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Quantif ing the fall in mortalit associated with interventions related to h pertensive diseases of pregnanc

Abstract

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Introduction

The fifth Millennium Development Goal has set targets for the reduction of maternal mortality by 2015, but progress has been slow [1,2]. Effective interventions to reduce maternal deaths exist but they are often not available to women in poor countries [3]. Where resources are limited, information on the costs and health effects of interventions is thought to be important to aid decisions on how to reach the MDG-goals [4]. Such information may help to determine what can be achieved with existing resources, and to decide how additional funds can be used to maximise the chances of achieving the MDG-goals [4].

WHO estimates that 88 to 98 percent of maternal deaths are avoidable with moderate levels of health care [5]. This deceptively simple statement hides the complexities underlying the assessment of the health effects of interventions [6]. First, evidence of the efficacy of interventions needs to be available. In maternal health, reliable evidence of an effect on maternal mortality is rarely available and reliance on lower quality evidence – by current scientific standards - is often necessary [3]. Second, a distinction needs to be made between efficacy and effectiveness. Effectiveness, taking into account the coverage and quality of service delivery is thought to be more representative of the real world, but it requires robust evidence from a large range of programme settings. Third, interventions act on disease incidence,

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We searched PubMed for articles quantifying the impact of maternal health interventions on the reduction of maternal mortality at the population level, using the terms interventions, maternal mortality and effectiveness in our search. Reference lists from all relevant articles were checked. We included articles reporting the effect of preventive or curative interventions on HDP-related mortality, regardless of the definitions used. Information was extracted on interventions, the health systems level at which the intervention was delivered, the mortality outcome, the reported risk reduction on mortality outcomes, the methods for estimat-

routine calcium supplementation in pregnancy [40] and antiplatelet agents during pregnancy in women at risk of pre-eclampsia [41] and three treatment interventions: Magnesium sulphate (MgS04) for the treatment of eclampsia (3 reviews) [42-44] MgS04 for the treatment of pre-eclampsia [45], and hypertensive drugs for the treatment of mild to moderate hypertension in pregnancy [46]. The review documenting the effect of oral beta-blockers for hypertension [47] is not reported separately because beta-blockers are included in a later review of hypertensive drugs [46]. All studies are randomized controlled trials, and the quality of the trials is generally high. The number of deaths reported was sufficient in only one review [42] and one review combined death with severe morbidity to increase the number of adverse events [40].

There is no doubt that treating women with eclampsia with MgS04 reduces the risk of maternal death compared to diazepam (RR 0.59 95% CI 0.37-0.94), though the effect against placebo is not known. MgS04 is also effective for the treatment of pre-eclampsia: treating women with pre-eclampsia with MgS04 reduces their risk of eclampsia (RR 0.41 95% CI 0.29-0.58) and placental abruption (RR 0.64 95% CI 0.50-0.83), though there is insufficient evidence to draw conclusions with regard to the risk of death. The efficacy of the treatment of hypertension in pregnancy is less clear. Antihypertensive drugs in women with mild to moderate hypertension do not lower the risk of pre-eclampsia and there are insufficient numbers of events to assess their effect on risk of eclampsia or maternal death. Antihypertensive drugs do halve the risk of developing severe hypertension (RR 0.50 95% CI 0.41-0.61) [46].

Routine calcium supplementation during pregnancy halves the risk of pre-eclampsia (RR 0.45 95% CI 0.31-0.65), and reduces the occurrence of a composite outcome of death or serious morbidity (RR 0.80 95% CI 0.65-0.97). The reduction in the risk of pre-eclampsia is greatest for women at high risk of pre-eclampsia (5 trials, 587 women: RR 0.22, 95% CI 0.12-0.42), and for those with low baseline calcium intake (8 trials, 10,678 women: RR 0.36, 95% CI 0.20-0.65). There is a 17% reduction in the risk of pre-eclampsia with the use of antiplatelet agents – mostly low dose aspirin - during pregnancy in women at risk of pre-eclampsia (RR 0.83 95% CI 0.77-0.89). However, there are no significant differences between antiplatelet agents and placebo in the risk of eclampsia or maternal death.

Population models quantifying the impact of the prevention or treatment of HDP on mortality from HDP at the population level

We found 15 studies quantifying the effect of maternal health interventions on reducing maternal mortality at the population level, ten of which are included here (Additional File 2). Five studies were excluded because they did not report on HDP specifically [48-51] or because findings were only presented in a chart with no information on assumptions or the data underlying the chart [52].

The approach to classifying interventions varies greatly (Additional File 2). Most authors include a health systems dimension aimed at separating interventions that can be delivered at the primary or health centre level from those that require hospital treatment, though definitions are rarely provided and there is no consistency in the types of interventions that are deemed effective at the various levels. At the hospital level, effective interventions usually consist of MgS04 for the treatment of eclampsia [53-59], and later studies also include MgS04 for the treatment of pre-eclampsia. [55,58-60] Caesarean section is generally listed as part of the hospital package, and Graham et al (2006) [55] also include calcium supplementation, low dose aspirin, antioxidants and antihypertensive drugs as effective interventions at the hospital level.

Primary care interventions tend to focus on screeningon:-11(ea)--2(

eclampsia. [80] Treatment of severe hypertension is essential, but the choice of drug is not obvious, and an experienced clinician needs to decide on a case by case basis [46]. MgS04 has been suggested for use at the primary care level, but MgS04 is difficult to administer, and health centres need to refer women to hospital, even if they are able to give a loading those.

Table 4 suggests potential effect estimates for the reduction of HDP related mortality based on this review. We postulate that health centres without access to referral care can contribute to a 20% reduction in death from HDP

with qualified staff and drugs, much greater reductions can

P rido ine (vitamin B6) supplementation in pregnanc . *C c a e Databa e f S te atc Re e* Issue 2, Art. No.:CD000179.

Oestrogen supplementation, mainl dieth lstilbestrol, for preventing miscarriages and other adverse pregnanc outcomes. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD004353.

Progesterone for preventing pre-eclampsia and its complications. *C c a e Databa e f S te atc Re e* Issue 4, Art. No.:CD006175.

Marine oil, and other prostaglandin precursor, supplementation for pregnanc uncomplicated b pre-eclampsia or intrauterine growth restriction. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD003402.

Garlic for preventing pre-eclampsia and its complications. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD006065.

Diuretics for preventing pre-eclampsia. *C c a e Databa e f S te atc Re e* Issue 1, Art. No.:CD004451.

Nitric o ide for preventing pre-eclampsia and its complications. *C c a e Databa e f S te atc Re e* Issue 2, Art. No.:CD006490.

Energ and protein intake in pregnanc . *C c a e Databa e f S te atc Re e* Issue 4, Art. No.:CD000032.

Altered dietar salt for preventing pre-eclampsia, and its complications. *C c a e Databa e f S te atc Re e* Issue 4, Art. No.:CD005548.

Reduced salt intake compared to normal dietar salt, or high intake, in pregnanc . *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD001687.

E ercise or other ph sical activit for preventing pre-eclampsia and its complications. *C c a e Databa e f S te atc Re e* Issue 2, Art. No.:CD005942.

Bed rest with or without hospitalisation for h pertension during pregnanc . *C c a e Databa e f S te atc Re e* Issue 4, Art. No.:CD003514.

Low-dose dopamine for women with severe pre-eclampsia. *C c a e Databa e f S te atc Re e* Issue 1, Art. No.: CD003515.

Plasma volume e pansion for treatment of pre-eclampsia. *C c a e Databa e f S te atc Re e* Issue 4, Art. No.:CD001805.

Interventionist versus e pectant care for severe pre-eclampsia before term. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD003106.

Drugs for treatment of ver high blood pressure during pregnanc . *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD001449.

Rest during pregnanc for preventing pre-eclampsia and its complications in women with normal blood pressure. *C c a e Databa e f S te atc Re e* Issue 2, Art. No.:CD005939.

Coen me Q10 supplementation during pregnanc reduces the risk of pre-eclampsia. *I t J G aec Ob tet* 105

et a Induction of labour versus e pectant monitoring for gestational h pertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. *La cet* 374

Calcium supplementation during pregnanc for preventing h pertensive disorders and related problems. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.: CD001059 (updated 1 Februar 2010).

Antiplatelet agents for preventing pre-eclampsia and its complications. *C c a e Databa e f S te atc Re e* Issue 2, Art. No.:CD004659.

Magnesium sulphate versus dia epam for eclampsia. *C c a e Databd e f S te atc Re e* Issue 4, Art. No.:CD000127.

Magnesium sulphate versus phen toin for women with eclampsia.

Magnesium sulphate versus l tic cocktail for eclampsia. *C c a e Databa e f S te atc Re e* Issue 3, Art. No.: CD002960.

Magnesium sulphate and other anticonvulsants for women with pre-eclampsia.

Antih pertensive drug therap for mild to moderate h pertension during pregnanc . *C c a e Databa e f S te atc Re e* Issue 1, Art. No.:CD002252.

Oral beta-blockers for mild to moderate h pertension during pregnanc . *C c a e Databa e f S te atc Re e* Issue 3, Art. No.:CD002863.

S stematic review of effect of communit -level interventions to reduce maternal mortalit . *BMC P e ac a d C db t* 9

Saving maternal lives in resource-poor settings: facing realit . *Hea t P c* 89

The cost-effectiveness of fort health interventions in Guinea. *Hea t P c a d Pa* 13

Estimation of potential effects of improved communit -based drug provision, to augment health-facilit strengthening, on maternal mortalit due to post-partum haemorrhage and sepsis in sub-Saharan Africa: an equit -effectiveness model. *La cet* 374

Safe motherhood interventions in low-income countries: an economic justification and evidence of cost effectiveness. *Hea t P c* 53

Mother Bab Package: Implementing Safe Motherhood in countries.

Can skilled attendance at deliver reduce maternal mortalit in developing countries? Safe Motherhood Strategies: a Review of the Evidence. *St d e Hea t Se ce O a at a d P c* 17

Chapter 26. Maternal and perinatal conditions. *D ea e c t te de e c te*

Setting priorities for safe motherhood interventions in resource scarce settings. *Pa e e a ed f t e 2004 P at A cat f A e ca Meet*

Cost effectiveness anal sis of strategies for maternal and neonatal health in developing countries. *BMJ* 331

The costs, benefits and cost-effectiveness of interventions to reduce maternal morbidit and mortalit in Me ico. *PL S O e* 2

Alternative Strategies to Reduce Maternal Mortalit in India: A Cost-Effectiveness Anal sis. *PL S Med* 7(4)

Alma-Ata: Rebirth and revision 6. Interventions to address maternal, newborn, and child survival: what difference can integrated primar health care strategies make. *La cet* 372

Safe motherhood programs: Options and Issues.

Could a simple antenatal package combining micronutritional supplementation with presumptive treatment of infection prevent maternal deaths in sub-Saharan Africa? *BMC P e ac a d C db t* 7

Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. *La cet* 345

Dietar calcium supplementation for prevention of pre-eclampsia and related problems: a s stematic review and commentar . *BJOG* , 114,

Report on confidential enquiries into maternal deaths in England and Wales 1982-84. *De a t e t f Hea t . Re t ea t a d c a bject* 34

Eclampsia in the United Kingdom. *BMJ* 309,

Incidence and predictors of severe obstetric morbidit : case control stud . *BMJ* 322,

Incidence of severe pre-eclampsia, postpartum haemorrhage and sepsis as a surrogate marker for severe maternal morbidit in a European population-based stud : the MOMS-B surve . *BJOG* 112,

Severe maternal morbidit in Canada, 1991–2001. *CMAJ* 173,

Eclampsia in the United Kingdom 2005. *BJOG* , 114,

Severe maternal morbidit during pregnanc , deliver and puerperium in the Netherlands: a nationwide population-based stud of 371 000 pregnancies. *BJOG* 115,

Severe acute maternal morbidit : a pilot stud of a definition of a near miss. *B t J a f Ob tet c a d G aec* 105,

Maternal mortalit and "near-miss" in rural North India. *I te at a J a f G ec & Ob tet c* 68,

Can enquiries into severe acute maternal morbidit act as a surrogate for maternal death enquiries? *B t J a f Ob tet c a d G aec* 110,

Maternal mortalit and associated near-misses among emergenc intrapartum obstetric referrals in Mulago hospital, Kampala, Uganda. *Ea t Af ca Med ca J a* 2003,

Near miss obstetric events and maternal deaths in Sagamu, Nigeria: a retrospective stud . *Re d ct e Hea t* 2,

Obstetric near miss and deaths in public and private hospitals in Indonesia. *B Med Ce t a P e a c a d C db t* 8,

Priorities in emergenc obstetric care in Bolivia – maternal mortalit and near miss morbidit in metropolitan La Pa . *BJOG* 116,

Management of pre-eclampsia. *BMJ* 332,

Responsiveness to life-threatening obstetric emergencies in two hospitals in Abidjan, C te d'Ivoire. *T ca Med c e a d I te at a Hea t* 9,

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