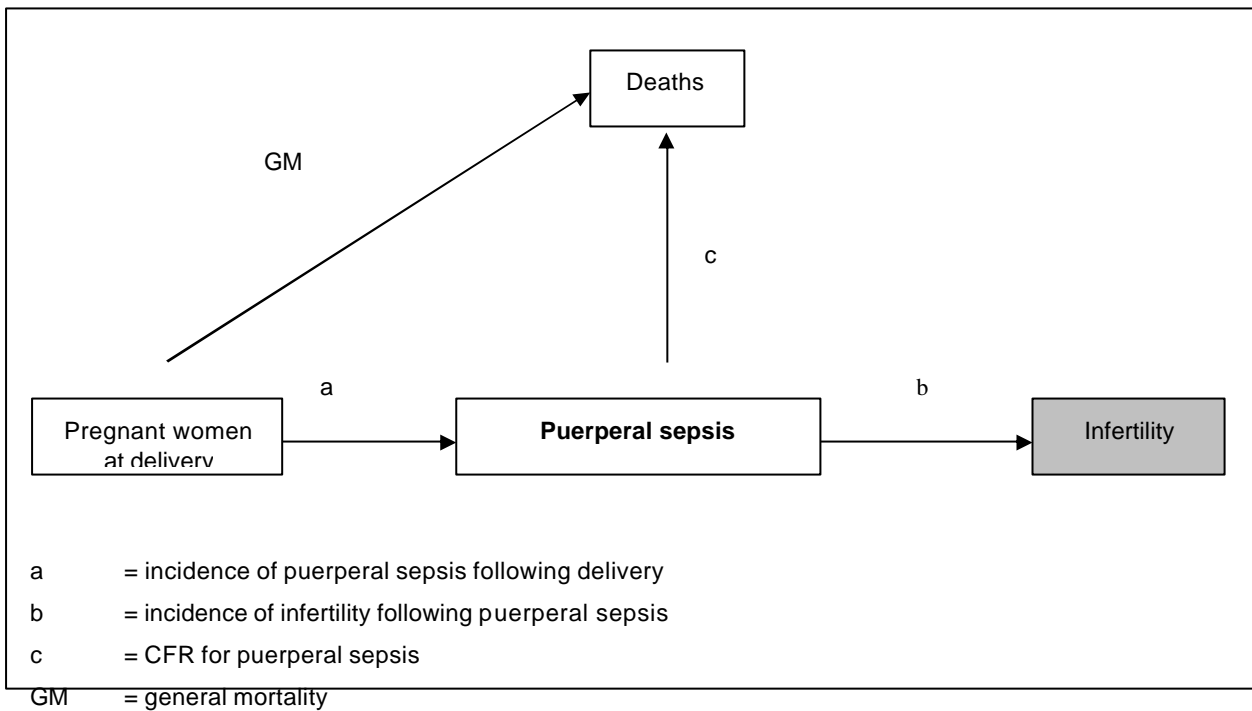
**Table 4.1. Proportion of maternal deaths due to puerperal sepsis**

Region	Setting	Type of study	Year	Total maternal deaths	Proportion maternal deaths due to sepsis	Ref
AFRO D						
Guinea-Bissau	the 5 northern regions of Guinea-Bissau (82% of population)	RAMOS	1989-1996	111	9.9	23
Guinea-Bissau	all country	RAMOS	1989-1990	145	15.9	24
Ghana	Ejisu health district	community based survey of maternal mortality	1985-1990	44	6.8	25
Burkina Faso, Mali, Mauritania, Niger, Senegal, Cote d'Ivoire (AFRO E)	5 urban areas and 1 rural area	population based prospective study	1994-1996	55	10.9	26
AMRO B						
Mexico	3 states in Mexico	Verbal autopsy to validate information from vital statistics records	1995	145	15	27
SEARO D						
Bangladesh	Verbal autopsy in demographic surveillance system	Matlab area, Bangladesh	1987-1993	174	5.7	28

**Table 4.2. Case fatality rates for puerperal sepsis – epidemiological studies**

Region	Setting	Type of study	Year	Incidence per 100 live births	Case fatality rate (%)	Ref.
AFRO D						
Nigeria	Ife State hospital, <i>Ife-Ife</i>	retrospective hospital based	1986-1995	1.70	4.10	9
Niger	Niamey, 6 maternity wards	maternity wards-based, longitudinal	1994-1996	0.22 (95% CI: 95-434)	50	11
Burkina Faso, Mali, Mauritania, Niger, Senegal, Cote d'Ivoire*	Ouagadougou, Bamako, Nouakchott, Niamey, Kaolack region, Abidjan*	population-based, multicentre; door-to-door census of all pregnant women	Dec 1994- June 1996	0.09 (95% CI 0.05-0.14)	33.30%	12
South Africa	Kalafong and Pretoria Academic	prospective descriptive multicentre study:	Sept 1996- aug	0.07	30.00	13



**Figure 5.1. Maternal sepsis disease model.**

*YLDs to be calculated for boxes in gray*

**Table 5.1. Comparison between GBD 1990 and GBD 2000 disease models**

	<b>GBD 1990</b>	<b>GBD 2000</b>
Stages/Sequelae	Episodes of puerperal infections (including mastitis and surgical site infections) Infertility	Episodes of puerperal sepsis (excluding mastitis and surgical site infections) Infertility
Incidence rates	A range from 5% in developed countries and FSE, up to 10% Sub-Saharan Africa	A range from 2.7% to 5.7%
Proportion puerperal infection resulting in infertility	Between 5% in developed countries to 12% in developing countries	As for GBD 1990, adjusting for differences in case definition
Assumptions on duration of infertility	Up to age 44	Up to age 49
Mortality	Proportional mortality model 3-17% of all maternal deaths (15% globally)	Proportional mortality model 2-19% of all maternal deaths (15% globally)
Disability weight for infertility	0.180 both treated and untreated	0.180 both treated and untreated

## 6. Regional incidence, prevalence and mortality estimates

**Table 6.2. Maternal sepsis: age-specific incidence, prevalence and mortality rate estimates for WHO epidemiological subregions, 2000.**

Subregion	Incidence/1000 women 15-49	Prevalence of infertility/1000 women 15-49	Mortality/100,000 women 15-49
AFRO D	6.91	24.87	25.45
AFRO E	7.09	24.63	28.46
AMRO A	1.40	3.41	0.01
AMRO B	2.85	12.82	0.49
AMRO D	5.45	21.00	1.82
EMRO B	3.25	11.82	0.40
EMRO D	4.96	19.08	1.54
EURO A	1.14	2.55	0.01
EURO B1	1.72	8.77	0.05
EURO B2	2.16	9.70	0.18
EURO C	0.96	5.85	0.14
SEARO B	2.83	12.37	1.35
SEARO D	5.10	21.65	8.20
WPRO A	1.16	2.53	0.01
WPRO B1	1.93	11.06	0.22
WPRO B2	3.30	13.35	2.58
WPRO B3	4.86	18.46	2.77

## 7. Global burden of maternal sepsis in 2000

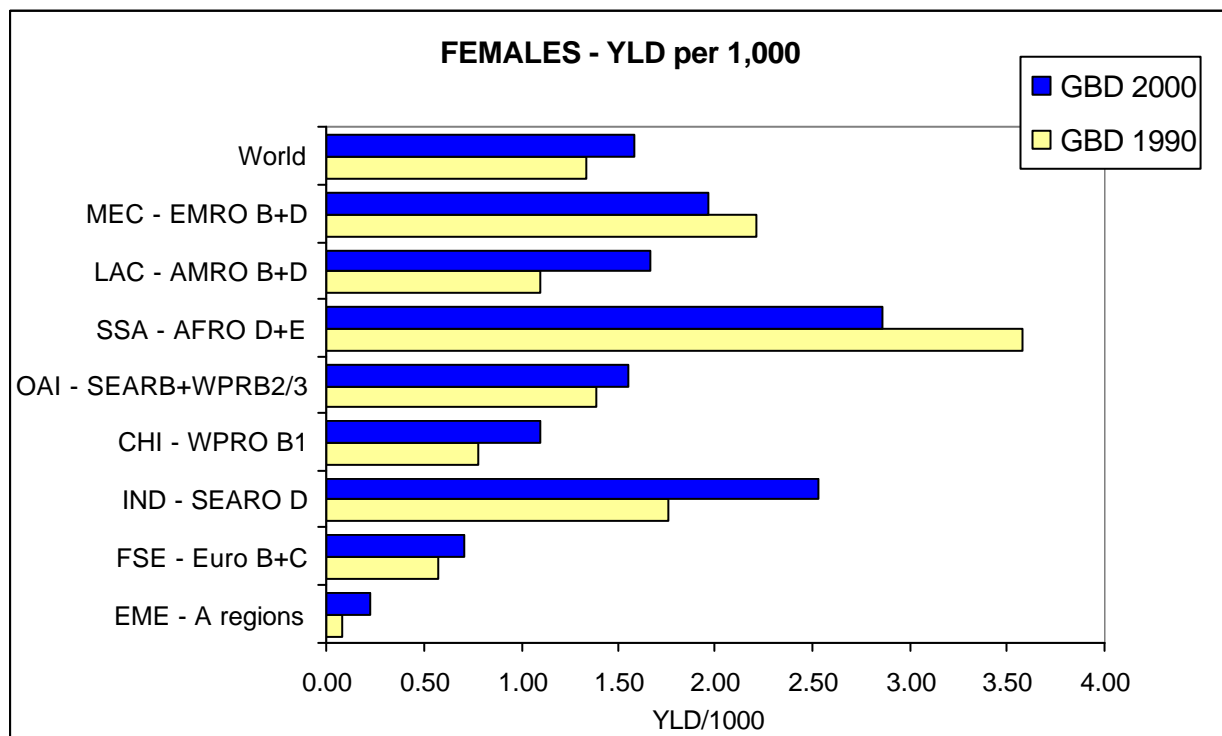
General methods used for the estimation of the global burden of disease are given elsewhere<sup>31</sup>. The tables and graphs below summarise the global burden of maternal sepsis estimates for the GBD 2000 and compare them with the maternal sepsis estimates from the GBD 1990<sup>32</sup>.

**Table 7.1. Maternal sepsis: global total deaths, YLD, YLL and DALY estimates, 1990 and 2000.**

	GBD 1990	GBD 2000
Deaths ('000)	68	77
YLD('000)	3,476	4,731
YLL('000)	1,976	2,170
DALY('000)	5,452	6,901

**Table 7.2. Maternal sepsis: YLD, YLL and DALY estimates for WHO epidemiological subregions, 2000.**

Subregion	YLD/100,000	YLL/100,000	YLD('000)	YLL('000)	DALY('000)
AFRO D	296.7	313.0	498	525	1,023
AFRO E	275.2	442.8	467	752	1,219
AMRO A	26.7	0.2	42	0	42
AMRO B	151.0	12.9	337	29	366
AMRO D	262.4	21.5	94	8	102
EMRO B	159.5	9.2	107	6	113
EMRO D	233.7	32.1	159	22	181
EURO A	19.5	0.1	41	0	41
EURO B1	91.2	0.8	76	1	77
EURO B2	111.8	3.4	29	1	30
EURO C	48.9	1.9	64	2	66
SEARO B	149.6	46.4	295	91	386
SEARO D	253.0	105.1	1,653	686	2,339
WPRO A	19.7	0.0	15	0	15
WPRO B1	110.2	3.6	727	24	751
WPRO B2	166.3	27.1	119	19	139
WPRO B3	225.7	69.4	8	2	10
World	157.7	72.3	4,731	2,170	6,901

**Figure 7.1. Maternal sepsis YLD rates, by sex, broad regions, 1990 and 2000.**

## Conclusions

One of the main limitations in estimated the global burden of puerperal sepsis, as well as for the other maternal conditions, is that epidemiological studies are currently using different definitions of the condition, rendering those studies difficult to compare. More efforts are needed to develop standard definitions, that researchers can refer to, and that may allow comparability of their work.

These are version 3 estimates for the GBD 2000. Apart from the uncertainty analysis, updating estimates to reflect revisions of mortality estimates and any new or revised epidemiological data or evidence, it is not intended to undertake any major addition revision of these estimates.

We welcome comments and criticisms of these draft estimates, and information on additional sources of data and evidence. Please contact Colin Mathers (Evidence and Information for Policy, WHO Geneva) on email [mathersc@who.int](mailto:mathersc@who.int).

## Acknowledgements

We particularly wish to thank Stephen Lim, who carried out final revisions of the estimates and documentation during the second half of 2003.

We also wish to thank colleagues from Reproductive Health Research department who provided comments and suggestions on data sources and assumptions, particularly Carla Abouzahr, Metin Gulmezoglu, Jose Villar, Luc De Bernis and Ana Betran. We also thank the many staff of the Global Program on Evidence for Health Policy who contributed to the development of life tables and cause of death analysis. In particular we thank Omar Ahmad, Brodie Ferguson, Mie Inoue, Alan Lopez, Rafael Lozano Doris Ma Fat, Christopher Murray and Chalipati Rao. This study has been supported by a grant from the National Institute on Aging, USA.

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