

# Global burden of hypertensive disorders of pregnancy in the year 2000

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## 1. Introduction

Hypertensive disorders of pregnancy (HDP) represent a group of conditions associated with high blood pressure during pregnancy, proteinuria and in some cases convulsions. The most serious consequences for the mother and the baby result from pre-eclampsia and eclampsia. These are associated with vasospasm, pathologic vascular lesions in multiple organ systems, increased platelet activation and subsequent activation of the coagulation system in the micro-vasculature<sup>1</sup>. Eclampsia is usually a consequence of pre-eclampsia consisting of central nervous system seizures which often leave the patient unconscious; if untreated it may lead to death. The long-term sequelae of both pre-eclampsia or eclampsia are not well evaluated, and the burden of hypertensive disorders of pregnancy stems mainly from deaths.

In the GBD 1990 hypertensive disorders of pregnancy ranked 75<sup>th</sup> in terms of DALYs and were responsible for 6% of the burden of all maternal conditions. It was estimated that deaths due to hypertensive disorders of pregnancy represented 13% of all maternal deaths. This draft paper summarises the data and methods used to produce the Version 2 estimates of burden of hypertensive disorders of pregnancy for the year 2000.

## 2. Case and sequelae definitions

The classification of HDP is difficult because of limited knowledge about its etiology and the lack of conformity of definitions<sup>1</sup>. A WHO Study Group recommended the definitions listed in Table 2.1. Further amendments to these definitions have been made by the American College of Obstetricians and Gynaecologists, particularly for clinical purposes<sup>2</sup>. According to these, pre-eclampsia superimposed is likely in women with hypertension alone who develop new proteinuria, or in women with pre-existing hypertension and proteinuria who have sudden increase in blood pressure or proteinuria, thrombocytopenia, or increases in hepatocellular enzymes.

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**Table 2.1 Types of hypertension during pregnancy (WHO 1987)**

Gestational hypertension	Hypertension without the development of significant proteinuria (<0.3 g/l), after 20 weeks of gestation or during labour and/or within 48 hours of delivery
Unclassified hypertension in pregnancy	Hypertension found when blood pressure is recorded for the first time after 20 weeks of gestation or during labour and/or within 48 hours of delivery <sup>a)</sup>
Gestational proteinuria	Development of significant proteinuria ( $\geq 0.3$ g/l) after 20 weeks of gestation or during labour and/or within 48 hours of delivery
Pre-eclampsia	Development of gestational hypertension and significant proteinuria after 20 weeks of gestation or during labour and/or within 48 hours of delivery
Eclampsia	Convulsions ante, intra- or postpartum
Underlying hypertension or renal disease	Underlying hypertension, or renal disease, or other known causes of hypertension (such as pheochromocytoma)
Pre-existing hypertension or renal hypertension and or proteinuria in pregnancy	Pre-existing hypertension, pre-existing renal disease, pre-existing other causes of hypertension
Superimposed pre-eclampsia/eclampsia	a) Pre-existing hypertension with superimposed pre-eclampsia or eclampsia (a worsening of hypertension, with an increase in diastolic blood pressure to at least of 15 mm Hg above non-pregnancy values, accompanied by the development or worsening of proteinuria b) pre-existing renal disease with superimposed pre-eclampsia or eclampsia

<sup>a)</sup> This type of hypertension should be reclassified as gestational hypertension if blood pressure returns to normal during postnatal period, although some of these patients may have underlying hypertension caused by renal disease

The definitions used by GBD 2000 are listed in table 2.2

**Table 2.2 GBD 2000 case and sequelae definitions for hypertensive disorders of pregnancy**

Cause category	GBD 2000 Code	ICD 9 codes	ICD 10 codes
Hypertensive disorders of pregnancy	U045	642	O10-O16

Sequela	Definition
Cases	Pre-eclampsia: Gestational hypertension with significant proteinuria ( $\geq 0.3$ g/l) after 20 weeks of gestation or during labor and/or within 48 hours of delivery (WHO 1987)  Eclampsia: convulsions occurring ante-, intra- or postpartum, associated with high blood pressure and proteinuria

### 3. Incidence

Assessing the epidemiology of pre-eclampsia is difficult due to lack of conformity of the definitions described above. There may also be measurement bias and errors in the ascertainment of both hypertension and proteinuria. Because uniform diagnostic criteria are not always followed by those

who study and report on hypertensive disorders of pregnancy, reported incidence may not be readily comparable between sites<sup>1</sup>.

As a result, incidence of pre-eclampsia and eclampsia was based on a systematic review by Villar et al. (unpublished) in which only studies where investigators made efforts to control and/or assure the diagnosis of pre-eclampsia and eclampsia (blood pressure and proteinuria measurements, documentation of seizure, etc.) were included. Some studies lacking details of diagnostic quality assessment, but whose data demonstrated overall good quality were also included. The data included in the review was population based and came from recently published reports as well as a series of large recent data sets available to WHO. Estimates of incidence were stratified into data from developing countries and more developed countries.

The pooled incidence of pre-eclampsia for developing countries was estimated to be 3.4%. This figure was used for all WHO sub-regions B through to E. Two developed country studies were included in the review for the incidence of pre-eclampsia. The incidence of pre-eclampsia was estimated at 2.8% from the Norwegian Birth Registry for the period 1967-1998. The South East Thames Study estimated pre-eclampsia incidence to be 0.4% for the period 1997-1998. A pooled incidence rate was not estimated as it was not possible to disaggregate the Norwegian study by year. The 0.4% incidence rate estimate from the South East Thames Study was therefore used as the estimate of pre-eclampsia incidence for all WHO A sub-regions.

Incidence for eclampsia from the systematic review was 2.3% of pre-eclampsia cases for developing regions and 0.8% of pre-eclampsia cases for developed regions.

**Table 3.1. Regional incidence rates for pre-eclampsia and eclampsia**

WHO region	Pre-eclampsia incidence rate (% births)	Eclampsia incidence rate (as % pre-eclampsia)
AFRO D	2.8	2.3
AFRO E	2.8	2.3
AMRO A	0.4	0.8
AMRO B	2.8	2.3
AMRO D	2.8	2.3
EMRO B	2.8	2.3
EMRO D	2.8	2.3
EURO A	0.4	0.8
EURO B1	2.8	2.3
EURO B2	2.8	2.3
EURO C	2.8	2.3
SEARO B	2.8	2.3
SEARO D	2.8	2.3
WPRO A	0.4	0.8
WPRO B1	2.8	2.3
WPRO B2	2.8	2.3
WPRO B3	2.8	2.3

### 3.3 Time trends in hypertensive disorders of pregnancy

An assessment of the time trends of hypertensive disorders of pregnancy is difficult, due to lack of consensus about the definitions used. Eclampsia is easier to recognise and incidence surveys have been undertaken in England and Wales since 1922; these show a continuous decline in both incidence and deaths from the condition<sup>1</sup>. As the incidence of eclampsia is influenced by the availability and quality of antenatal care<sup>1</sup>, eclampsia mortality remains important in settings of high maternal mortality<sup>3</sup>. Epidemiological studies conducted during the last decade show no decline in the incidence of eclampsia in developing countries, suggesting an urgent need to better identify women at risk and to improve access to treatment.

### 3.4 Risk factors for the development of hypertensive disorders of pregnancy

Several risk factors have been found to be associated with an increased risk of developing pre-eclampsia: the presence of type 1 diabetes, gestational diabetes, twin birth and obesity (body mass index >29)<sup>4</sup>. The likelihood of progression from gestational hypertension to pre-eclampsia may be increased by a prior miscarriage<sup>5,6</sup>. A study on a large cohort of Latin American and Caribbean women identified the following risk factors for developing pre-eclampsia: nulliparity, multiple pregnancy, history of chronic hypertension, gestational diabetes, maternal age over 35 years, fetal malformation and obesity<sup>7</sup>. Using the same source of data (the Latin American and Caribbean Perinatal System database) Conde-Agudelo et al. showed that interpregnancy intervals longer than 59 months are associated with an increased risk of pre-eclampsia and eclampsia<sup>8</sup>. Error! Bookmark not defined.

## 4. Mortality and case fatality

Although eclampsia is responsible for the majority of deaths associated with hypertensive disorders of pregnancy, death can occur in the absence of convulsions<sup>1</sup>. Evidence on case fatality rates of eclampsia is limited to mainly hospital-based studies (table 4.1) where rates are likely to be higher.

As for other maternal conditions, deaths due to hypertensive disorders of pregnancy were estimated using a proportional mortality model. A first set of regional estimates of total number of maternal deaths have been produced using the methodology developed for WHO/UNICEF 1995 estimates of maternal mortality<sup>8</sup>. Available information on cause of death distributions in each region, including data from vital registration systems<sup>9</sup>, were then used to estimate the proportion of different causes of maternal mortality<sup>10</sup>. Table 4.2 presents available data on the proportion of deaths due to eclampsia among all maternal deaths.

Based on this evidence, the GBD 2000 study estimates the following case fatality rates for hypertensive disorders of pregnancy (Table 4.3). As discussed above, case fatality reports from hospital-based studies may be biased due to a selected high risk population.

**Table 4.1. Case fatality rates for eclampsia**

Region	Setting	Type of study	Year	Incidence per 100 live births	Case fatality rate (%)	References
AFRO D						
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	1994-1996	0.19	18.4	Pruel A, Bouvier-Colle MH et al, Bull WHO 2000
Burkina Faso	University hospital, maternity wards, Ouagadougou	retrospective hospital based	1992-1995	0.88	15.7	Pruel A, Bouvier-Colle MH et al, Bull WHO 2000
Niger	Niamey, 6 maternity wards	maternity wards-based, longitudinal	1997	0.22	5.9	Pruel A et al, Afr J reprod Health 1998
AFRO E						
South Africa	Kalafong and Pretoria Academic hospitals	prospective descriptive multicentre study: audit of maternal near miss (daily case notes review)	Sept 1996-aug 1997	0.28	26.3	Buga Ga, East Afr Med J, 1999
South Africa	Ga-Rankuwa Hospital	Retrospective hospital based	Jan 1994-Dec 1995	0.36	21.2	
AMRO D						
Peru	Hospital Nacional Cayetano	hospital based prospective	1991-1997	0.4	8.0	Conde-Agudelo A et al, BMJ 2000
EURO A						
UK	279 hospitals in UK with a consultant obstetric unit	prospective hospital based and questionnaires to physicians	1992	0.05	1.8	Knuist M, Int J Obstet Gyn, 1998
SEARO B						
Thailand	Rajavithi Hospital, Bangkok	hospital based retrospective review	1988-1997	0.05	3.3	Chinayon P, J Med Assoc Thai 1988

**Table 4.2. Proportion of maternal deaths due to eclampsia**

Region	Setting	Type of study	Year	Total maternal deaths	Proportion maternal deaths associated with eclampsia	Ref.
<b>AFRO D</b>						
Guinea-Bissau	The 5 northern regions of Guinea-Bissau (82% of population)	RAMOS*	1989-1996	144	5.1	11
Guinea-Bissau	All country	RAMOS	1989-1990	145	4.6	12
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	13
<b>AMRO A</b>						
USA	Non federal Maryland hospitals	retrospective hospital based	1984-1997	135	22.2	14
<b>SEARO D</b>						
Bangladesh	Matlab area, Bangladesh	Verbal autopsy in demographic surveillance system	1987-1993	174	17.2	15
India	RG Kar Med Coll Hospital, Calcutta, India	Retrospective hospital based	1995-1997	203	53.2	16

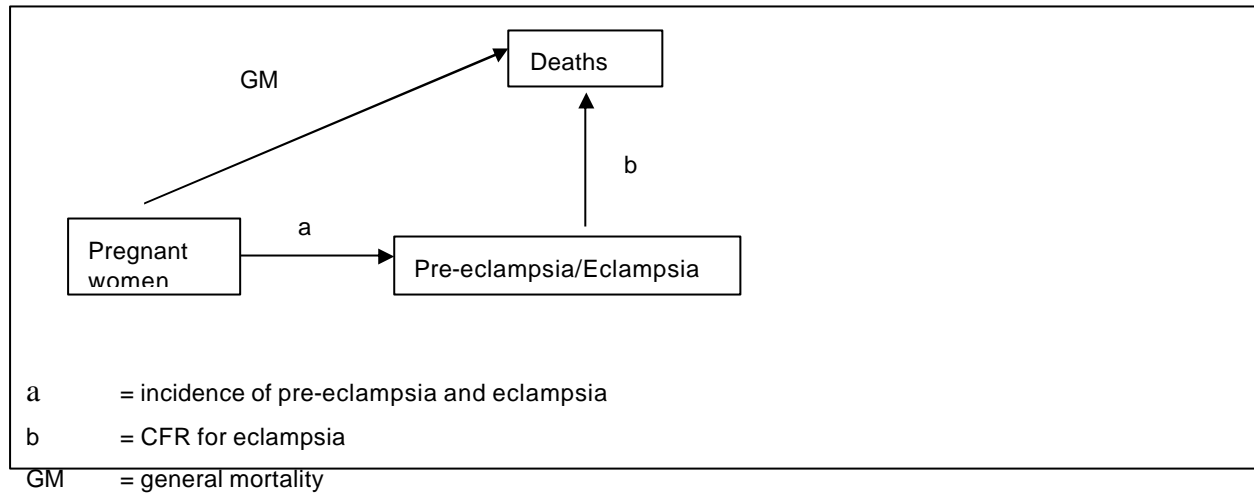
\*RAMOS = Reproductive Age Mortality Study

## 5. Disease model for hypertensive disorders of pregnancy

A disease model was developed for hypertensive disorders of pregnancy as described in figure 5.1. During pregnancy, delivery or shortly thereafter (within 6 weeks), women with hypertensive disorders of pregnancy may have renal or liver damage, pulmonary oedema and cerebral haemorrhage. However, no long-term follow-up studies have been performed to evaluate the consequences of eclampsia over time. A retrospective study at the King Edward VIII hospital in Durban, South Africa, identified 140 cases of neurological complication during pregnancy among 14,881 deliveries within one year<sup>17</sup>. All but one of these cases had eclampsia, and all of them recovered completely before discharge. A study from Norway using record linkage from 2 registers between 1967 and 1992, the national medical birth register and the national register of causes of

death, showed that women who had pre-eclampsia may have an increased risk of death from cardiovascular causes in later life than non-pre-eclamptic women<sup>18</sup>.

**Figure 5.1. Hypertensive disorders of pregnancy disease model.**



In the GBD 2000 neurological complications were therefore no longer considered as sequelae of eclampsia and pre-eclampsia. Long-term follow-up studies are needed to evaluate the extent to which women with hypertensive disorders of pregnancy and particularly eclampsia, will develop long-term complications.

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

	<b>GBD 1990</b>	<b>GBD 2000</b>
Stages/Sequelae <sup>e</sup>	Hypertensive disorders of pregnancy Neurological sequelae	Pre-eclampsia / Eclampsia
Incidence rates	Eclampsia: 0.5% of live births in developing countries and 0.1% in developed countries  Assumptions made for the rest of HDP led to a world average of 5.5%	Pre-eclampsia: 2.8% of live births for developing countries and 0.4% of live births in developed countries.  Eclampsia: 2.3% of pre-eclampsia in developing countries and 0.8% of pre-eclampsia in developed countries  Assumed pre-eclampsia/eclampsia account for 50% of all hypertensive
Case fatality	2.9-16.4%	0.1% to 4.0%
Mortality	13% of all maternal deaths	14% of all maternal deaths

## 6. Regional incidence, prevalence and mortality estimates

**Table 6.1. Hypertensive disorders of pregnancy: age-specific incidence and mortality rate estimates for WHO epidemiological subregions, 2000.**

<b>Subregion</b>	<b>Age-specific Incidence/1000 women 15-49</b>	<b>Age-specific mortality/100,000 women 15-49</b>
AFRO D	11.50	18.46
AFRO E	11.72	20.49
AMRO A	0.41	0.11
AMRO B	5.21	2.10
AMRO D	7.16	9.32
EMRO B	6.94	1.05
EMRO D	7.83	4.46
EURO A	0.34	0.05
EURO B1	3.67	0.58
EURO B2	4.80	0.72
EURO C	2.25	0.10
SEARO B	5.26	2.76
SEARO D	7.75	8.59
WPRO A	0.35	0.03
WPRO B1	3.76	0.07
WPRO B2	5.86	4.27
WPRO B3	9.03	4.68
World	5.35	4.56

## 7. Global burden of hypertensive disorders of pregnancy in 2000

General methods used for the estimation of the global burden of disease are given elsewhere<sup>19</sup>. The tables and graphs below summarise the global burden of hypertensive disorders of pregnancy estimates for the GBD 2000 and compare them with the hypertensive disorders of pregnancy estimates from the GBD 1990<sup>20</sup>.

**Table 7.1. Hypertensive disorders of pregnancy: global total YLD, YLL and DALY estimates, 1990 and 2000.**

	<i>GBD 1990</i>	<i>GBD 2000</i>
Deaths ('000)	57	73
YLD('000)	75	-
YLL('000)	1,656	2,231
DALY('000)	1,731	2,231

**Table 7.2. Hypertensive disorders of pregnancy: 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	0	293.2	0	492	492
AFRO E	0	344.0	0	584	584
AMRO A	0	1.9	0	3	3
AMRO B	0	48.2	0	108	108
AMRO D	0	199.7	0	71	71
EMRO B	0	21.1	0	14	14
EMRO D	0	105.2	0	72	72
EURO A	0	0.7	0	1	1
EURO B1	0	8.4	0	7	7
EURO B2	0	4.7	0	1	1
EURO C	0	1.3	0	2	2
SEARO B	0	74.4	0	147	147
SEARO D	0	107.2	0	700	700
WPRO A	0	0.3	0	0	0
WPRO B1	0	1.0	0	6	6
WPRO B2	0	26.9	0	19	19
WPRO B3	0	74.8	0	2	2
World	0	74.3	0	2,231	2,231

## 8. Conclusions

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).

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## References

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- 1 AbouZahr C, Guidotti R. Hypertensive disorders of pregnancy. In: Murray, CJL and Lopez, AD, eds., *Health dimensions of sex and reproduction: the global burden of sexually transmitted diseases, maternal conditions, perinatal disorders, and congenital anomalies*. WHO 1998.
- 2 Report on the national high blood pressure education program working group on high blood pressure in pregnancy. *American Journal of Obstetrics and Gynaecology*, 2000, 183:s1-s22.
- 3 The Magpie trial Collaborative Group. Do women with pre-eclampsia and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. *Lancet*, 2002, 359(9321):1877-90.
- 4 Ros HS, Cnattingius S, Lipworth L. Comparison of risk factors for pre-eclampsia and gestational hypertension in a population-based cohort study. *American Journal of Epidemiology*, 1998, 147(11):1062-70.
- 5 Saudan P, Brown MA, Buddle ML et al. Does gestational hypertension become pre-eclampsia? *British Journal of Obstetrics and Gynaecology*, 1998, 105:1177-84.
- 6 Lankoande J, Ouedraogo A, Ouedraogo CM, et al. [Gynecology-obstetrics at the Yalgado-Ouedraogo National Hospital Center. Eclampsia: epidemiologic, clinical and prognostic aspects] *Santé*, 1997, 7(4):231-5.
- 7 Conde-Agudelo A, Beliza JM Risk factors for pre-eclampsia in a large cohort of Latin American and Caribbean women. *BJOG*, 2000, 107(1):75-83.
- 8 Maternal mortality in 1995: estimates developed by WHO, UNICEF, UNFPA. WHO/RHR/01.9

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- 9 Statistics from EUPHIN network database: <http://www.euphin.dk/hfa/Phfa.asp> (last accessed 28<sup>th</sup> March 2002)
- 10 Mathers CD, Stein C, Tomijima N, Ma Fat D, Rao C, Inoue M, Lopez AD, Murray CJL. (2002). *Global Burden of Disease 2000: Version 2 methods and results*. Geneva, World Health Organization (GPE Discussion Paper No. 50).
- 11 Hoj L, Stensballe J, Aaby P. Maternal mortality in Guinea-Bissau: the use of verbal autopsy in a multi-ethnic population. *Int J Epidemiol*, 1999 Feb, 28(1):70-6.
- 12 Oosterbann M. Guinea-Bissau: what women know about the risks, an anthropological study. *World Health Statistics Quarterly*, 1995, 48(1): 39-43. WHO, Geneva.
- 13 Bouvier-Colle MH, Ouedraogo C, Dumont A, et al. Maternal mortality in West Africa. Rates, causes and substandard care from a prospective survey. *Acta Obstet Gynecol Scand*, 2001 Feb, 80(2):113-9.
- 14 Panchal S, Arria AM, Labhsetwar SA. Maternal mortality during hospital admission for delivery: a retrospective analysis using a state-maintained database. *Anesth Analg*, 2001 Jul, 93(1):134-41.
- 15 Ronsmans C, Vanneste AM, Chakraborty J, Van Ginneken JA. A comparison of three verbal autopsy methods to ascertain levels and causes of maternal deaths in Matlab, Bangladesh. *Int J Epidemiol*, 1998 Aug, 27(4):660-6.
- 16 Majhi AK, Mondal A, Mukherjee GG. Safe motherhood - a long way to achieve. *J Indian Med Assoc*, 2001 Mar, 99(3):132-7.
- 17 Okanloma KA, Moodley J. Neurological complications associated with pre-eclampsia and eclampsia syndrome. *International Journal of Gynaecology and Obstetrics*, 2000, 71:223-5.
- 18 Irgens HU, Reisaeter L, Irgens LM et al. Long term mortality of mothers and fathers after pre-eclampsia: population-based cohort study. *BMJ*, 2001, 323:1213-7.
- 19 Murray CJL, Lopez AD eds. *The Global Burden of Disease. A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020*. WHO 1996.
- 20 Murray CJL, Lopez AD, eds. *Global Health Statistics. A compendium of incidence, prevalence and mortality estimates for over 200 conditions*. WHO, 1996.