Magnesium sulphate and other anticonvulsants for women with pre-eclampsia (Review)

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ABSTRACT

Background
Pre-eclampsia is a relatively common complication of pregnancy. Eclampsia, the occurrence of one or more convulsions (fits) in association with the syndrome of pre-eclampsia, is a rare but serious complication. Anticonvulsants are used in the belief they help prevent eclamptic fits and so improve outcome.

Objectives
The objective was to assess the effects of anticonvulsants for pre-eclampsia on the women and their children.

Search strategy
We searched the Cochrane Pregnancy and Childbirth Group trials register (28 November 2002), and the Cochrane Controlled Trials Register (The Cochrane Library, Issue 3, 2002).

Selection criteria
Randomised trials comparing anticonvulsants with placebo or no anticonvulsants or comparisons of different anticonvulsants in women with pre-eclampsia.

Data collection and analysis
Two reviewers assessed trial quality and extracted data independently.

Main results
Six trials (11,444 women) compared magnesium sulphate with placebo or no anticonvulsant. There was more than a halving in the risk of eclampsia associated with magnesium sulphate (relative risk (RR) 0.41, 95% confidence interval (CI) 0.29 to 0.58; number needed to treat (NNT) 100, 95% CI 50 to 100). The risk of dying was non-significantly reduced by 46% for women allocated magnesium sulphate (RR 0.54, 95% CI 0.26 to 1.10). For serious maternal morbidity RR 1.08, 95% CI 0.89 to 1.32. Side effects were more common with magnesium sulphate (24% versus 5%; RR 5.26, 95% CI 4.59 to 6.03; NNT for harm 6, 95% CI 6 to 5). The main side effect was flushing. Risk of placental abruption was reduced for women allocated magnesium sulphate (RR 0.64, 95% CI 0.50 to 0.83; NNT 100, 95% CI 50 to 1000). Women allocated magnesium sulphate had a small increase (5%) in the risk of caesarean section (95% CI 1% to 10%). There was no overall difference in the risk of stillbirth or neonatal death (RR 1.04, 95% CI 0.93 to 1.15).

Magnesium sulphate was better than phenytoin for reducing the risk of eclampsia (two trials 2241 women; RR 0.05, 95% CI 0.00 to 0.84), but with an increased risk of caesarean section (RR 1.21, 95% CI 1.05 to 1.41). It was also better than nimodipine (1 trial, 1650 women; RR 0.33, 95% CI 0.14 to 0.77).

Authors' conclusions
Magnesium sulphate more than halves the risk of eclampsia, and probably reduces the risk of maternal death. It does not improve outcome for the baby, in the short term. A quarter of women have side effects, particularly flushing.

PLAIN LANGUAGE SUMMARY

Magnesium sulphate helps prevent eclamptic fits in pregnant women at increased risk

Some women have high blood pressure with protein in their urine during pregnancy (pre-eclampsia). Most women with mild pre-eclampsia give birth without problems. However, severe pre-eclampsia can cause problems with the liver, blood clotting etc, and some women have fits (eclampsia). These problems can cause severe difficulties for the babies. Sometimes mothers and babies die because of these problems, particularly in low-income countries. This review showed magnesium sulphate reduced the number of women having fits but did not improve the babies' health. The magnesium sulphate had side effects for the mother, mostly flushing.

BACKGROUND

Pre-eclampsia is a multisystem disorder that is usually associated with raised blood pressure and proteinuria but, when severe, can involve the woman's liver, kidneys, clotting system, or brain. The placenta is also involved with an increased risk of poor growth and early delivery for the baby. It is a relatively common complication of pregnancy, and can occur at any time during the second half of pregnancy or the first few weeks after delivery.

For many women who have mild pre-eclampsia the outcome is good, but severe disease can lead to death or serious problems for the woman and/or her baby.

Eclampsia, defined as the occurrence of one or more convulsions (fits) in association with the syndrome of pre-eclampsia, is a rare but serious complication. In the UK it is associated with one in 2000 deliveries (Douglas 1994), while in low and middle income countries it complicates between one in 100 and one in 1700 deliveries (WHO 1988). Eclampsia probably accounts for 50,000 deaths a year worldwide, which is about 10% of direct maternal deaths (Duley 1992). One aim of antenatal care is to detect pre-eclampsia in the hope that the onset of serious complications (including eclampsia) can be delayed or prevented. Anticonvulsants were introduced for women with pre-eclampsia in the belief that they would prevent the first fit, and so improve outcome. Predicting who is at risk of an eclamptic fit is difficult, as only around 1 to 2% of those with even very severe pre-eclampsia will fit. This has contributed to the wide variation in policies for prophylactic anticonvulsants (Duley 1994). In the USA, for example, an estimated 5% of pregnant women receive magnesium sulphate before delivery (USA - Texas 1995), whilst in the UK a quarter of obstetricians do not use any prophylactic anticonvulsant and only 40% report using magnesium (Gulmezoglu 1998).

The principal question is whether a policy of using an anticonvulsant for women with pre-eclampsia does more good than harm, to both her and her baby, than a policy of not using an anticonvulsant. A variety of anticonvulsants have been suggested for the care of women with pre-eclampsia but, over the last 10 to 20 years, the most widely used worldwide have been magnesium sulphate, diazepam and phenytoin. Recent evidence places magnesium sulphate as the drug of choice (compared to diazepam or phenytoin) for control of the first fit and for preventing recurrence of convulsions for women with eclampsia (Collab Trial 1995; Duley 2002; Duley 2002a). This has increased interest in its use to prevent the first fit for women with pre-eclampsia. Further impetus to the need for proper evaluation of magnesium sulphate has come from suggestions that for very low birthweight infants (less than 1500 g), or those born before 34 weeks' gestation, it may reduce the risk of cerebral palsy (Nelson 1995) and/or increase the risk of paediatric death (Scudiero 2000; Mittendorf 1998). Others have argued that there is unlikely to be a link between exposure to magnesium sulphate before preterm birth and an increase in mortality (Grether 1998). There are no reliable data on the possible effects on development of term babies.

There are potential hazards associated with the use of magnesium sulphate. Adverse effects may be rare (such as respiratory and cardiac arrest) or subtle (such as impact on developmental of the infant). As magnesium sulphate is thought to be a smooth muscle relaxant, it is also used as a tocolytic to prevent preterm birth for women in threatened preterm labour. If it does relax the smooth muscles in the uterus, although the evidence suggests it does not (Crowther 2003), this might lead to an increase in caesarean section, postpartum haemorrhage or retained placenta. There are also side effects, such as nausea, flushing and muscle weakness, and we need to know more about their frequency and severity. As we do not have any reliable way of predicting who will develop eclampsia, the number of women potentially eligible for anticonvulsant therapy is large. For magnesium sulphate to be worthwhile, it must therefore be very safe as well as effective.

Magnesium sulphate therapy usually starts with an intravenous loading dose. Traditionally this has been 4 g, but 6 g is advocated by some. Therapy is then continued, usually either for 24 hours in total or until 12 to 24 hours after delivery. This maintenance therapy can be either by a series of intramuscular injections, or by an intravenous infusion. The intramuscular maintenance regimen is usually 10 g given with the loading dose, and then 5 g every four hours. The intravenous infusion is usually 1 g/hour, although 2 g/hour is used by some.

Other aspects of the care of women with very high blood pressure or severe pre-eclampsia are covered by other reviews. These include drugs for very high blood pressure (Duley 2002b), plasma vol-

ume expansion (Duley 2002c) and timing of delivery (Churchill 2002). Comparisons of the dose and route of administration for magnesium sulphate will be dealt with in a future review.

OBJECTIVES

The primary aim was to assess the benefits and hazards (for women and their babies) of anticonvulsant therapy when used for women with pre-eclampsia. If anticonvulsant therapy is indeed beneficial, secondary aims were to evaluate the differential effects of the various agents and to evaluate the possible effects of anticonvulsants for women with different levels of severity of pre-eclampsia.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All randomised trials of the administration of an anticonvulsant to women with pre-eclampsia, including trials that compare anticonvulsant with none or with placebo, and trials that compare one drug with another. Quasi randomised trials were excluded.

Types of participants

Any women with pre-eclampsia, regardless of whether before or after delivery, whether a singleton or multiple pregnancy, or whether an anticonvulsant had been given before trial entry. If women with eclampsia had also been entered into the trial, only data for women with pre-eclampsia were included in this review.

As sufficient data are now available, the planned subgroup analysis by severity of pre-eclampsia is now included in the review. Severe pre-eclampsia includes those with two or more signs or symptoms of imminent eclampsia, or blood pressure of at least 170/110 mmHg and 3+ proteinuria or, if on antihypertensive agents, 150/100 mmHg and 2+ proteinuria If the definition of severe pre-eclampsia was not specified, women were still included in this catergory if the authors described them as having severe pre-eclampsia. Women who did not have any of these criteria were classified as not severe pre-eclampsia.

Types of intervention

All randomised comparisons of an anticonvulsant, or other agents used specifically to prevent eclampsia, with placebo (or no anticonvulsant). Also, comparisons of one such drug with another.

Anticonvulsant drugs which have been used for pre-eclampsia include magnesium sulphate, diazepam (valium), phenytoin, nimodipine, and chlormethiazole.

Types of outcome measures

For all women: eclampsia, measures of serious maternal morbidity related to either pre-eclampsia or anticonvulsant use (such as renal failure, cardiac arrest, liver failure, stroke, coagulopathy and respiratory depression), and use of health service resources (such as dialysis, ventilation, admission to intensive care, length of stay).

For women randomised before delivery: induction of labour, length of labour, caesarean section, retained placenta and postpartum haemorrhage.

For the baby: death, measures of serious neonatal morbidity (such as low Apgar scores, intraventricular haemorrhage) and of infant and child development (such as cerebral palsy), use of health service resources (such as admission to special care nursery, ventilation, length of stay in hospital and special needs in the community) and measures of long term development (such as cerebral palsy and serious impairment).

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group trials register (28 November 2002).

The Cochrane Pregnancy and Childbirth Group's trials register is maintained by the Trials Search Co-ordinator and contains trials identified from:
1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. monthly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness search of a further 37 journals.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

In addition, the Cochrane Controlled Trials Register (The Cochrane Library Issue 3, 2002) was searched using the terms pregnan* pre-eclamp* preeclamp* hypertensi* anticonvuls* magnesium sul* diazepam phenytoin.

METHODS OF THE REVIEW

Two reviewers independently assessed for eligibility. Two reviewers independentaly extracted and double entered data. Discrepancies were resolved by discussion. If the two reviewers could not agree, the third reviewer was consulted. There was no blinding of authorship or results. Whenever possible, we sought unpublished data from investigators. We assigned a quality score for concealment of allocation to each trial, using the following criteria:

(A) adequate concealment of allocation;
(B) unclear whether adequate concealment of allocation;
(C) inadequate concealment of allocation.

We excluded quasi-randomised trials, for example those using alternate allocation.

In addition, we assigned to each reported outcome quality scores for completeness of follow up and blinding of the assessment of outcome using the following criteria:

For completeness of follow-up:

(A) less than 3% of participants excluded;
(B) 3% to 9.9% of participants excluded;
(C) 10% to 19.9% of participants excluded.

Excluded: If not possible to enter data based on intention to treat, and/or 20% of participants were excluded from that outcome.

For blinding of assessment of outcome:

(A) Double blind, neither caregiver nor participant knew or were likely to guess the allocated treatment.
(B) Single blind, either the caregiver or the participant knew the allocation. Or, the trial is described as double blind, but side effects of one or other treatment mean that it is likely that for a substantial proportion of participants (greater than 40%) the allocation could be correctly identified.
(C) No blinding, both caregiver and participant knew (or were likely to guess) the allocated treatment; or, blinding not mentioned.

Excluded: no blinding, and the outcomes were very subjective.

We performed statistical analyses using the Review Manager software (RevMan 2000), with results presented as relative risks (RR) and risk difference (RD). From 1/RD the number needed to treat (NNT) for benefits or harm were calculated. For each measure the 95% confidence intervals are given. The fixed effects model was used for calculating relative risk. If there was clear heterogeneity between the studies in any one outcome, a random effects model was used. Possible factors in the heterogeneity were also explored, including study quality, clinical factors as determined by the prespecified subgroup analyses, and the play of chance.

Subgroup analyses for the main outcomes were planned by severity of pre-eclampsia at trial entry (see above for definition), whether delivered or not, gestation at trial entry (above or below 34 weeks), and whether anticonvulsants had already been given. The main outcomes were maternal death, eclampsia, severe maternal morbidity, total fetal and neonatal deaths, and death or serious morbidity for the baby (such as greater than seven days in a special care baby unit). Subgroups by dose and route of administration for magnesium sulphate were planned for maternal death, eclampsia, baby deaths and side effects.

DESCRIPTION OF STUDIES

For a full description of the characteristics of included studies, see table of 'Characteristics of included studies':

Six studies (228 women) were excluded. For three, no clinical outcomes were reported. One used quasi random allocation, one was abandoned due to excess maternal sedation and, in the last, data for women with eclampsia were not reported separately from pre-eclampsia.

Thirteen studies were included. One trial (Magpie Trial 2002) was considerably larger than any others, with 10,141 women recruited. Two other studies had more than 1000 women (USA - Texas 1995; Nimodipine SG 2003), six had 100 to 1000 women (South Africa 1994; South Africa 1998; USA - Maryland 1993; USA - Memphis 1997; USA - Tennessee 2001) and the remaining five studies had less than 100 women (Denmark 2000; Malaysia 1994; Mexico 1992; Taiwan 1995; USA - Alabama 1995).

Most trials used magnesium sulphate for one treatment arm. Six trials (11,444 women) compared magnesium sulphate with placebo or no treatment, three compared it with phenytoin (2295 women), two with diazepam (66 women), and one with nimodipine (1750 women). One trial compared magnesium chloride with methyl dopa (33 women).

In the largest study (Magpie Trial 2002) around half the women used the intravenous route for maintenance therapy of magnesium sulphate (1 g/hour), and the other half used the intramuscular route. The other big study (USA - Texas 1995) used the intramuscular route for maintenance magnesium sulphate therapy, as did two of the smaller studies (Malaysia 1994; South Africa 1994). The remaining studies used the intravenous route. The smaller studies used the intravenous route for magnesium sulphate maintenance therapy. The studies from South Africa (South Africa 1998), Mexico (Mexico 1992), and Taiwan (Taiwan 1995) used a dose of 1g/hour. The USA studies all used a dose of 2 g/hour.

The trials conducted in the USA largely included women with mild to moderate pre-eclampsia. Trials from other parts of the world included women with more severe disease. All of the trials were restricted to women who had not yet given birth, except for the Magpie Trial in which 13% of women were randomised in the 24 hours after delivery.

METHODOLOGICAL QUALITY

The quality of the studies included in this review range from excellent to poor. In the largest study (Magpie Trial 2002), concealment of allocation was secure, and completeness of follow up was 99%. For the other bigger studies the procedure used to conceal allocation was not described in one (USA - Texas 1995) and in two others the procedure used for trial entry did not give secure concealment of allocation (Nimodipine SG 2003; South Africa 1998). In one of these 17% of women were lost to follow up (South Africa 1998). This study also recruited over a long time period, 13+ years. Apart from the Magpie Trial 2002, few studies attempted to blind administration of the allocated treatment. This may be inevitable in comparisons of one agent against another when the monitoring during administration is very different. However, two studies evaluating a single agent did not use a placebo (South Africa 1994; Taiwan 1995). If blinding in the assessment of outcome was not mentioned, it was assumed not to have been done, and this was the case for all the trials that were not placebo controlled.

RESULTS

MAGNESIUM SULPHATE VERSUS PLACEBO OR NO ANTICONVULSANT

Eclampsia

Six trials (11,444 women) compared magnesium sulphate with placebo or no anticonvulsant. Taken together, these studies show more than a halving in the risk of eclampsia associated with the use of magnesium sulphate (RR 0.41, 95% confidence interval (CI) 0.29 to 0.58; risk difference (RD) -0.01 95% CI -0.02 to -0.01, NNT for benefit 100, 95% CI 50 to 100). The relative risk is consistent regardless of severity of pre-eclampsia. For women with severe pre-eclampsia at trial entry: RR 0.37, 95% CI 0.22 to 0.64, RD -0.02, 95% CI -0.03 to -0.01; NNT for benefit 50, 95% CI 34 to 100. For women who did not have severe pre-eclampsia: RR 0.44, RD -0.01, 95% CI -0.01 to -0.00; NNT for benefit 100, 95% CI 100 to 500) It is also consistent regardless of whether the women were antepartum at trial entry, and of gestation at trial entry. The only exception is the small subgroup of women who had another anticonvulsant before trial entry, and this result may reflect the play of chance.

Maternal death

Two trials (10,795 women) reported maternal deaths. The risk of dying was reduced by 46% for women allocated magnesium sulphate rather than placebo or no anticonvulsant, although this did not achieve statistical significance (RR 0.54, 95% CI 0.26 to 1.10). This effect was consistent regardless of severity of pre-eclampsia, whether antepartum at trial entry, gestation at trial entry or whether an anticonvulsant had been given before trial entry.

Maternal morbidity

For the two trials (10,332 women) reporting serious maternal morbidity the relative risk was 1.08 (95% CI 0.89 to 1.32). This lack of evidence for any overall effect was consistent across the subgroups. For the individual measures of serious morbidity, such as pneumonia, renal failure and liver failure, there was also no clear evidence of an overall difference in effect between the two groups. Two trials (10,795 women) reported use of antihypertensive therapy after trial entry. There was a small (3%) reduction in the need for antihypertensive therapy associated with the use of magnesium sulphate rather than placebo or no anticonvulsant (RR 0.97, 95% CI 0.95 to 0.99).

Side effects and toxicity

Toxicity (absent or reduced tendon reflexes and/or respiratory depression) was uncommon, occurring in around 1% of women given magnesium sulphate and 0.5% of those allocated placebo. There was no clear evidence of an overall difference in the risk of absent or reduced tendon reflexes (RR 1.00, 95% CI 0.70 to 1.42). The risk of respiratory depression, or other respiratory problems, was increased for women allocated magnesium sulphate, however (RR 1.98, 95% CI 1.24 to 3.15; RD 0.0049, 95% CI 0.000 to 0.01; NNT for harm 206, 95% CI 1000 to 100)

Side effects were more common amongst women allocated magnesium sulphate rather than placebo or no anticonvulsant (24% versus 5%; RR 5.26, 95% CI 4.59 to 6.03; RD 0.19, 95% CI 0.18 to 0.21; NNT for harm 6, 95% CI 6 to 5). By far the most common side effect was flushing (20% versus 2%). Although other side effects were much less common, all were increased for women allocated magnesium sulphate. Other reported side effects included nausea and/or vomiting, slurred speech, muscle weakness, hypotension (low blood pressure), dizziness, drowsiness or confusion, and headache

Problems at the injection site were also more common for women allocated magnesium sulphate rather than placebo. Problems were more common with intramuscular use in both the active treatment and placebo groups (intramuscular: 12% versus 8%; intravenous 5% versus 2%). For intramuscular use the risk of problems was increased by 1.5 for women allocated magnesium sulphate rather than placebo (RR 1.48, 95% CI 1.25 to 1.79; RD 0.04, 95% CI 0.02 to 0.06; NNT for harm, 25, 95% CI 50 to 17) and for intravenous use it was trebled (RR 3.05, 95% CI 2.15 to 4.32; RD 0.03, 95% CI 0.02 to 0.04; NNT for harm 34, 95% CI 50 to 25).

Complications of pregnancy, labour and delivery

The risk of placental abruption was reduced for women allocated magnesium sulphate rather than placebo (RR 0.64, 95% CI 0.50 to 0.83; RD -0.01, 95% CI -0.02 to 0.00; NNT 100, 95% CI 50 to 1000). The risk of caesarean section was high in both groups (50% versus 47%). For women allocated magnesium sulphate this risk was a little higher (5% increase) than for those allocated placebo or no anticonvulsant (six trials, 10,108 women) (RR 1.05, 95% CI 1.01 to 1.10; RD 0.03, 95% CI 0.01 to 0.04; NNT for harm

34, 95% CI 100 to 25). There was no evidence of a clinically important effect on the need for induction of labour (RR 0.99, 95% CI 0.94 to 1.04). The was no clear evidence of an effect on the risk of postpartum haemorrhage (RR 0.96, 95% CI 0.88 to 1.05) or on manual removal of placenta (RR 0.90, 95% CI 0.72 to 1.12).

Stillbirth and neonatal death

There was no overall difference in the risk of stillbirth or neonatal death (three trials, 9961 women), although a small increase or decrease in mortality associated with the use of magnesium sulphate remains possible (RR 1.04, 95% CI 0.93 to 1.15). The result is consistent regardless of gestation at trial entry. For the composite outcome of death or in special care baby unit there is no clear evidence of a clinically important difference (RR 1.01, 95% CI 0.95 to 1.08).

Neonatal morbidity

There was no clear evidence of a difference in neonatal morbidity between the two groups, for example admission to special care baby unit (RR 1.01, 95% CI 0.96 to 1.06), admission to special care baby unit for more than seven days (RR 1.02, 95% CI 0.93 to 1.11), intubation at the place of delivery (RR 1.01, 95% CI 0.82 to 1.24).

MAGNESIUM SULPHATE VERSUS PHENYTOIN

Two trials (2241 women) compared magnesium sulphate with phenytoin. Magnesium sulphate appears to be better than phenytoin at reducing the risk of eclampsia (RR 0.05, 95% CI 0.00 to 0.84; RD 0.009, 95% CI -0.015 to 0.003; NNT 111, 95% CI 67 to 333), although the number of events is small (0 versus 10), and the summary statistic is not robust (see above). However, there is an increase in the risk of caesarean section associated with the use of magnesium sulphate rather than phenytoin (RR 1.21, 95% CI 1.05 to 1.41; RD 0.048, 95% CI 0.012 to 0.084; NNT for harm 21 95% CI 83 to 12). There is no information on other important measures of maternal morbidity. Also, the confidence intervals for estimates of the differential effects on measures of morbidity and mortality for the baby are all wide and cross the no effect line.

MAGNESIUM SULPHATE VERSUS DIAZEPAM

The two trials (66 women) comparing magnesium sulphate with diazepam are too small for any reliable conclusions about their differential effects.

MAGNESIUM SULPHATE VERSUS NIMODIPINE

One trial compared magnesium sulphate with nimodipine (1650 women). The risk of eclampsia was lower for women allocated magnesium sulphate rather than nimodipine (0.8% versus 2.6%; RR 0.33, 95% CI 0.14 to 0.77; RD -0.02, 95% CI -0.03 to -0.00; NNT for benefit with magnesium sulphate 50, 95% CI 34 to 1000). The only other clear differences were an increase in respiratory problems associated with magnesium sulphate compared to nimodipine (1.3% versus 0.4%; RR 3.61, 95% CI 1.01 to 12.91), and a greater need for additional antihypertensive drugs associated with magnesium sulphate rather than nimodipine (54% versus 46%, RR 1.19, 95% CI 1.08 to 1.31).

Mortality for the baby is not reported. There was no evidence of any clear differences in morbidity between the two regimens.

MAGNESIUM SALTS VERSUS METHYL DOPA

One trial compared magnesium chloride with nimodipine (31 women) and it was too small for any reliable conclusions about potential differential effects.

DISCUSSION

Over 11,000 women have been randomised into trials comparing an anticonvulsant with none, and for all these studies the anticonvulsant evaluated was magnesium sulphate. Magnesium sulphate is associated with a halving in the risk of eclampsia, and it seems likely that there is also a clinically important reduction in the risk of maternal death. There is no clear evidence that these benefits are reflected in any reduction in other measures of serious maternal morbidity, or any substantive effect on stillbirth or neonatal mortality. A small increase or decrease in mortality for the baby associated with the use of magnesium sulphate has not been excluded, although the lack of any effect on the composite outcome of death or in special care nursery for more than seven days provides additional reassurance. The only other effects are that there appears to be a reduction in the risk of placental abruption associated with magnesium sulphate, and a small increase (5%) in the risk of caesarean section.

The reduction in placental abruption is not reflected in any overall effect on mortality or morbidity for the baby. This is not surprising, as the number of women who had a placental abruption was small, even in the placebo group. The difference between the groups in the number with a placental abruption was 49 women. Even a moderate impact, for example a 15% reduction in morality, would only represent seven deaths and would therefore be unlikely to influence the overall mortality.

Longer term follow up of the children is required to provide reassurance that the short term safety continues into childhood.

The halving of the risk of eclampsia is consistent across the subgroups. In particular the reduction in relative risk is similar regardless of severity of pre-eclampsia. As eclampsia is more common amongst women with severe pre-eclampsia than amongst those with moderate or mild pre-eclampsia, the number of women who would need to be treated to prevent one case of eclampsia is greater for non-severe pre-eclampsia. Few women in this review had mild pre-eclampsia, and the non-severe category primarily includes women with moderate disease. The number needed to treat is likely to be considerably higher for mild pre-eclampsia.

About a quarter of women will report side effects associated with magnesium sulphate, but the vast majority of these are flushing. Almost all the data on side effects and safety come from studies that used either the intramuscular regimen for maintenance therapy, or the intravenous route with 1 g per hour, and for around 24 hours. The use of higher doses and longer duration cannot be supported by these data. In particular, the reassurance about safety and lack of serious side effects cannot be extrapolated to higher doses or longer duration of therapy.

For most of the women in the comparison of magnesium sulphate with placebo or no anticonvulsant, the magnesium sulphate regimen was administered by the local hospital staff within their normal clinical practice, and without serum monitoring. Clinical monitoring of respiration, tendon reflexes and urine output was used for the majority of women.

The comparisons of one anticonvulsant with another provide further evidence that magnesium sulphate is the anticonvulsant of choice for women with pre-eclampsia.

AUTHORS' CONCLUSIONS

Implications for practice

Magnesium sulphate should be considered for women with pre-eclampsia for whom there is concern about the risk of eclampsia. As it is an inexpensive drug, it is especially suitable for use in low income countries. Intravenous administration is preferable, where there are appropriate resources, as side effects and injection site problems seem lower. Duration of treatment should not normally exceed 24 hours, and if the intravenous route is used for maintenance therapy the dose should not exceed 1 g/hour. Serum monitoring is not necessary. Administration and clinical monitoring of magnesium sulphate can be done by medical, midwifery or nursing staff, provided they are appropriately trained.

The trials in this review included women only after admission to hospital. Whether a loading dose of magnesium sulphate should be used for women at primary care level before they are transferred to hospital is unclear. Other factors in this decision are likely to include how long it will take to get the woman to hospital, the support that is available during transfer, and severity of her pre-eclampsia.

Implications for research

Remaining questions about the use of magnesium sulphate include what is the minimum effective dose; when is the optimal time to give it; should it be used at primary care level for women being transferred for secondary or tertiary care; is it cost effective; and what are the long term consequences of exposure for the mother and her child. Data on outcome after disharge from hospital and cost effectiveness will be available in one to two years from the Magpie Trial (Magpie Trial 2002). Any new agents for eclampsia prophylaxis should be compared in large randomised trials with magnesium sulphate.

FEEDBACK

Alford, February 2004

Summary

Pre-eclampsia can be prevented if the mother is checked for reverse T3 hypothyroidism and treated properly with liothyronine (Cytomel--T3). It normalizes the incubator temperature and prevents the hypotension that leads to the pre-eclampsia.

Author's reply

A reply from the authors will be published as soon as it is available.

Contributors

Comment received from RM Alford, February 2004.

POTENTIAL CONFLICT OF INTEREST

Lelia Duley is a principal investigator for the Magpie Trial, which compared magnesium sulphate with placebo.

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None.

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REFERENCES

References to studies included in this review

Denmark 2000 *{published data only}*

Rudnicki M, Frolich A, Pilsgaard K, Nyrnberg L, Moller M, Sanchez M, et al. Comparison of magnesium and methyl dopa for the control of blood pressure in pregnancies complicated with hypertension. *Gynecologic and Obstetric Investigation* 2000;**49**:231–5.

Magpie Trial 2002 *{published and unpublished data}*

Bricker L, Magpie Trial Collaborative Group. The Magpie Trial: magnesium sulphate versus placebo for women with pre-eclampsia. XVI FIGO World Congress of Obstetrics and Gynecology; 2000 Sept 3-8; Washington DC, USA 2000;Book 2:47.

Duley L, Campbell L. The Magpie Trial: magnesium sulphate for pre-eclampsia, evaluating the effects on women and their babies. *MIDIRS Midwifery Digest* 1999;**9**:48–51.

Duley L, Magpie Trial Collaborative Group. The Magpie Trial: magnesium sulphate versus placebo for women with pre-eclampsia. *Hypertension in Pregnancy* 2000;**19**(Suppl 1):63.

Duley L, Neilson JP. Magnesium sulphate and pre-eclampsia. Trial needed to see whether it's as valuable in pre-eclampsia as in eclampsia. *BMJ* 1999;**319**:3–4.

Duley L, Watkins K. Magnesium sulphate for treatment of pre-eclampsia: a trial to evaluate the effects on women and their babies. *Contemporary Reviews in Obstetrics and Gynaecology* 1998;**10**(4):267–74.

* Magpie Trial Collaborative Group. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial. *Lancet* 2002;**359**:1877–90.

Moodley J, Magpie Trial Collaborative Group. The Magpie Trial: magnesium sulphate versus placebo for women with pre-eclampsia. Women's Health - into the new millenium. Proceedings of the 4th International Scientific Meeting of the Royal College of Obstetricians and Gynaecologists; 1999 October 3-6; Cape Town, South Africa, 1999:25.

Malaysia 1994 *{published and unpublished data}*

Adeeb N, Hatta AZ, Shariff J. Comparing magnesium sulphate to diazepam in managing severe pre-eclampsia and eclampsia. 10th World Congress of the International Society for the Study of Hypertension in Pregnancy; 1996 August 4-8; Seattle, Washington, USA, 1996: 246.

Adeeb N, Ho CM. Comparing magnesium sulphate versus diazepam in the management of severe pre-eclampsia and eclampsia. 9th International Congress of the International Society for the Study of Hypertension in Pregnancy; 1994 March 15-18; Sydney, Australia; 1994:38.

Mexico 1992 *{published data only}*

Walss Rodriguez RJ, Levario AR. Anticonvulsant treatment of severe pre-eclampsia: comparison of diazepam and magnesium sulfate. *Ginecologia y Obstetricia de Mexico* 1992;**60**:331–5.

Nimodipine SG 2003 *{published data only}*

Belfort M, Anthony J, Saade G, Nimodipine Study Group. Interim report of the nimodipine vs. magnesium sulfate for seizure prophylaxis in severe preeclampsia study: an international randomized controlled trial. *American Journal of Obstetrics and Gynecology* 1998;**178** (1 Pt 2):S7.

Belfort M, Saade G, Yared M, Abedejos P, Dorman K. Change in estimated cerebral perfusion pressure following nimodipine or magnesium sulfate in patients with severe preeclampsia. *American Journal of Obstetrics and Gynecology* 1998;**178**:S114.

* Belfort MA, Anthony J, Saade GR, Allen JC, for the Nimodipine Study Group. A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia. *New England Journal of Medicine* 2003;**348**:304–11.

Belfort MA, Saade GR, Yared M, Grunewald C, Herd A, Varner MA, et al. Change in estimated cerebral perfusion pressure after treatment with nimodipine or magnesium sulfate in patients with pre-eclampsia. *American Journal of Obstetrics and Gynecology* 1999;**181**:402–7.

South Africa 1994 *{published data only}*

Moodley J, Moodley J. Prophylactic anticonvulsant therapy in hypertensive crises of pregnancy - the need for a large randomized trial. *Hypertension in Pregnancy* 1994;**13**:245–52.

South Africa 1998 *{published data only}*

Anthony J, Rush R. A randomised controlled trial of intravenous magnesium sulphate versus placebo. *British Journal of Obstetrics and Gynaecology* 1998;**105**:809–10.

* Coetzee E, Dommisse J, Anthony J. A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre-eclampsia. *British Journal of Obstetrics and Gynaecology* 1998;**105**:300–3.

Coetzee E, Dommisse J, Anthony J. Are anticonvulsants necessary in the management of severe gestational proteinuric hypertension. *International Journal of Gynaecology and Obstetrics* 1994;**46**:121.

Coetzee E, Dommisse J, Anthony J. The prediction and prevention of seizures in 571 patients with severe pre-eclampsia. 10th World Congress of the International Society for the Study of Hypertension in Pregnancy; 1996 August 4-8; Seattle, Washington, USA, 1996: 124.

Coetzee EJ, Anthony J, Dommisse AJ. Does magnesium sulphate prevent eclampsia in severe gestational proteinuria hypertension. *Prenatal and Neonatal Medicine* 1996;**1**(Suppl 1):9.

Coetzee EJ, Dommisse AJ. Eclampsia: not a preventable disease in the South African context. Proceedings of the 13th conference on Prioirities in Perinatal Care; 1994; South Africa, 1994:3-5.

Moodley J, Pattinson RC, Hofmeyr GJ. A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre-eclampsia [letter; comment]. *British Journal of Obstetrics and Gynaecology* 1999;**106**(3):289–90.

Woods D, Anthony J, Dommisse J, Coetzee E. Can magnesium sulphate before delivery reduce the risk of hypoxic-ischaemic en-

cephalopathy. Proceedings of the 15th Conference on Priorities in Perinatal Care in South Africa; March 5-8; Goudini Spa, South Africa, 1996.

Taiwan 1995 *{published data only}*

Chen FP, Chang SD, Chu KK. Expectant management in severe preeclampsia: does magnesium sulfate prevent the development of eclampsia. *Acta Obstetricia et Gynecologica Scandinavica* 1995;**74**: 181–5.

USA - Alabama 1995 *{published data only}*

* Atkinson MW, Guinn D, Owen J, Hauth JC. Does magnesium sulfate affect the length of labor induction in women with pregnancy-associated hypertension?. *American Journal of Obstetrics and Gynecology* 1995;**173**:1219–22.

Atkinson MW, Guinn D, Owen J, Hauth JC. Does magnesium sulfate prolong labor induction in women with gestational hypertension?. *American Journal of Obstetrics and Gynecology* 1995;**172**:384.

USA - Maryland 1993 *{published data only}*

* Friedman SA, Lim KH, Baker C, Repke JT. Phenytoin vs magnesium sulfate in preeclampsia: a pilot study. *American Journal of Perinatology* 1993;**10**:233–8.

Friedman SA, Lim KH, Baker CA, Repke JT. A comparison of phenytoin infusion versus magnesium sulphate infusion in preeclampsia. Proceedings of the 10th annual meeting of the Society of Perinatal Obstetricians; 1990; Houston, Texas, USA, 1990:16.

Repke JT, Friedman SA, Lim KH, Baker CA. Magnesium sulfate vs phenytoin in preeclampsia: preliminary results from a randomized clinical trial. Proceedings of 9th Annual Meeting of the Society of Perinatal Obstetricians; 1989 Feb 1-4; New Orleans, Louisiana, USA, 1989:123.

USA - Memphis 1997 *{published data only}*

Witlin A, Friedman S, Sibai B. The effect of magnesium sulfate therapy on the duration of labor in women with mild preeclampsia at term: a randomized double-blind, placebo-controlled trial. *American Journal of Obstetrics and Gynecology* 1997;**176**(1 Pt 2):S15.

* Witlin AG, Friedman SA, Sibai BM. The effect of magnesium sulfate therapy on the duration of labor in women with mild preeclampsia at term: a randomized, double-blind, placebo-controlled trial. *American Journal of Obstetrics and Gynecology* 1997;**76**:623–7.

USA - Tennessee 2001 *{published data only}*

Livingston J, Livingston L, Mabie B, Sibai B. The efficacy of magnesium sulfate in women with mild preeclampsia: a double blinded placebo controlled trial. *Hypertension in Pregnancy* 2002;**20**(Suppl 1):42.

Livingston J, Livingston L, Ramsey R, Kao L, Mabie B, Sibai B. Magnesium sulfate in women with mild preeclampsia: a double blind placebo controlled trial. *American Journal of Obstetrics and Gynecology* 2001;**185**(Suppl 6):S75.

* Livingston JC, Livingston LW, Ramsey R, Mabie BC, Sibai BM. Magnesium sulfate in women with mild preeclampsia: a randomised controlled trial. *Obstetrics and Gynecology* 2003;**101**(2):217–20.

USA - Texas 1995 *{published data only}*

Leveno KJ, Alexander JM, McIntire DD, Lucas MJ. Does magnesium sulfate given for the prevention of eclampsia affect the outcome of labor?. *American Journal of Obstetrics and Gynecology* 1998;**178**:707–12.

* Lucas MJ, Leveno KJ, Cunningham MD. A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. *New England Journal of Medicine* 1995;**333**:201–5.

References to studies excluded from this review

China 2000

Dianrong S, Lirong Y, Yinglin L. A comparison of phentolamine and magnesium sulphate in pre-eclampsia. *International Journal of Gynecology and Obstetrics* 2000;**68**:259–60.

South Africa 1996

Payne AJ, Naidu S, Moodley J, Hoffmann M, Gouws F. Non-invasive assessment of the maternal cerebral circulation by transcranial doppler ultrasound in the hypertensive crises of pregnancy. *American Journal of Obstetrics and Gynecology* 1996;**174**:320.

Tanzania 1994

Ramsay M, Rimoy G, Rubin P. Are anticonvulsants necessary to prevent eclampsia? Proceedings of the 9th International Congress of the International Society for the Study of Hypertension in Pregnancy; 1994 March 15-18; Sydney, Australia, 1994:279.

Ramsay MM, Rimoy GH, Rubin PC. Are anticonvulsants necessary to prevent eclampsia. *Lancet* 1994;**343**:540–1.

UK 1989

Slater RM, Wilcox FL, Smith WD, Maresh M. Phenytoin in pre-eclampsia. *Lancet* 1989;**ii**:1224–5.

USA - Texas 1991

Appleton M, Kuehl T, Raebel M, Adams H, Pickens J, Koops B, et al. Magnesium sulfate vs. phenytoin in pregnancy-induced hypertension. *American Journal of Obstetrics and Gynecology* 1991;**164**:273.

Appleton MP, Kuehl TJ, Raebel MA, Adams HR, Knight AB, Gold WR. Magnesium sulfate versus phenytoin for seizure prophylaxis in pregnancy-induced hypertension. *American Journal of Obstetrics and Gynecology* 1991;**165**:907–13.

USA - Texas 1992

Belfort MA, Moise KJ. Effect of magnesium sulfate on maternal brain blood flow in preeclampsia: a randomized, placebo-controlled study. *American Journal of Obstetrics and Gynecology* 1992;**167**:661–6.

Belfort MA, Moise KJ, Saade G. The effect of magnesium sulfate on maternal retinal blood flow in pregnancy-induced hypertension: a randomized placebo-controlled study. Proceedings of 39th Annual Meeting of the Society for Gynecologic Investigation; 1992; San Antonio, USA, 1992:233.

Belfort MA, Saade GR, Moise KJ. The effect of magnesium sulfate on maternal retinal blood flow in preeclampsia: a randomized placebo-controlled study. *American Journal of Obstetrics and Gynecology* 1992; **167**:1548–53.

References to studies awaiting assessment

Rudnicki 1990

Rudnicki M, Junge J, Frolich A, Ornvold K, Fischer-Rasmussen W. Magnesium supplement in pregnancy-induced hypertension. A clinicopathological study. *APMIS* 1990;**98**:1123–7.

Rudnicki 1991
Rudnicki M, Frolich A, Rasmussen WF, McNair P. The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. *Acta Obstetricia et Gynecologica Scandinavica* 1991;**70**:445–50.

Additional references

Churchill 2002
Churchill D, Duley L. Interventionist versus expectant care for severe pre-eclampsia before term (Cochrane Review). *The Cochrane Library* 2002, Issue 3.

Collab Trial 1995
The Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the Collaborative Eclampsia Trial. *Lancet* 1995;**345**:1455–63.

Crowther 2003
Crowther CA, Hiller JE, Doyle LW. Magnesium sulphate for preventing preterm birth in threatened preterm labour (Cochrane Review). *The Cochrane Library* 2003, Issue 1. Art. No.: CD001060. DOI:10.1002/14651858.CD001060.

Douglas 1994
Douglas KA, Redman CWG. Eclampsia in the United Kingdom. *BMJ* 1994;**309**:1395–400.

Duley 1992
Duley L. Maternal mortality associated with hypertensive disorders of pregnancy in Africa, Asia, Latin America and the Caribbean. *British Journal of Obstetrics and Gynaecology* 1992;**99**:547–53.

Duley 1994
Duley L, Johanson R. Magnesium sulphate for pre-eclampsia and eclampsia: the evidence so far. *British Journal of Obstetrics and Gynaecology* 1994;**101**:565–7.

Duley 2002
Duley L, Henderson-Smart D. Magnesium sulphate versus diazepam for eclampsia (Cochrane Review). *The Cochrane Library* 2002, Issue 3. Art. No.: CD000127. DOI:10.1002/14651858.CD000127.

Duley 2002a
Duley L, Henderson-Smart D. Magnesium sulphate versus phenytoin for eclampsia (Cochrane Review). *The Cochrane Library* 2002, Issue 3. Art. No.: CD000128. DOI:10.1002/14651858.CD000128.

Duley 2002b
Duley L, Henderson-Smart D. Drugs for rapid treatment of very high blood pressure during pregnancy (Cochrane Review). *The Cochrane Library* 2002, Issue 3.

Duley 2002c
Duley L, Henderson-Smart DJ. Plasma volume expansion (Cochrane Review). *The Cochrane Library* 2002, Issue 3.

Grether 1998
Grether JK, Hoogstrate J, Selvin S, Nelson KB. Magnesium sulphate tocolysis and risk of neonatal death. *American Journal of Obstetrics and Gynecology* 1998;**178**:1–6.

Gulmezoglu 1998
Gülmezoglu M, Duley L. Use of anticonvulsants in eclampsia and pre-eclampsia: survey of obstetricians in the United Kingdom and the Republic of Ireland. *BMJ* 1998;**316**:975–6.

Mittendorf 1998
Mittendorf R, Covert R, Boman J, Khoshnood B, Kwang-Sun L, Siegler M. Is tocolytic magnesium sulphate associated with increased total paediatric mortality?. *Lancet* 1997;**350**:1517–8.

Nelson 1995
Nelson KB, Grether JK. Can magnesium sulfate reduce the risk of cerebral palsy in very low birthweight infants?. *Pediatrics* 1995;**95**:263–9.

Scudiero 2000
Scudiero R, Khoshnood B, Pryde PG, Lee KS, Wall S. Perinatal death and tocolytic magnesium sulfate. *Obstetrics and Gynecology* 2000;**96**:178–82.

WHO 1988
World Health Organization International Collaborative Study of Hypertensive Disorders of Pregnancy. Geographic variation in the incidence of hypertension in pregnancy. *American Journal of Obstetrics and Gynecology* 1988;**158**:80–3.

References to other published versions of this review

Duley 2003
Duley L, Gülmezoglu AM, Henderson-Smart DJ. Anticonvulsants for women with pre-eclampsia (Cochrane Review). *The Cochrane Library* 2003, Issue 1.

* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	Denmark 2000
Methods	Numbered sealed opaque envelopes. 2 exclusions from MgSO4 group (1 withdrawal, 1 had methyl dopa).
Participants	33 nulliparous women with singleton pregnancy and BP > 140/90 mmHg x 2 over 3 hr. Excluded: pre-existing HT, cardiac or renal disease, BP > 180/120 mmHg after hydralazine.

Characteristics of included studies (*Continued*)

Interventions	MgCl2: 80 mmol IV in first 24 hr, then 40 mmol in next 24 hr. Then 15 mmol/day MgOH2 orally until 3 days after delivery. Methyl dopa: 250 mg x 4/day. Day after delivery reduced by 250 mg/day.
Outcomes	Women: additional antihypertensive. Baby: admission to SCBU.
Notes	
Allocation concealment	A – Adequate

Study	**Magpie Trial 2002**
Methods	Either minimisation via central telephone service (2037 women), or consecutively numbered, sealed treatment packs, stratified by centre (8104 women). Computer generated allocation sequence. 5 women excluded: 2 each group no data available, 1 in MgSO4 group entered into wrong trial. Recruitment stopped early following interim analysis.
Participants	10141 women with uncertainty about whether to use MgSO4, before birth or 24 hours postpartum, DBP >/= 90 mmHg, SBP >/= 140 mmHg x 2 30-30 min apart, .>/= 1+ proteinuria. Excluded: hypersensitivity to Mg, hepatic coma with risk of renal failure, myasthenia gravis.
Interventions	MgSO4: 4 g IV bolus. Then either 1 g/hr iv infusion or 10 g im with bolus followed by 5 g every 4 hr. Continued for 24 hr. 2 centres in Bangladesh used 5 g im then 2.5 g every 4 hr. Placebo: by identical regimen. Dose halved if oliguria. Clinical monitoring alone for all women.
Outcomes	Woman: death, eclampsia, respiratory depression, pneumonia, cardiac arrest, renal failure, coagulopathy, liver failure, pulmonary oedema, stroke, side effects, caesarean section, postpartum haemorrhage, transfusion, admission to high care. Baby: death, gestation at birth, Apgar < 7 at 5 min, intubation at place of delivery, ventilation, admission SCBU, death or SCBU > 7 days.
Notes	Multicentre trial, 175 centres in 33 countries. 85% recruitment in middle-low income countries. In MgSO4, 4999 women received allocated treatment, in placebo group 4993 women. Not known whether anticonvulsant before trial entry for 26 MgSO4 and 37 placebo. Outcome at delivery and for the baby only included for women randomised before birth.
Allocation concealment	A – Adequate

Study	**Malaysia 1994**
Methods	Consecutive sealed envelopes, no other information.
Participants	28 women with PE (DBP > 110mmHg + proteinuria) and 11 women with eclampsia (data not included in this review).
Interventions	MgSO4: 'Pritchard's regimen', no other information. Diazepam: not stated.
Outcomes	Woman: death, eclampsia, caesarean section. Baby: death.
Notes	Interim data on an ongoing study, published in abstract form only. Additional information from verbal presentation.
Allocation concealment	B – Unclear

Characteristics of included studies (*Continued*)

Study	**Mexico 1992**
Methods	Numbered opaque envelopes, no other information.
Participants	38 women > 28 weeks gestation with SBP >/= 150 mmHg, DBP >/= 110 mmHg, proteinuria 2+, no previous treatment, at least one symptom (of headache, blurred vision, epigastric pain) and no epilepsy.
Interventions	MgSO4: 4 g IV over 15 min, then 1 g/hr infusion. Diazepam: 30 mg in 500 ml 5% glucose IV at 60 microg/hr. If convulsions, bolus of 10 mg IV.
Outcomes	Woman: eclampsia, caesarean section. Baby: mean Apgar scores (1 and 5 min).
Notes	Nifedipine for BP control.
Allocation concealment	B – Unclear

Study	**Nimodipine SG 2003**
Methods	Randomisation stratified by centre, blocks of 6. Sealed opaque envelopes. Recruitment 1995-2000. 100 women (6%) excluded from analysis: 99 did not get allocated treatment, 1 withdrawn. Recruitment stopped early following interim analysis.
Participants	1750 women with PE, planned delivery and no previous MgSO4. BP >/=140/90 and 1+ proteinuria plus one of: headache, clonus, visual disturbance, epigastric pain, oliguria, pulmonary oedema, raised liver enzymes, haemolysis, oligohydramnios, IUGR.
Interventions	Nimodipine: 60 mg 4 hrly, orally. MgSO4: according to local protocol. Either 4 g iv then 1 g/hr, or 6 g iv then 2 g/hr. All continued either for 24 hr total, or until 24 hr after delivery. Serum monitoring not required.
Outcomes	Woman: eclampsia, stroke, coagulopathy, respiratory problems, cardiac failure, antihypertensive drugs, side effects, abruption, caesarean section, PPH. Baby: RDS, hypotonia, intubation, hypotension.
Notes	Recruitment at 14 hospitals in 8 countries. Data for stillbirths and neonatal deaths not reported.
Allocation concealment	B – Unclear

Study	**South Africa 1994**
Methods	Consecutively numbered sealed opaque envelopes.
Participants	228 women with severe PE: DBP >/= 110 mmHg for 4-6 hours, proteinuria +, and delivery imminent. Excluded if prior anticonvulsant (except phenobarbitone) or antihypertensive.
Interventions	MgSO4: 4 g IV over 20 min and 10 g IM (5 g into each buttock), then 5 g 4 hourly for 24 hours. Control: no anticonvulsant.
Outcomes	Woman: eclampsia, pulmonary oedema, renal failure, caesarean section. Baby: death (stillbirth, neonatal death).
Notes	For both groups, immediate BP control with dihydralazine (69%) or nifedipine (25%). Most women had phenobarbitone before entry.
Allocation concealment	A – Adequate

Study	**South Africa 1998**
Methods	Allocation by sealed opaque envelopes containing card marked solution A or B. Cards, but not envelopes, consecutively numbered. Envelopes distributed in batches of 20, with equal numbers of A and B. Solutions prepared by pharmacy, and identity of A and B changed periodically. 123 excluded as envelopes and data sheets

	lost. Review of hospital records suggests no eclampsia amongst these women. Further 14 post randomisation exclusions (4 delivered before treatment, 3 no solution available, 4 MgSO4 before entry, 2 no consent, 1 anuric). None had eclampsia.
Participants	822 women with severe PE: at least 2 of DBP >/= 110 mmHg, significant proteinuria, symptoms of imminent eclampsia. Also, > 16 years, no previous anticonvulsant (except clonazepam).
Interventions	MgSO4: 4 g IV in 200 ml saline over 20 min, then Ig/hr (200 ml over 4 hr) until 24 hr after delivery. Placebo: 200 ml over 20 min, then 200 ml over 4 hours until 24 hr after delivery. Treatment stopped if urine output < 30 ml/hr. Serum monitoring not required.
Outcomes	Woman: death, eclampsia, toxicity, antihypertensive therapy, caesarean section. Child: stillbirths.
Notes	All women given clonazepam 1 mg. Recruitment over 13 years, 1982-95.
Allocation concealment	C – Inadequate

Study	**Taiwan 1995**
Methods	'Randomised', no other information.
Participants	64 women with BP >/= 150/100 mmHg, plus at least one of 11 listed features of severe PE. Excluded if intrauterine death, chronic hypertension or eclampsia.
Interventions	MgSO4: 4 g IV over 10 min, then 1 g/hr until 24 hours after delivery. Control: no anticonvulsant.
Outcomes	Women: eclampsia, caesarean section, abruption. Baby: Apgar score (1 min).
Notes	8 women excluded, probably before randomisation but this is not completely clear. Women less than 34 weeks (32/64) managed conservatively, and duration of MgSO4 therapy not clear.
Allocation concealment	B – Unclear

Study	**USA - Alabama 1995**
Methods	'Blinded computer-generated random number tables'.
Participants	54 women with singleton pregnancy requiring medical induction of labour for PIH, and with an unfavourable cervix.
Interventions	MgSO4: 4 g IV and then an infusion of 2 g/hr. Phenytoin: 15 mg/kg IV over 2 hours, then 200 mg IV every 8 hours.
Outcomes	Woman: caesarean section, mean length of labour. Baby: mean Apgar scores, cord pH.
Notes	
Allocation concealment	B – Unclear

Study	**USA - Maryland 1993**
Methods	Sealed opaque envelopes, sequence generated from random number table.
Participants	103 women with BP >/= 140/90 mmHg or rise in SBP of >/= 30 mmHg, or rise in DBP of >/= 15 mmHg, plus either >/= + proteinuria , or significant oedema, or eclampsia. Also, 2 women with eclampsia (data not included in this review). Excluded if MgSO4 before admission, history of seizure disorder, cardiac arrhythmia, phenytoin sensitivity or myasthenia gravis.
Interventions	MgSO4: 6 g IV, then infusion of 2 g/hr. Mg levels every 6 hours.

Characteristics of included studies (*Continued*)

	Phenytoin: 1000, 1250 or 1500 mg, depending on weight. Serum levels 1-2 hours later to determine next dose (0-500 mg), once stable checked every 12 hours. Both regimens continued for 24 hours after delivery.
Outcomes	Woman: eclampsia. No other outcomes reported separately for women with pre-eclampsia and eclampsia. Baby: none reported.
Notes	12 post randomisation exclusions because twin pregnancy (8 women), no medical record (1), and lost envelopes (3).
Allocation concealment	B – Unclear

Study	**USA - Memphis 1997**
Methods	Sealed, sequentially numbered opaque envelopes.
Participants	135 women who were at least 37 weeks gestation with recent onset PE (BP >/= 140/90 mmHg and proteinurea >/= 300 mg in 24 hr). Excluded if severe PE, fetal malpresentation, congenital anomalies, nonreassuring fetal testing, contraindication to trial of labour.
Interventions	MgSO4: 6 g IV bolus over 15-20 min, then infusion of 2 g/hr. Continued until 12 hr post partum. Placebo: saline solution administered by an identical regimen.
Outcomes	Woman: duration of labour, use of oxytocin, caesarean, post partum haemorrhage, infection, side effects, severe pre-eclampsia. Baby: Apgar.
Notes	64% of women had labour induced, and 91% had an epidural.
Allocation concealment	A – Adequate

Study	**USA - Tennessee 2001**
Methods	'Randomised placebo controlled trial'. No further information.
Participants	222 women with mild pre-eclampsia during labour. Excluded: chronic HT, severe PE.
Interventions	MgSO4: 6 g IV, then infusion of 2 g/hr. Placebo: matching regimen. Clinical monitoring.
Outcomes	Women: progression to severe PE, eclampsia, HELLP, caesarean section, toxicity. Baby: meconium.
Notes	Abstract only. 33 women who progressed to severe pre-eclampsia were unblinded and given MgSO4.
Allocation concealment	B – Unclear

Study	**USA - Texas 1995**
Methods	Numbered opaque envelopes, no other information.
Participants	2138 women with BP >/= 140/90 mmHg. Excluded if postpartum or delivery imminent, epilepsy, or eclampsia.
Interventions	MgSO4: 10 g (50% solution) IM (5 g in each buttock), then 5 g IM every 4 hours. If severe pre-eclampsia, an additional 4 g IV (20% solution) before the first IM dose. Phenytoin: 1000 mg IV over 1 hour. 10 hours later, 500 mg orally. If eclampsia developed, all women received MgSO4.
Outcomes	Woman: eclampsia, caesarean section, induction of labour.

	Baby: death (stillbirth, neonatal death), Apgar score, admission to special care baby unit.
Notes	Only 18% of women had 2+ or more proteinuria, and 4% received an antihypertensive. Of the 1049 women allocated phenytoin, 17 also received MgSO4, and 139 did not receive it because of 'logistic' problems (not clear if these women had MgSO4 instead). No reporting of compliance for those allocated MgSO4.
Allocation concealment	C – Inadequate

BP: blood pressure
DBP: diastolic BP
hr: hour
hrly: hourly
IM: intramuscular
IV: intravenous
Mg: magnesium
MgSO4: magnesium sulphate
min: minute
PE: pre-eclampsia
PIH: pregnancy induced hypertension
SBP: systolic BP
SCBU: special care baby unit
PPH: postpartum haemorrhage
RDS: respiratory distress syndrome

Characteristics of excluded studies

Study	Reason for exclusion
China 2000	No clinical outcomes reported. Participants: 84 women with PE at 34-42 weeks. Interventions: magnesium sulphate vs phentolamine.
South Africa 1996	No clinical outcomes reported. Outcome for women with eclampsia not reported separately to pre-eclampsia. Participants: 24 women with eclampsia (also in Collaborative Eclampsia Trial) and 18 with pre-eclampsia. Interventions: magnesium sulphate versus phenytoin.
Tanzania 1994	Quasi randomised, alternate allocation. Participants: 59 women >/= 26 weeks' gestation, with DBP 90 mmHg or more, and proteinuria. Excluded if seizures in this pregnancy, any anticonvulsant drugs, or epilepsy. Interventions: diazepam 10 mg orally, then 5 mg 8 hourly vs no anticonvulsant. Outcomes: death, fits, cerebrovascular accident, cardiac failure. None reported for baby. All women received nifedipine for BP control, with methyl dopa if required.
UK 1989	Trial abandoned due to excessive maternal sedation with clonazepam, and neonatal feeding difficulties, jitteriness and drowsiness. No data available. Interventions: phenytoin versus clonazepam.
USA - Texas 1991	Data for the woman with eclampsia not reported separately from the women with pre-eclampsia. Methods: 'prospectively randomised'. Participants: 1 woman with eclampsia, 11 with severe PE, 38 with mild PIH. Interventions: magnesium sulphate versus phenytoin. Outcomes: fits.
USA - Texas 1992	No clinical outcomes reported. Participants: 12 women with pre-eclampsia.

Characteristics of excluded studies (*Continued*)

	Intervention: magnesium sulphate vs placebo.

DBP: diastolic blood pressure
PE: pre-eclampsia
PIH: pregnancy induced hypertension
vs: versus

ANALYSES

Comparison 01. Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	3	10795	Relative Risk (Fixed) 95% CI	0.54 [0.26, 1.10]
02 Eclampsia	7	11444	Relative Risk (Fixed) 95% CI	0.41 [0.29, 0.58]
03 Serious maternal morbidity	3	10332	Relative Risk (Fixed) 95% CI	1.08 [0.89, 1.32]
04 Pulmonary oedema	3	10560	Relative Risk (Fixed) 95% CI	0.97 [0.60, 1.57]
05 Pneumonia	1	10110	Relative Risk (Fixed) 95% CI	2.33 [0.90, 6.07]
06 Renal failure	1	10110	Relative Risk (Fixed) 95% CI	0.80 [0.55, 1.17]
07 Renal dialysis	2	10338	Relative Risk (Fixed) 95% CI	0.70 [0.21, 2.32]
08 Liver failure	1	10110	Relative Risk (Fixed) 95% CI	0.78 [0.54, 1.11]
09 Coagulopathy	1	10110	Relative Risk (Fixed) 95% CI	0.85 [0.62, 1.16]
10 Stroke	1	10110	Relative Risk (Fixed) 95% CI	0.50 [0.13, 2.00]
11 Cardiac arrest	1	10110	Relative Risk (Fixed) 95% CI	0.80 [0.21, 2.98]
12 Respiratory arrest	1	10110	Relative Risk (Fixed) 95% CI	2.50 [0.49, 12.88]
13 Any antihypertensive therapy	2	10795	Relative Risk (Fixed) 95% CI	0.97 [0.95, 0.99]
14 Rapid acting antihypertensives			Relative Risk (Fixed) 95% CI	Subtotals only
15 Progression from mild to severe pre-eclampsia	2	357	Relative Risk (Fixed) 95% CI	0.91 [0.53, 1.55]
16 Toxicity			Relative Risk (Fixed) 95% CI	Subtotals only
17 Given calcium gluconate	2	10795	Relative Risk (Fixed) 95% CI	1.35 [0.63, 2.88]
18 Side effects			Relative Risk (Fixed) 95% CI	Subtotals only
19 Problems at injection site	2	9992	Relative Risk (Fixed) 95% CI	1.78 [1.52, 2.08]
20 Placental abruption	2	8838	Relative Risk (Fixed) 95% CI	0.64 [0.50, 0.83]
21 Caesarean section	6	10108	Relative Risk (Fixed) 95% CI	1.05 [1.01, 1.10]
22 Induction of labour	1	8774	Relative Risk (Fixed) 95% CI	0.99 [0.94, 1.04]
23 Postpartum haemorrhage	2	8909	Relative Risk (Fixed) 95% CI	0.96 [0.88, 1.05]
24 Manual removal of retained placenta	1	8774	Relative Risk (Fixed) 95% CI	0.90 [0.72, 1.12]
25 Blood transfusion	1	8774	Relative Risk (Fixed) 95% CI	0.91 [0.77, 1.09]
26 Stillbirths and neonatal deaths	4	9961	Relative Risk (Fixed) 95% CI	1.04 [0.93, 1.15]
27 Mortality for the fetus or infant (by time of death)			Relative Risk (Fixed) 95% CI	Subtotals only
28 Death or in special care baby unit > 7 days	2	9024	Relative Risk (Fixed) 95% CI	1.02 [0.95, 1.08]
29 Apgar score < 7 at 5 minutes	1	8260	Relative Risk (Fixed) 95% CI	1.02 [0.85, 1.22]
30 Intubated at place of birth	1	8260	Relative Risk (Fixed) 95% CI	1.01 [0.82, 1.24]
31 Admission to special care baby unit	1	8260	Relative Risk (Fixed) 95% CI	1.01 [0.96, 1.06]
32 In special care baby unit > 7 days	1	8260	Relative Risk (Fixed) 95% CI	1.02 [0.93, 1.11]

Comparison 02. Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	3	10795	Relative Risk (Fixed) 95% CI	0.53 [0.26, 1.09]
02 Eclampsia	6	11222	Relative Risk (Fixed) 95% CI	0.41 [0.29, 0.58]
03 Serious maternal morbidity	2	10110	Relative Risk (Fixed) 95% CI	1.07 [0.88, 1.30]

Comparison 03. Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	3	9460	Relative Risk (Fixed) 95% CI	0.56 [0.26, 1.20]
02 Eclampsia	6	9887	Relative Risk (Fixed) 95% CI	0.40 [0.27, 0.57]
03 Serious maternal morbidity	2	8775	Relative Risk (Fixed) 95% CI	1.09 [0.89, 1.34]
04 Stillbirths and neonatal deaths	4	9961	Relative Risk (Fixed) 95% CI	1.04 [0.94, 1.14]
05 Death or in special care baby unit > 7 days	2	9024	Relative Risk (Fixed) 95% CI	1.02 [0.97, 1.07]

Comparison 04. Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	3	10732	Relative Risk (Fixed) 95% CI	0.53 [0.26, 1.09]
02 Eclampsia	6	11159	Relative Risk (Fixed) 95% CI	0.41 [0.29, 0.58]
03 Serious maternal morbidity	2	10047	Relative Risk (Fixed) 95% CI	1.06 [0.87, 1.29]
04 Stillbirths and neonatal deaths	4	9901	Relative Risk (Fixed) 95% CI	1.03 [0.93, 1.14]
05 Death or in special care baby unit > 7 days	2	8965	Relative Risk (Fixed) 95% CI	1.01 [0.95, 1.08]

Comparison 05. Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	3	10795	Relative Risk (Fixed) 95% CI	0.53 [0.26, 1.09]
02 Eclampsia	7	11444	Relative Risk (Fixed) 95% CI	0.41 [0.29, 0.58]
03 Stillbirths and neonatal deaths	4	9961	Relative Risk (Fixed) 95% CI	1.03 [0.93, 1.14]
04 Any reported side effects	3	10127	Relative Risk (Fixed) 95% CI	5.16 [4.52, 5.89]

Comparison 06. Magnesium sulphate versus phenytoin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Eclampsia	2	2241	Relative Risk (Fixed) 95% CI	0.05 [0.00, 0.84]
02 Complications of labour			Relative Risk (Fixed) 95% CI	Subtotals only
03 Caesarean section	2	2195	Relative Risk (Fixed) 95% CI	1.21 [1.05, 1.41]
04 Mortality for the fetus or infant			Relative Risk (Fixed) 95% CI	Subtotals only
05 Infant morbidity			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 07. Magnesium sulphate versus diazepam

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Eclampsia	2	66	Relative Risk (Fixed) 95% CI	3.00 [0.13, 69.31]
02 Caesarean section	2	66	Relative Risk (Fixed) 95% CI	0.98 [0.76, 1.27]
03 Stillbirths and neonatal deaths			Relative Risk (Fixed) 95% CI	Subtotals only

Comparison 08. Magnesium sulphate versus nimodipine

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Eclampsia	1	1650	Relative Risk (Fixed) 95% CI	0.33 [0.14, 0.77]
02 Stroke	1	1650	Relative Risk (Fixed) 95% CI	Not estimable
03 Coagulopathy	1	1650	Relative Risk (Fixed) 95% CI	0.59 [0.14, 2.47]
04 Respiratory problems	1	1650	Relative Risk (Fixed) 95% CI	3.61 [1.01, 12.91]
05 Cardiac failure	1	1650	Relative Risk (Fixed) 95% CI	4.93 [0.24, 102.49]
06 Respiratory depression	1	1650	Relative Risk (Fixed) 95% CI	3.61 [1.01, 12.91]
07 Antihypertensive drug	1	1650	Relative Risk (Fixed) 95% CI	1.19 [1.08, 1.31]
08 Oliguria	1	1650	Relative Risk (Fixed) 95% CI	1.15 [0.79, 1.68]
09 Side effects			Relative Risk (Fixed) 95% CI	Subtotals only
10 Placental abruption	1	1650	Relative Risk (Fixed) 95% CI	1.31 [0.46, 3.77]
11 Caesarean section	1	1650	Relative Risk (Fixed) 95% CI	1.03 [0.94, 1.13]
12 Postpartum haemorrhage	1	1650	Relative Risk (Fixed) 95% CI	2.46 [1.09, 5.56]
13 Respiratory distress syndrome	1	1564	Relative Risk (Fixed) 95% CI	1.23 [0.84, 1.81]
14 Neonatal hypotonia	1	1564	Relative Risk (Fixed) 95% CI	1.78 [0.91, 3.46]
15 Baby intubated	1	1564	Relative Risk (Fixed) 95% CI	1.37 [0.91, 2.05]
16 Neonatal hypotension	1	1564	Relative Risk (Fixed) 95% CI	0.32 [0.06, 1.58]

Comparison 09. Magnesium salts versus methyl dopa

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Other antihypertensive therapy	1	31	Relative Risk (Fixed) 95% CI	0.93 [0.61, 1.43]
02 Admission to special care baby unit	1	31	Relative Risk (Fixed) 95% CI	1.21 [0.08, 17.71]

INDEX TERMS

Medical Subject Headings (MeSH)

Anticonvulsants [*therapeutic use]; Magnesium Sulfate [therapeutic use]; Pre-Eclampsia [*drug therapy]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

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

Authors Duley L, Gülmezoglu AM, Henderson-Smart DJ

Contribution of author(s)	All three reviewers contributed to developing the methods. M Gulmezoglu and L Duley extracted and double checked the data. All three reviewers have contributed to the text of the review.
Issue protocol first published	1996/4
Review first published	1996/4
Date of most recent amendment	18 May 2005
Date of most recent SUBSTANTIVE amendment	25 February 2003
What's New	The search strategy has been updated. Sub-group analyses are now included in the comparisons tables. New included trials identified: Magpie Trial, Denmark 2000, USA - Tenessee 2001. Also new excluded trials.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	28 November 2002
Date authors' conclusions section amended	28 November 2002
Contact address	Prof Lelia Duley Obstetric Epidemiologist Centre for Epidemiology and Biostatistics University of Leeds Academic Unit, Fieldhouse Bradford Teaching Hospitals Foundation Trust, Bradford Royal Infirmary, Duckworth Lane Bradford West Yorkshire BD9 6RJ UK E-mail: l.duley@leeds.ac.uk Tel: +44 1274 383079
DOI	10.1002/14651858.CD000025
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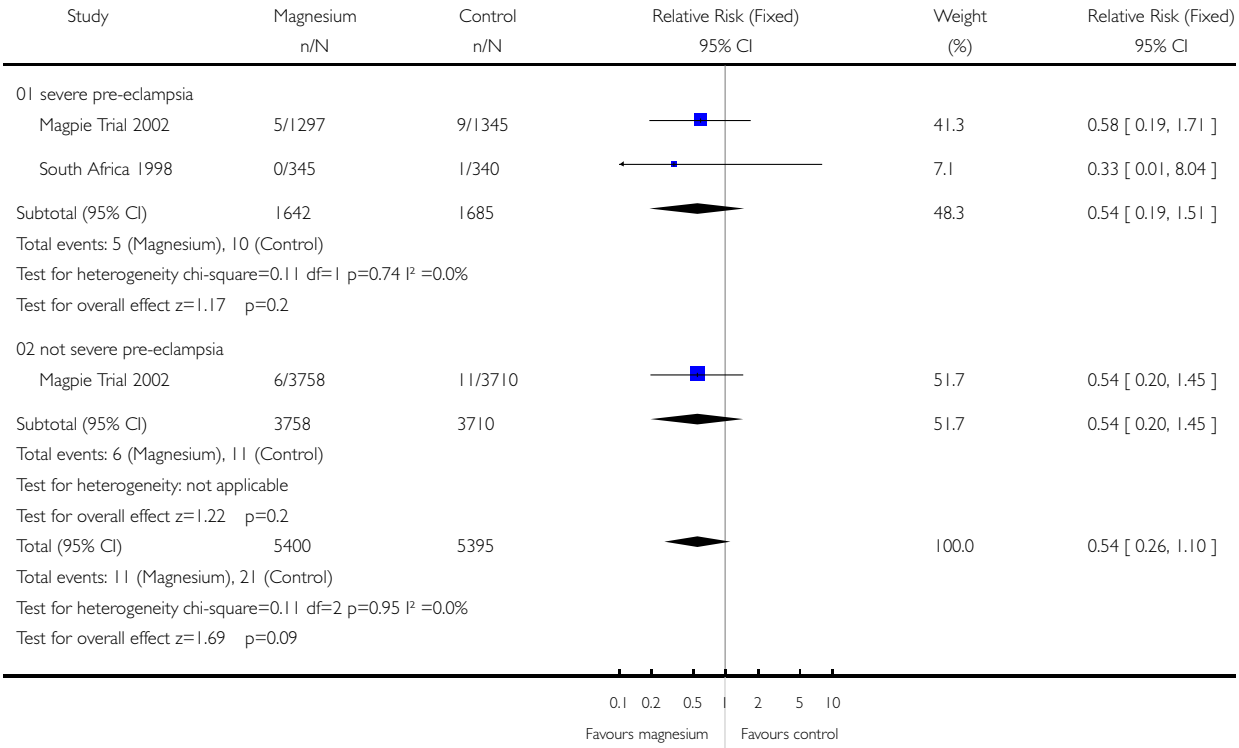
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 01 Maternal death

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 01 Maternal death



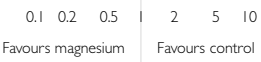
Analysis 01.02. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 02 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 02 Eclampsia

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 severe pre-eclampsia					
Magpie Trial 2002	15/1297	37/1345		33.7	0.42 [0.23, 0.76]
South Africa 1994	1/112	0/116		0.5	3.11 [0.13, 75.46]
South Africa 1998	1/345	11/340		10.3	0.09 [0.01, 0.69]
Subtotal (95% CI)	1754	1801		44.4	0.37 [0.22, 0.64]
Total events: 17 (Magnesium), 48 (Control)					
Test for heterogeneity chi-square=3.73 df=2 p=0.15 I^2 =46.4%					
Test for overall effect z=3.58 p=0.0003					
02 not severe pre-eclampsia					
Magpie Trial 2002	25/3758	59/3710		55.1	0.42 [0.26, 0.67]
× Taiwan 1995	0/34	0/30		0.0	Not estimable
USA - Memphis 1997	1/67	0/68		0.5	3.04 [0.13, 73.42]
× USA - Tennessee 2001	0/109	0/113		0.0	Not estimable
Subtotal (95% CI)	3968	3921		55.6	0.44 [0.28, 0.69]
Total events: 26 (Magnesium), 59 (Control)					
Test for heterogeneity chi-square=1.46 df=1 p=0.23 I^2 =31.7%					
Test for overall effect z=3.53 p=0.0004					
Total (95% CI)	5722	5722		100.0	0.41 [0.29, 0.58]
Total events: 43 (Magnesium), 107 (Control)					
Test for heterogeneity chi-square=5.22 df=4 p=0.27 I^2 =23.4%					
Test for overall effect z=5.02 p<0.00001					



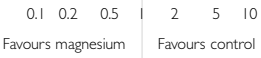
Analysis 01.03. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 03 Serious maternal morbidity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 03 Serious maternal morbidity

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 severe pre-eclampsia					
Magpie Trial 2002	89/1297	75/1345		40.4	1.23 [0.91, 1.66]
Subtotal (95% CI)	1297	1345		40.4	1.23 [0.91, 1.66]
Total events: 89 (Magnesium), 75 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.37 p=0.2					
02 not severe pre-eclampsia					
Magpie Trial 2002	107/3758	108/3710		59.6	0.98 [0.75, 1.27]
× USA - Tennessee 2001	0/109	0/113		0.0	Not estimable
Subtotal (95% CI)	3867	3823		59.6	0.98 [0.75, 1.27]
Total events: 107 (Magnesium), 108 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.16 p=0.9					
Total (95% CI)	5164	5168		100.0	1.08 [0.89, 1.32]
Total events: 196 (Magnesium), 183 (Control)					
Test for heterogeneity chi-square=1.28 df=1 p=0.26 I^2 =22.0%					
Test for overall effect z=0.77 p=0.4					



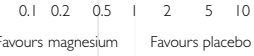
Analysis 01.04. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 04 Pulmonary oedema

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 04 Pulmonary oedema

Study	Magnesium n/N	Placebo/no magnesium n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	32/5055	33/5055		97.1	0.97 [0.60, 1.57]
South Africa 1994	1/112	1/116		2.9	1.04 [0.07, 16.36]
× USA - Tennessee 2001	0/109	0/113		0.0	Not estimable
Total (95% CI)	5276	5284		100.0	0.97 [0.60, 1.57]
Total events: 33 (Magnesium), 34 (Placebo/no magnesium)					
Test for heterogeneity chi-square=0.00 df=1 p=0.96 I^2 =0.0%					
Test for overall effect z=0.12 p=0.9					



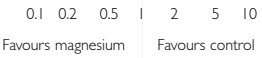
Analysis 01.05. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 05 Pneumonia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 05 Pneumonia

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	14/5055	6/5055		100.0	2.33 [0.90, 6.07]
Total (95% CI)	5055	5055		100.0	2.33 [0.90, 6.07]
Total events: 14 (Magnesium), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.74 p=0.08					



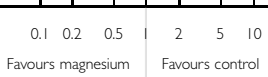
Analysis 01.06. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 06 Renal failure

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 06 Renal failure

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	49/5055	61/5055		100.0	0.80 [0.55, 1.17]
Total (95% CI)	5055	5055		100.0	0.80 [0.55, 1.17]
Total events: 49 (Magnesium), 61 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.15 p=0.3					



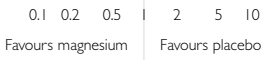
Analysis 01.07. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 07 Renal dialysis

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 07 Renal dialysis

Study	Magnesium n/N	Placebo/no magnesium n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	4/5055	5/5055		77.2	0.80 [0.21, 2.98]
South Africa 1994	0/112	1/116		22.8	0.35 [0.01, 8.38]
Total (95% CI)	5167	5171		100.0	0.70 [0.21, 2.32]
Total events: 4 (Magnesium), 6 (Placebo/no magnesium)					
Test for heterogeneity chi-square=0.23 df=1 p=0.63 I^2 =0.0%					
Test for overall effect z=0.59 p=0.6					



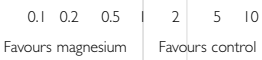
Analysis 01.08. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 08 Liver failure

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 08 Liver failure

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	52/5055	67/5055		100.0	0.78 [0.54, 1.11]
Total (95% CI)	5055	5055		100.0	0.78 [0.54, 1.11]
Total events: 52 (Magnesium), 67 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.38 p=0.2					



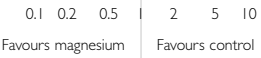
Analysis 01.09. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 09 Coagulopathy

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 09 Coagulopathy

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	73/5055	86/5055		100.0	0.85 [0.62, 1.16]
Total (95% CI)	5055	5055		100.0	0.85 [0.62, 1.16]
Total events: 73 (Magnesium), 86 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.04 p=0.3					



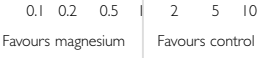
Analysis 01.10. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 10 Stroke

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 10 Stroke

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	3/5055	6/5055		100.0	0.50 [0.13, 2.00]
Total (95% CI)	5055	5055		100.0	0.50 [0.13, 2.00]
Total events: 3 (Magnesium), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.98 p=0.3					



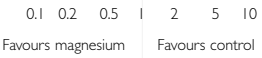
Analysis 01.11. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 11 Cardiac arrest

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 11 Cardiac arrest

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	4/5055	5/5055		100.0	0.80 [0.21, 2.98]
Total (95% CI)	5055	5055		100.0	0.80 [0.21, 2.98]
Total events: 4 (Magnesium), 5 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.33 p=0.7					



Analysis 01.12. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 12 Respiratory arrest

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 12 Respiratory arrest

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	5/5055	2/5055		100.0	2.50 [0.49, 12.88]
Total (95% CI)	5055	5055		100.0	2.50 [0.49, 12.88]
Total events: 5 (Magnesium), 2 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.10 p=0.3					

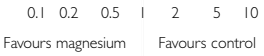
Analysis 01.13. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 13 Any antihypertensive therapy

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 13 Any antihypertensive therapy

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	3720/5055	3823/5055		93.7	0.97 [0.95, 1.00]
South Africa 1998	244/345	257/340		6.3	0.94 [0.85, 1.02]
Total (95% CI)	5400	5395		100.0	0.97 [0.95, 0.99]
Total events: 3964 (Treatment), 4080 (Control)					
Test for heterogeneity chi-square=0.67 df=1 p=0.41 I^2 =0.0%					
Test for overall effect z=2.64 p=0.008					



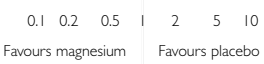
Analysis 01.14. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 14 Rapid acting antihypertensives

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 14 Rapid acting antihypertensives

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 intravenous or intramuscular hydralazine					
Magpie Trial 2002	977/5055	1040/5055		92.2	0.94 [0.87, 1.02]
South Africa 1994	68/112	90/116		7.8	0.78 [0.65, 0.94]
Subtotal (95% CI)	5167	5171		100.0	0.93 [0.86, 1.00]
Total events: 1045 (Treatment), 1130 (Control)					
Test for heterogeneity chi-square=3.59 df=1 p=0.06 I^2 =72.1%					
Test for overall effect z=2.01 p=0.04					
02 oral nifedipine					
Magpie Trial 2002	1469/5055	1560/4993		98.6	0.93 [0.88, 0.99]
South Africa 1994	27/112	22/116		1.4	1.27 [0.77, 2.09]
Subtotal (95% CI)	5167	5109		100.0	0.93 [0.88, 0.99]
Total events: 1496 (Treatment), 1582 (Control)					
Test for heterogeneity chi-square=1.48 df=1 p=0.22 I^2 =32.5%					
Test for overall effect z=2.24 p=0.03					



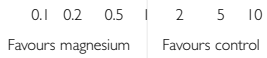
Analysis 01.15. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 15 Progression from mild to severe pre-eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 15 Progression from mild to severe pre-eclampsia

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
USA - Memphis 1997	8/67	6/68		24.2	1.35 [0.50, 3.69]
USA - Tennessee 2001	14/109	19/113		75.8	0.76 [0.40, 1.45]
Total (95% CI)	176	181		100.0	0.91 [0.53, 1.55]
Total events: 22 (Magnesium), 25 (Control)					
Test for heterogeneity chi-square=0.89 df=1 p=0.35 I^2 =0.0%					
Test for overall effect z=0.36 p=0.7					



Analysis 01.16. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 16 Toxicity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 16 Toxicity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 absent or reduced tendon reflexes					
Magpie Trial 2002	59/4999	60/4993		99.2	0.98 [0.69, 1.40]
South Africa 1998	1/345	0/340		0.8	2.96 [0.12, 72.32]
Subtotal (95% CI)	5344	5333		100.0	1.00 [0.70, 1.42]
Total events: 60 (Treatment), 60 (Control)					
Test for heterogeneity chi-square=0.45 df=1 p=0.50 I^2 =0.0%					
Test for overall effect z=0.01 p=1					
02 respiratory depression, or other respiratory problem					
Magpie Trial 2002	51/4999	26/4993		98.1	1.96 [1.22, 3.14]
South Africa 1998	1/345	0/340		1.9	2.96 [0.12, 72.32]
Subtotal (95% CI)	5344	5333		100.0	1.98 [1.24, 3.15]
Total events: 52 (Treatment), 26 (Control)					
Test for heterogeneity chi-square=0.06 df=1 p=0.80 I^2 =0.0%					
Test for overall effect z=2.87 p=0.004					
03 respiratory depression and absent tendon reflexes					

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Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	4/4999	0/4993		49.8	8.99 [0.48, 166.92]
South Africa 1998	1/345	0/340		50.2	2.96 [0.12, 72.32]
× USA - Tennessee 2001	0/109	0/113		0.0	Not estimable
Subtotal (95% CI)	5453	5446		100.0	5.96 [0.72, 49.40]
Total events: 5 (Treatment), 0 (Control)					
Test for heterogeneity chi-square=0.26 df=1 p=0.61 I^2 =0.0%					
Test for overall effect z=1.66 p=0.1					

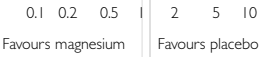
Analysis 01.17. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 17 Given calcium gluconate

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 17 Given calcium gluconate

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	14/5055	11/5055		95.6	1.27 [0.58, 2.80]
South Africa 1998	1/345	0/340		4.4	2.96 [0.12, 72.32]
Total (95% CI)	5400	5395		100.0	1.35 [0.63, 2.88]
Total events: 15 (Treatment), 11 (Control)					
Test for heterogeneity chi-square=0.25 df=1 p=0.62 I^2 =0.0%					
Test for overall effect z=0.77 p=0.4					



Analysis 01.18. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 18 Side effects

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 18 Side effects

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 feeling warm/flushed					
Magpie Trial 2002	987/4999	98/4993		89.2	10.06 [8.20, 12.33]
USA - Memphis 1997	45/67	12/68		10.8	3.81 [2.22, 6.53]
Subtotal (95% CI)	5066	5061		100.0	9.38 [7.74, 11.37]
Total events: 1032 (Treatment), 110 (Control)					
Test for heterogeneity chi-square=11.17 df=1 p=0.0008 I^2 =91.0%					
Test for overall effect z=22.87 p<0.00001					
02 nausea and/or vomiting					
Magpie Trial 2002	160/4999	18/4993		100.0	8.88 [5.46, 14.43]
Subtotal (95% CI)	4999	4993		100.0	8.88 [5.46, 14.43]
Total events: 160 (Treatment), 18 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=8.81 p<0.00001					
03 slurred speech					
USA - Memphis 1997	1/67	0/68		100.0	3.04 [0.13, 73.42]
Subtotal (95% CI)	67	68		100.0	3.04 [0.13, 73.42]
Total events: 1 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.69 p=0.5					
04 muscle weakness					
Magpie Trial 2002	72/4999	6/4993		100.0	11.99 [5.22, 27.54]
Subtotal (95% CI)	4999	4993		100.0	11.99 [5.22, 27.54]
Total events: 72 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=5.85 p<0.00001					
05 hypotension					
Magpie Trial 2002	38/4999	20/4993		100.0	1.90 [1.11, 3.26]
Subtotal (95% CI)	4999	4993		100.0	1.90 [1.11, 3.26]
Total events: 38 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.33 p=0.02					
06 dizziness					

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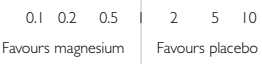
Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	37/4999	10/4993		100.0	3.70 [1.84, 7.42]
Subtotal (95% CI)	4999	4993		100.0	3.70 [1.84, 7.42]
Total events: 37 (Treatment), 10 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.67 p=0.0002					
07 drowsiness or confusion					
Magpie Trial 2002	20/4999	9/4993		100.0	2.22 [1.01, 4.87]
Subtotal (95% CI)	4999	4993		100.0	2.22 [1.01, 4.87]
Total events: 20 (Treatment), 9 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.99 p=0.05					
08 headache					
Magpie Trial 2002	36/4999	17/4993		100.0	2.12 [1.19, 3.76]
Subtotal (95% CI)	4999	4993		100.0	2.12 [1.19, 3.76]
Total events: 36 (Treatment), 17 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.55 p=0.01					
09 any reported side effects					
Magpie Trial 2002	1201/4999	228/4993		100.0	5.26 [4.59, 6.03]
Subtotal (95% CI)	4999	4993		100.0	5.26 [4.59, 6.03]
Total events: 1201 (Treatment), 228 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=23.92 p<0.00001					

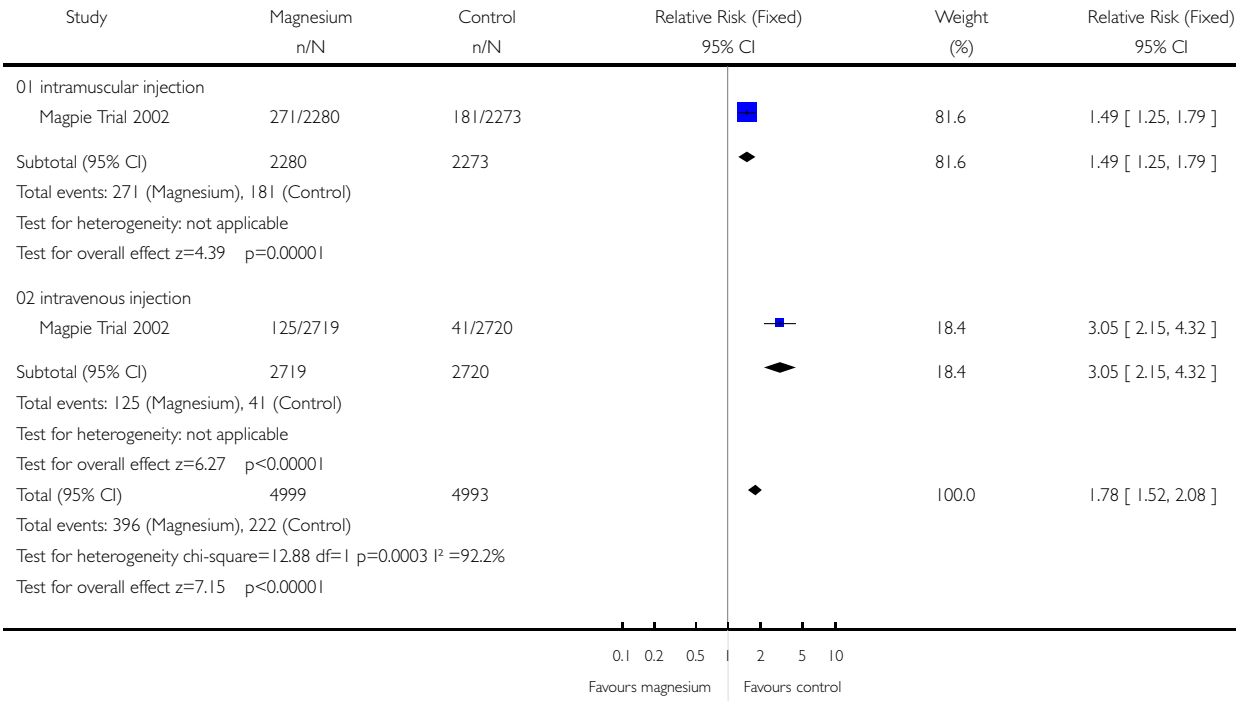


Analysis 01.19. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 19 Problems at injection site

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 19 Problems at injection site

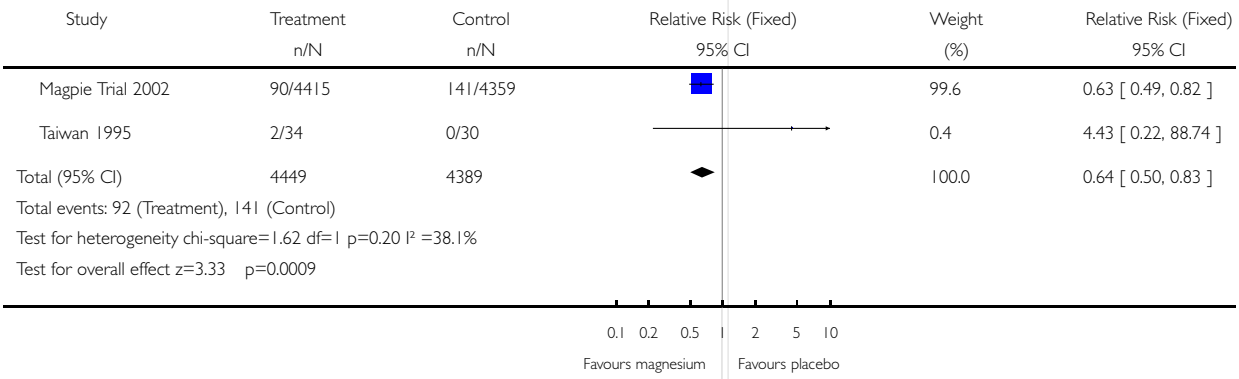


Analysis 01.20. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 20 Placental abruption

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 20 Placental abruption



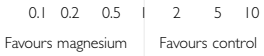
Analysis 01.21. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 21 Caesarean section

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 21 Caesarean section

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	2224/4415	2082/4359		87.9	1.05 [1.01, 1.10]
South Africa 1994	59/112	56/116		2.3	1.09 [0.84, 1.41]
South Africa 1998	173/345	165/340		7.0	1.03 [0.89, 1.20]
Taiwan 1995	28/34	22/30		1.0	1.12 [0.86, 1.47]
USA - Memphis 1997	11/67	14/68		0.6	0.80 [0.39, 1.63]
USA - Tennessee 2001	33/109	31/113		1.3	1.10 [0.73, 1.67]
Total (95% CI)	5082	5026		100.0	1.05 [1.01, 1.10]
Total events: 2528 (Treatment), 2370 (Control)					
Test for heterogeneity chi-square=0.99 df=5 p=0.96 I^2 =0.0%					
Test for overall effect z=2.57 p=0.01					



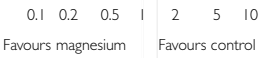
Analysis 01.22. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 22 Induction of labour

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 22 Induction of labour

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	1892/4415	1892/4359		100.0	0.99 [0.94, 1.04]
Total (95% CI)	4415	4359		100.0	0.99 [0.94, 1.04]
Total events: 1892 (Magnesium), 1892 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.52 p=0.6					



Analysis 01.23. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 23 Postpartum haemorrhage

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 23 Postpartum haemorrhage

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	750/4415	774/4359		99.9	0.96 [0.87, 1.05]
USA - Memphis 1997	4/67	1/68		0.1	4.06 [0.47, 35.38]
Total (95% CI)	4482	4427		100.0	0.96 [0.88, 1.05]
Total events: 754 (Treatment), 775 (Control)					
Test for heterogeneity chi-square=1.71 df=1 p=0.19 I^2 =41.5%					
Test for overall effect z=0.86 p=0.4					

Analysis 01.24. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 24 Manual removal of retained placenta

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 24 Manual removal of retained placenta

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	148/4415	162/4359		100.0	0.90 [0.72, 1.12]
Total (95% CI)	4415	4359		100.0	0.90 [0.72, 1.12]
Total events: 148 (Magnesium), 162 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.92 p=0.4					

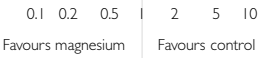
Analysis 01.25. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 25 Blood transfusion

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 25 Blood transfusion

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	224/4415	242/4359		100.0	0.91 [0.77, 1.09]
Total (95% CI)	4415	4359		100.0	0.91 [0.77, 1.09]
Total events: 224 (Magnesium), 242 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.00 p=0.3					



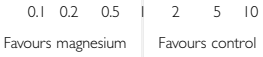
Analysis 01.26. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 26 Stillbirths and neonatal deaths

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 26 Stillbirths and neonatal deaths

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 severe pre-eclampsia					
Magpie Trial 2002	234/1185	240/1219		38.7	1.00 [0.85, 1.18]
South Africa 1994	20/117	25/118		4.1	0.81 [0.48, 1.37]
South Africa 1998	38/348	28/354		4.5	1.38 [0.87, 2.20]
Subtotal (95% CI)	1650	1691		47.3	1.02 [0.88, 1.18]
Total events: 292 (Magnesium), 293 (Control)					
Test for heterogeneity chi-square=2.42 df=2 p=0.30 I^2 =17.5%					
Test for overall effect z=0.30 p=0.8					
02 not severe pre-eclampsia					
Magpie Trial 2002	342/3353	318/3267		52.7	1.05 [0.91, 1.21]
Subtotal (95% CI)	3353	3267		52.7	1.05 [0.91, 1.21]
Total events: 342 (Magnesium), 318 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.63 p=0.5					
Total (95% CI)	5003	4958		100.0	1.04 [0.93, 1.15]
Total events: 634 (Magnesium), 611 (Control)					
Test for heterogeneity chi-square=2.50 df=3 p=0.48 I^2 =0.0%					
Test for overall effect z=0.67 p=0.5					



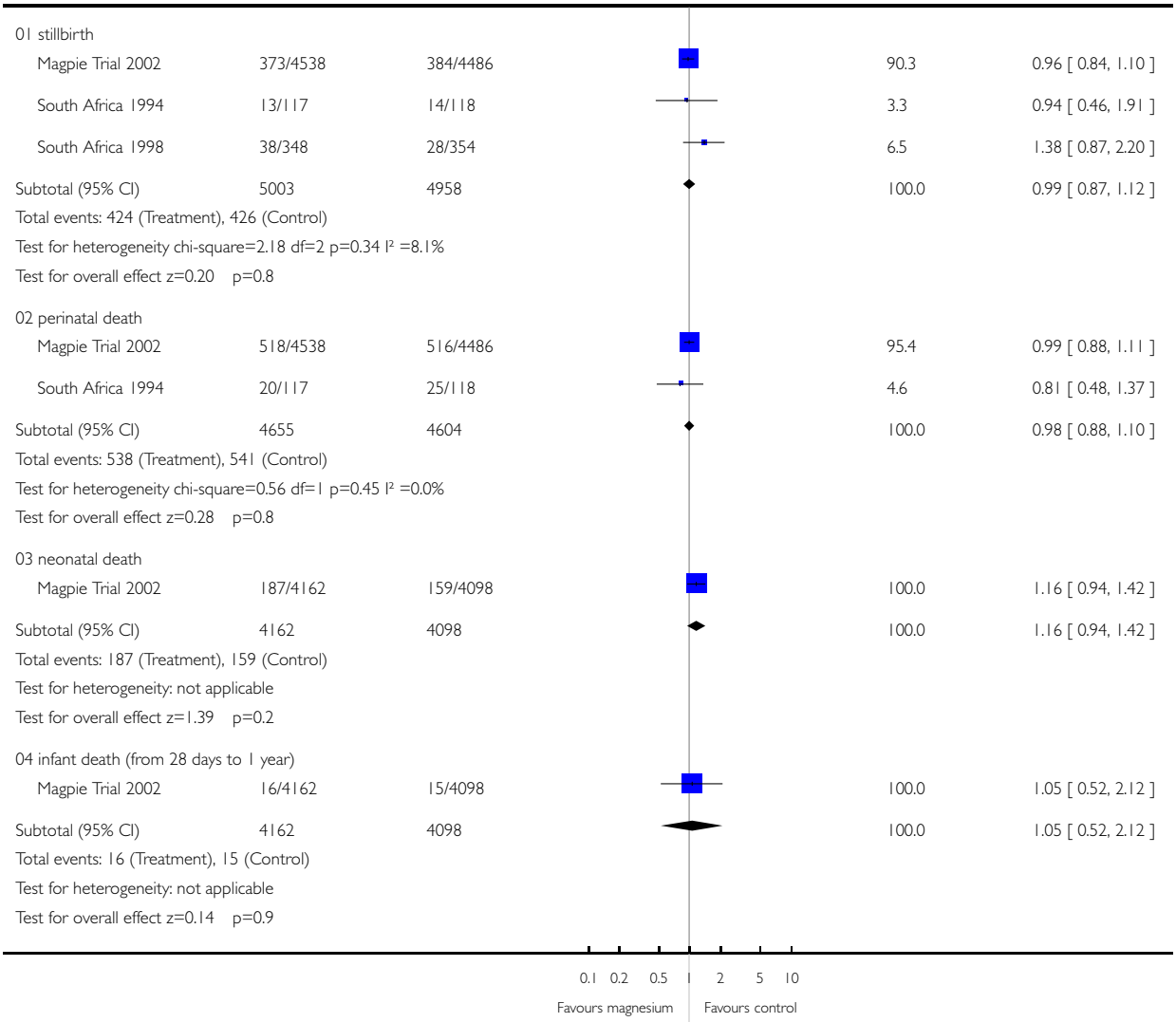
Analysis 01.27. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 27 Mortality for the fetus or infant (by time of death)

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 27 Mortality for the fetus or infant (by time of death)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 stillbirth					
Magpie Trial 2002	373/4538	384/4486		90.3	0.96 [0.84, 1.10]
South Africa 1994	13/117	14/118		3.3	0.94 [0.46, 1.91]
South Africa 1998	38/348	28/354		6.5	1.38 [0.87, 2.20]
Subtotal (95% CI)	5003	4958		100.0	0.99 [0.87, 1.12]
Total events: 424 (Treatment), 426 (Control)					
Test for heterogeneity chi-square=2.18 df=2 p=0.34 I^2 =8.1%					
Test for overall effect z=0.20 p=0.8					
02 perinatal death					
Magpie Trial 2002	518/4538	516/4486		95.4	0.99 [0.88, 1.11]
South Africa 1994	20/117	25/118		4.6	0.81 [0.48, 1.37]
Subtotal (95% CI)	4655	4604		100.0	0.98 [0.88, 1.10]
Total events: 538 (Treatment), 541 (Control)					
Test for heterogeneity chi-square=0.56 df=1 p=0.45 I^2 =0.0%					
Test for overall effect z=0.28 p=0.8					
03 neonatal death					
Magpie Trial 2002	187/4162	159/4098		100.0	1.16 [0.94, 1.42]
Subtotal (95% CI)	4162	4098		100.0	1.16 [0.94, 1.42]
Total events: 187 (Treatment), 159 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.39 p=0.2					
04 infant death (from 28 days to 1 year)					
Magpie Trial 2002	16/4162	15/4098		100.0	1.05 [0.52, 2.12]
Subtotal (95% CI)	4162	4098		100.0	1.05 [0.52, 2.12]
Total events: 16 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.14 p=0.9					



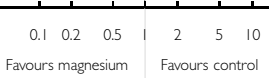
Analysis 01.28. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 28 Death or in special care baby unit > 7 days

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 28 Death or in special care baby unit > 7 days

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 severe pre-eclampsia					
Magpie Trial 2002	492/1185	544/1219		41.1	0.93 [0.85, 1.02]
Subtotal (95% CI)	1185	1219		41.1	0.93 [0.85, 1.02]
Total events: 492 (Magnesium), 544 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.54 p=0.1					
02 not severe pre-eclampsia					
Magpie Trial 2002	838/3353	758/3267		58.9	1.08 [0.99, 1.17]
Subtotal (95% CI)	3353	3267		58.9	1.08 [0.99, 1.17]
Total events: 838 (Magnesium), 758 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.70 p=0.09					
Total (95% CI)	4538	4486		100.0	1.02 [0.95, 1.08]
Total events: 1330 (Magnesium), 1302 (Control)					
Test for heterogeneity chi-square=5.32 df=1 p=0.02 I^2 =81.2%					
Test for overall effect z=0.52 p=0.6					



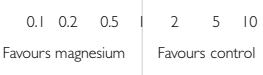
Analysis 01.29. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 29 Apgar score < 7 at 5 minutes

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 29 Apgar score < 7 at 5 minutes

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	235/4162	227/4098		100.0	1.02 [0.85, 1.22]
Total (95% CI)	4162	4098		100.0	1.02 [0.85, 1.22]
Total events: 235 (Magnesium), 227 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.21 p=0.8					



Analysis 01.30. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 30 Intubated at place of birth

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 30 Intubated at place of birth

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	175/4162	171/4098		100.0	1.01 [0.82, 1.24]
Total (95% CI)	4162	4098		100.0	1.01 [0.82, 1.24]
Total events: 175 (Magnesium), 171 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.07 p=0.9					

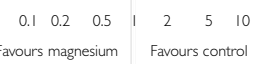
Analysis 01.31. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 31 Admission to special care baby unit

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 31 Admission to special care baby unit

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	1629/4162	1591/4098		100.0	1.01 [0.96, 1.06]
Total (95% CI)	4162	4098		100.0	1.01 [0.96, 1.06]
Total events: 1629 (Magnesium), 1591 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.29 p=0.8					



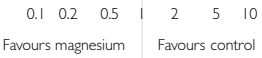
Analysis 01.32. Comparison 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia), Outcome 32 In special care baby unit > 7 days

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 01 Magnesium sulphate versus none/placebo (subgroups by severity of pre-eclampsia)

Outcome: 32 In special care baby unit > 7 days

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Magpie Trial 2002	810/4162	783/4098		100.0	1.02 [0.93, 1.11]
Total (95% CI)	4162	4098		100.0	1.02 [0.93, 1.11]
Total events: 810 (Magnesium), 783 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.41 p=0.7					



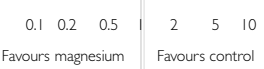
Analysis 02.01. Comparison 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry), Outcome 01 Maternal death

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry)

Outcome: 01 Maternal death

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 antepartum at trial entry					
Magpie Trial 2002	10/4416	17/4359		79.6	0.58 [0.27, 1.27]
South Africa 1998	0/345	1/340		7.0	0.33 [0.01, 8.04]
Subtotal (95% CI)	4761	4699		86.6	0.56 [0.26, 1.19]
Total events: 10 (Magnesium), 18 (Control)					
Test for heterogeneity chi-square=0.12 df=1 p=0.73 I^2 =0.0%					
Test for overall effect z=1.50 p=0.1					
02 postpartum at trial entry					
Magpie Trial 2002	1/639	3/696		13.4	0.36 [0.04, 3.48]
Subtotal (95% CI)	639	696		13.4	0.36 [0.04, 3.48]
Total events: 1 (Magnesium), 3 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.88 p=0.4					
Total (95% CI)	5400	5395		100.0	0.53 [0.26, 1.09]
Total events: 11 (Magnesium), 21 (Control)					
Test for heterogeneity chi-square=0.24 df=2 p=0.88 I^2 =0.0%					
Test for overall effect z=1.72 p=0.09					

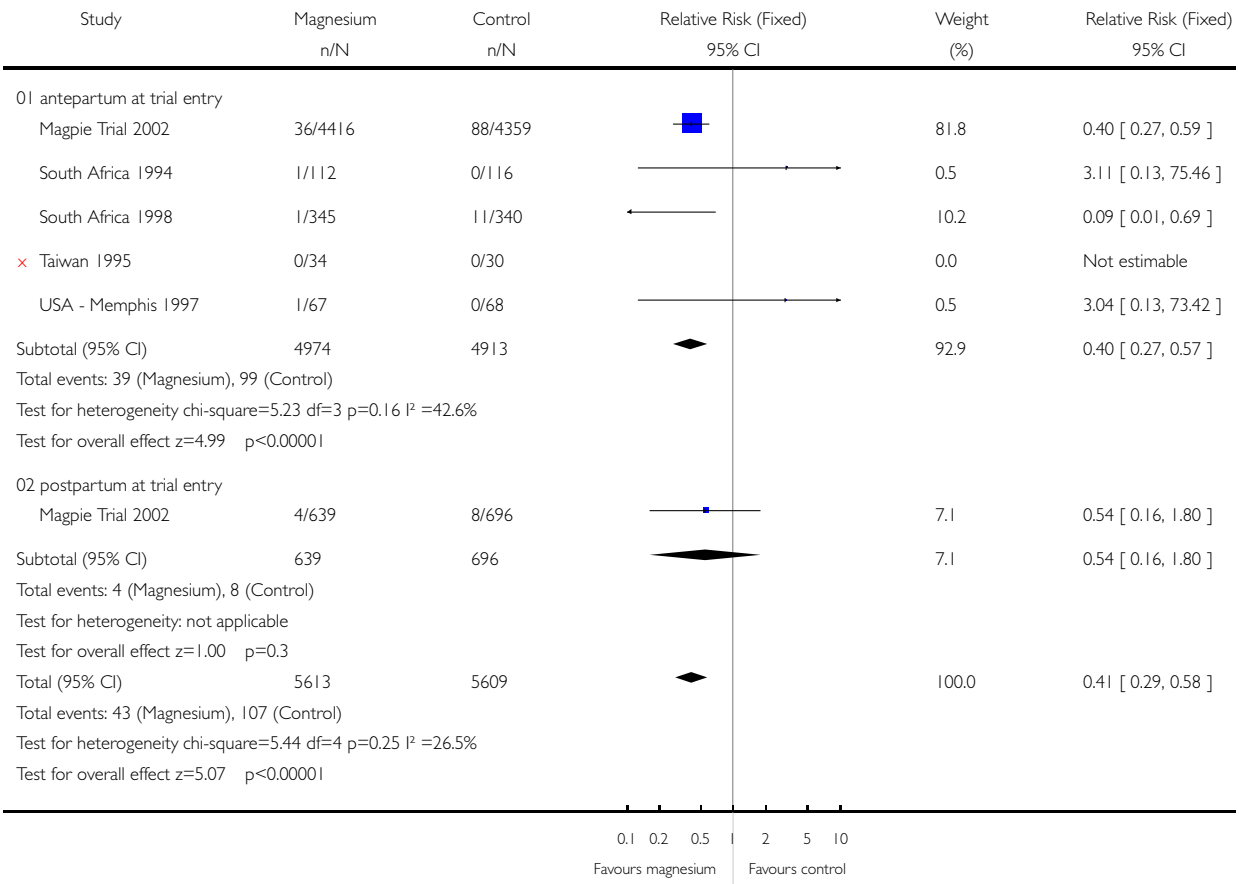


Analysis 02.02. Comparison 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry), Outcome 02 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry)

Outcome: 02 Eclampsia



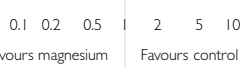
Analysis 02.03. Comparison 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry), Outcome 03 Serious maternal morbidity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 02 Magnesium sulphate versus none/placebo (subgroups by whether delivered at trial entry)

Outcome: 03 Serious maternal morbidity

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 antepartum at trial entry					
Magpie Trial 2002	180/4416	164/4359		90.1	1.08 [0.88, 1.33]
Subtotal (95% CI)	4416	4359		90.1	1.08 [0.88, 1.33]
Total events: 180 (Magnesium), 164 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.76 p=0.4					
02 postpartum at trial entry					
Magpie Trial 2002	16/639	19/696		9.9	0.92 [0.48, 1.77]
Subtotal (95% CI)	639	696		9.9	0.92 [0.48, 1.77]
Total events: 16 (Magnesium), 19 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.26 p=0.8					
Total (95% CI)	5055	5055		100.0	1.07 [0.88, 1.30]
Total events: 196 (Magnesium), 183 (Control)					
Test for heterogeneity chi-square=0.22 df=1 p=0.64 I^2 =0.0%					
Test for overall effect z=0.64 p=0.5					

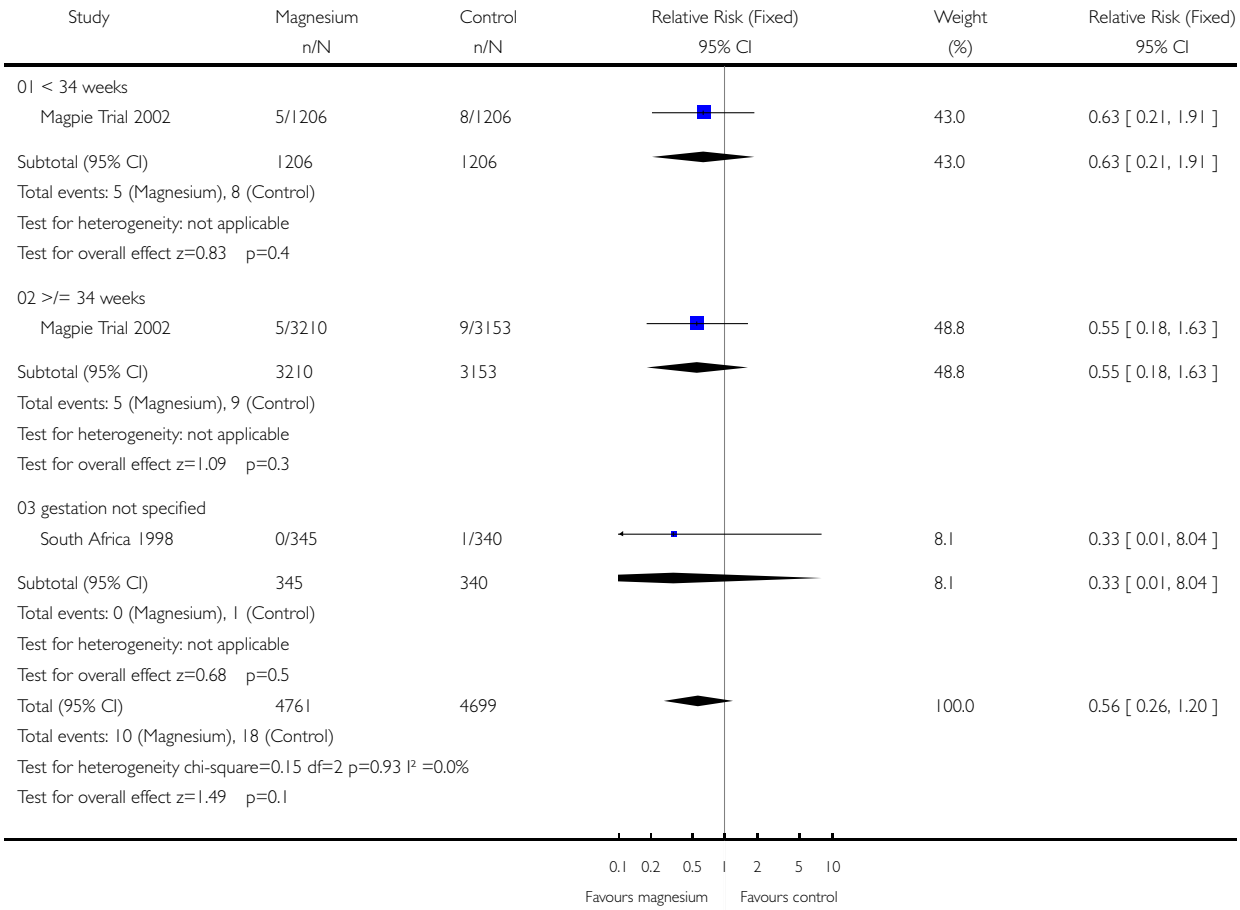


Analysis 03.01. Comparison 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry), Outcome 01 Maternal death

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome: 01 Maternal death

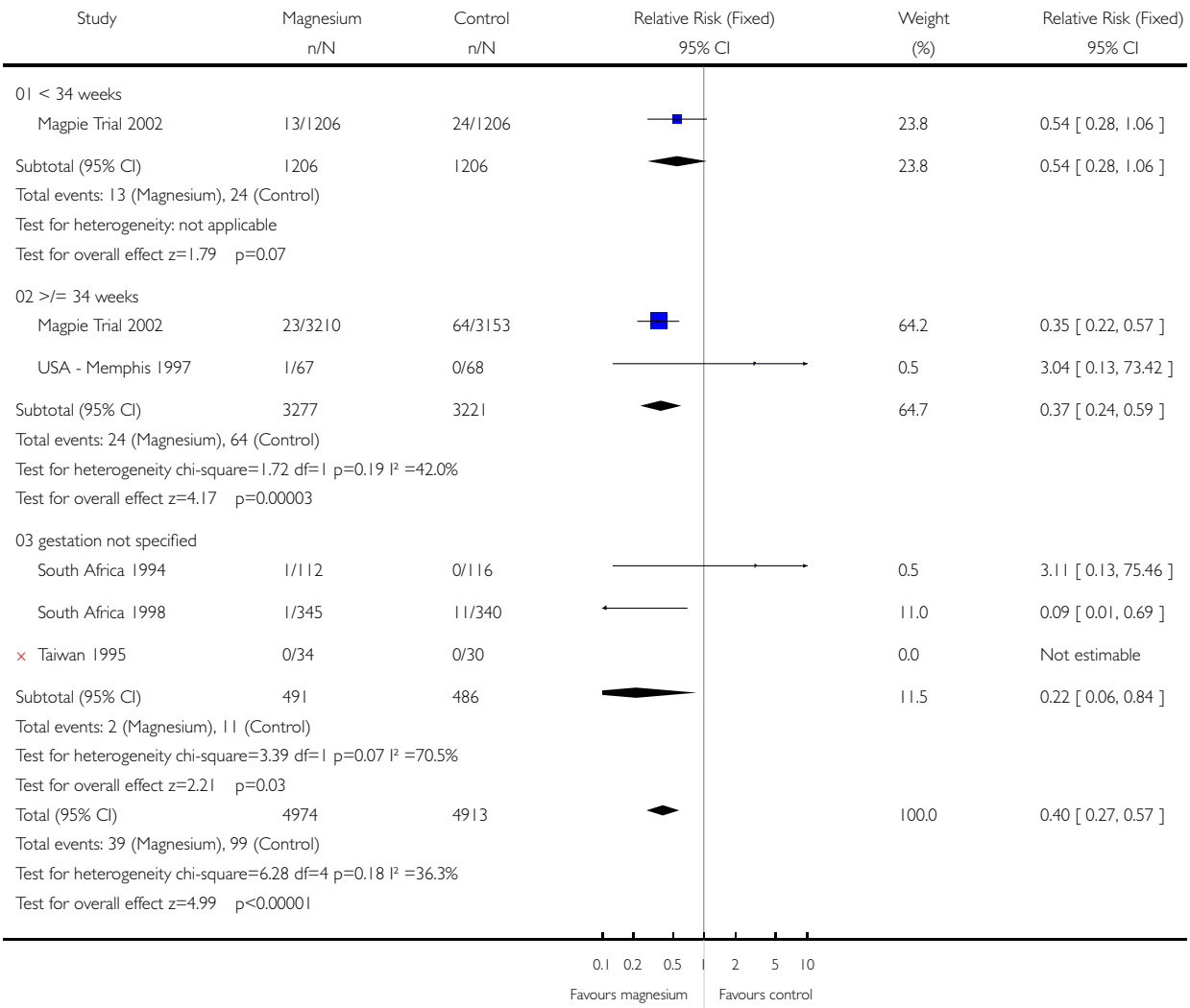


Analysis 03.02. Comparison 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry), Outcome 02 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome: 02 Eclampsia



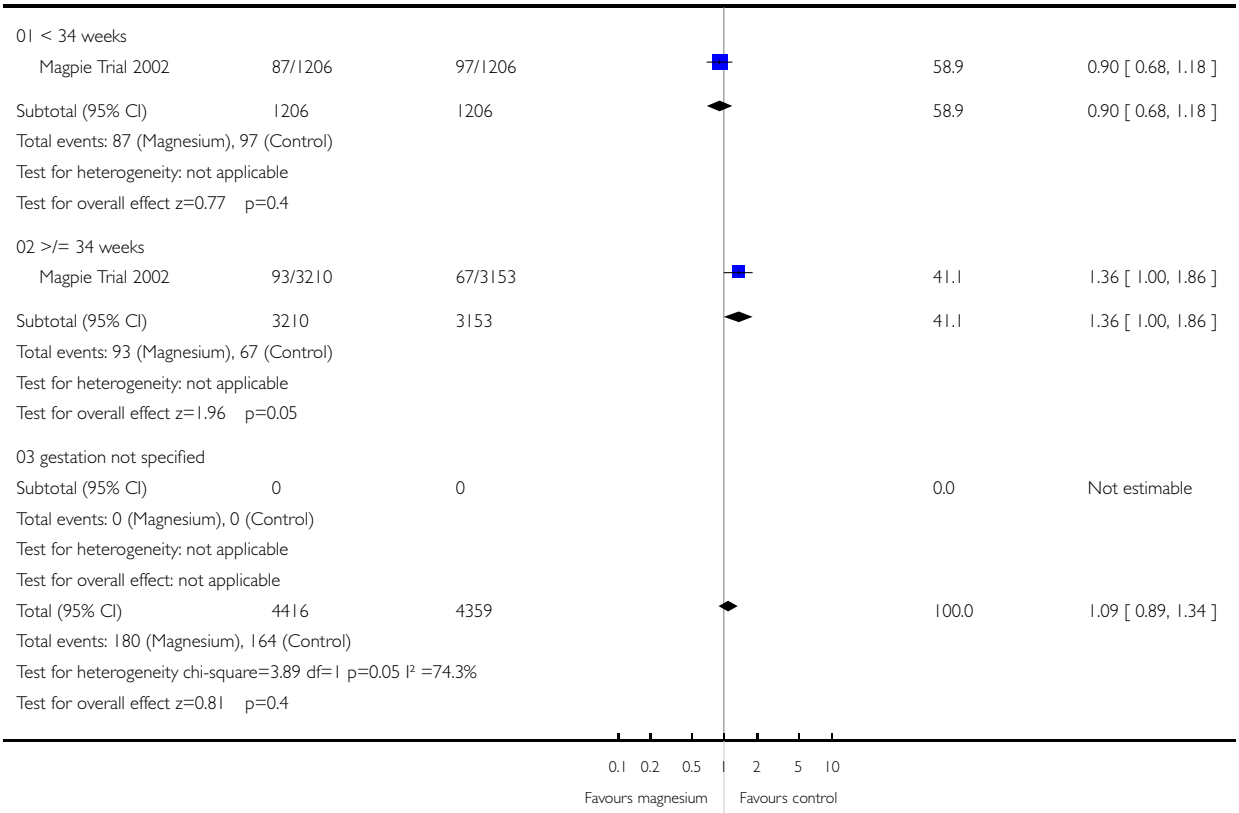
Analysis 03.03. Comparison 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry), Outcome 03 Serious maternal morbidity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome: 03 Serious maternal morbidity

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 < 34 weeks					
Magpie Trial 2002	87/1206	97/1206		58.9	0.90 [0.68, 1.18]
Subtotal (95% CI)	1206	1206		58.9	0.90 [0.68, 1.18]
Total events: 87 (Magnesium), 97 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.77 p=0.4					
02 >/= 34 weeks					
Magpie Trial 2002	93/3210	67/3153		41.1	1.36 [1.00, 1.86]
Subtotal (95% CI)	3210	3153		41.1	1.36 [1.00, 1.86]
Total events: 93 (Magnesium), 67 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.96 p=0.05					
03 gestation not specified					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Magnesium), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	4416	4359		100.0	1.09 [0.89, 1.34]
Total events: 180 (Magnesium), 164 (Control)					
Test for heterogeneity chi-square=3.89 df=1 p=0.05 I^2 =74.3%					
Test for overall effect z=0.81 p=0.4					



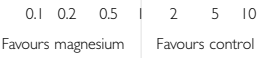
Analysis 03.04. Comparison 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry), Outcome 04 Stillbirths and neonatal deaths

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome: 04 Stillbirths and neonatal deaths

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 < 34 weeks					
Magpie Trial 2002	425/1217	418/1226		68.2	1.02 [0.92, 1.14]
Subtotal (95% CI)	1217	1226		68.2	1.02 [0.92, 1.14]
Total events: 425 (Magnesium), 418 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.43 p=0.7					
02 >/= 34 weeks					
Magpie Trial 2002	151/3321	140/3260		23.1	1.06 [0.85, 1.33]
Subtotal (95% CI)	3321	3260		23.1	1.06 [0.85, 1.33]
Total events: 151 (Magnesium), 140 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.50 p=0.6					
03 gestation not specified					
South Africa 1994	20/117	25/118		4.1	0.81 [0.48, 1.37]
South Africa 1998	38/348	28/354		4.5	1.38 [0.87, 2.20]
Subtotal (95% CI)	465	472		8.6	1.11 [0.78, 1.57]
Total events: 58 (Magnesium), 53 (Control)					
Test for heterogeneity chi-square=2.24 df=1 p=0.13 I^2 =55.3%					
Test for overall effect z=0.59 p=0.6					
Total (95% CI)	5003	4958		100.0	1.04 [0.94, 1.14]
Total events: 634 (Magnesium), 611 (Control)					
Test for heterogeneity chi-square=2.40 df=3 p=0.49 I^2 =0.0%					
Test for overall effect z=0.79 p=0.4					



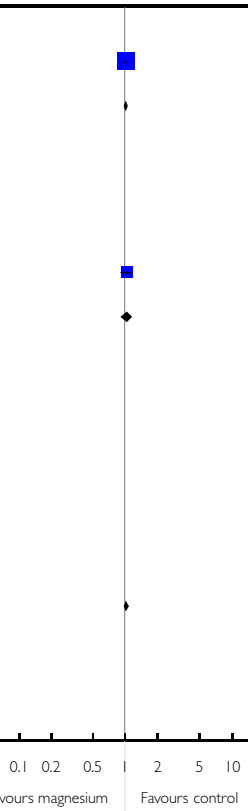
Analysis 03.05. Comparison 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry), Outcome 05 Death or in special care baby unit > 7 days

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 03 Magnesium sulphate versus none/placebo (subgroups by gestation at trial entry)

Outcome: 05 Death or in special care baby unit > 7 days

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 < 34 weeks					
Magpie Trial 2002	915/1217	906/1226		69.3	1.02 [0.97, 1.07]
Subtotal (95% CI)	1217	1226		69.3	1.02 [0.97, 1.07]
Total events: 915 (Magnesium), 906 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.73 p=0.5					
02 >/= 34 weeks					
Magpie Trial 2002	415/3321	396/3260		30.7	1.03 [0.90, 1.17]
Subtotal (95% CI)	3321	3260		30.7	1.03 [0.90, 1.17]
Total events: 415 (Magnesium), 396 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.43 p=0.7					
03 gestation not specified					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Magnesium), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	4538	4486		100.0	1.02 [0.97, 1.07]
Total events: 1330 (Magnesium), 1302 (Control)					
Test for heterogeneity chi-square=0.03 df=1 p=0.85 I^2 =0.0%					
Test for overall effect z=0.79 p=0.4					

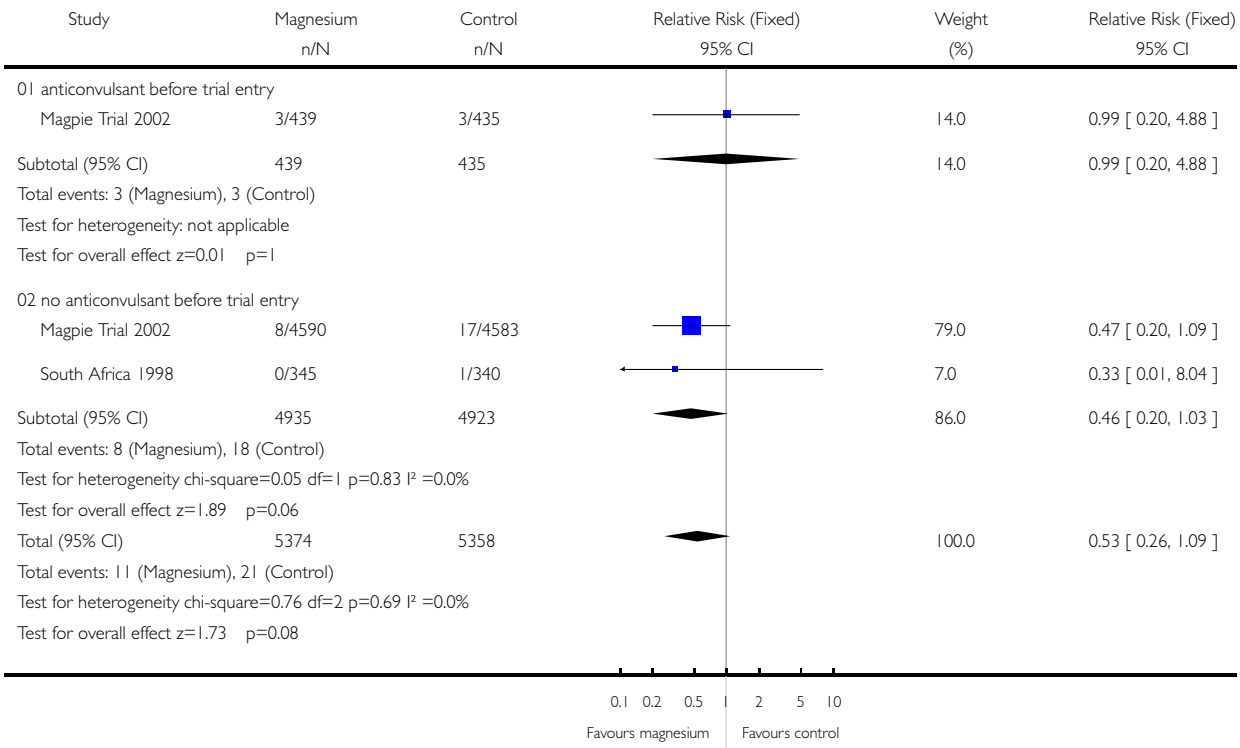


Analysis 04.01. Comparison 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry), Outcome 01 Maternal death

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome: 01 Maternal death



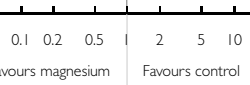
Analysis 04.02. Comparison 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry), Outcome 02 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome: 02 Eclampsia

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 anticonvulsant before trial entry					
Magpie Trial 2002	10/439	8/435		7.4	1.24 [0.49, 3.11]
Subtotal (95% CI)	439	435		7.4	1.24 [0.49, 3.11]
Total events: 10 (Magnesium), 8 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.46 p=0.6					
02 no anticonvulsant before trial entry					
Magpie Trial 2002	30/4590	88/4583		81.4	0.34 [0.23, 0.51]
South Africa 1994	1/112	0/116		0.5	3.11 [0.13, 75.46]
South Africa 1998	1/345	11/340		10.2	0.09 [0.01, 0.69]
× Taiwan 1995	0/34	0/30		0.0	Not estimable
USA - Memphis 1997	1/67	0/68		0.5	3.04 [0.13, 73.42]
Subtotal (95% CI)	5148	5137		92.6	0.34 [0.23, 0.50]
Total events: 33 (Magnesium), 99 (Control)					
Test for heterogeneity chi-square=5.31 df=3 p=0.15 I^2 =43.5%					
Test for overall effect z=5.47 p<0.00001					
Total (95% CI)	5587	5572		100.0	0.41 [0.29, 0.58]
Total events: 43 (Magnesium), 107 (Control)					
Test for heterogeneity chi-square=11.55 df=4 p=0.02 I^2 =65.4%					
Test for overall effect z=5.06 p<0.00001					

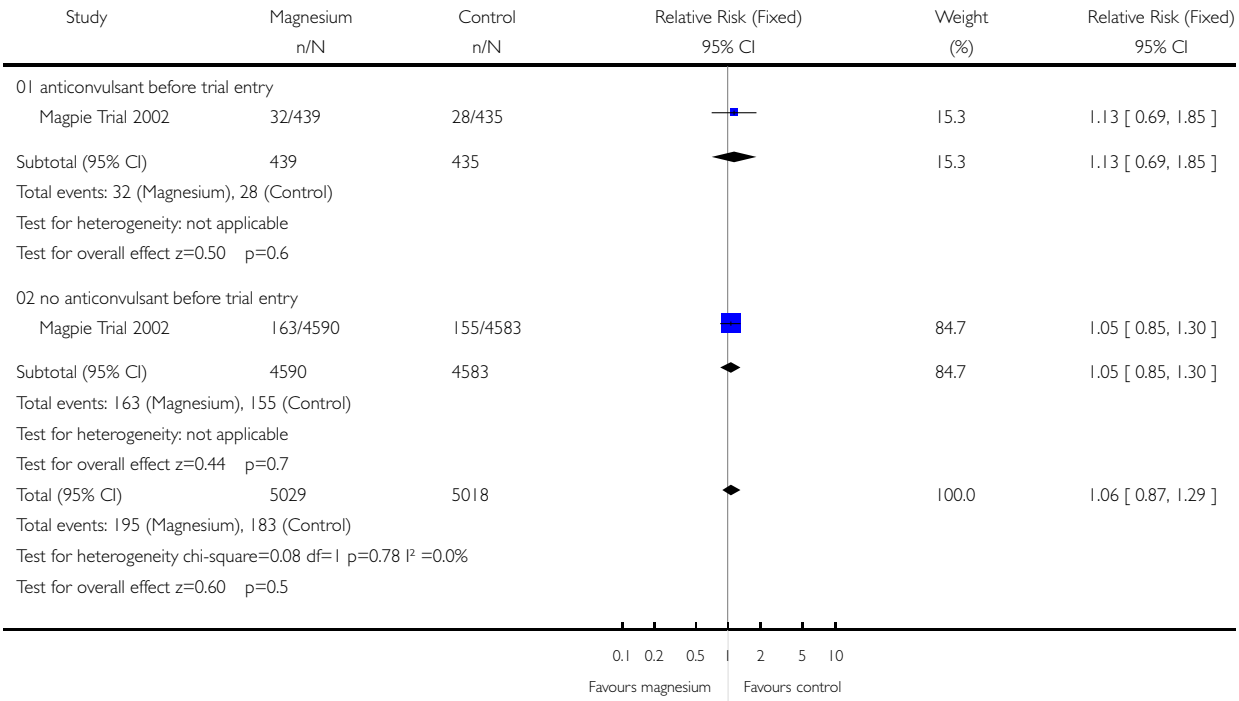


Analysis 04.03. Comparison 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry), Outcome 03 Serious maternal morbidity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome: 03 Serious maternal morbidity



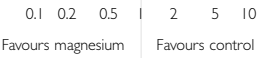
Analysis 04.04. Comparison 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry), Outcome 04 Stillbirths and neonatal deaths

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome: 04 Stillbirths and neonatal deaths

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 anticonvulsant before trial entry					
Magpie Trial 2002	92/408	60/396		10.0	1.49 [1.11, 2.00]
Subtotal (95% CI)	408	396		10.0	1.49 [1.11, 2.00]
Total events: 92 (Magnesium), 60 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.65 p=0.008					
02 no anticonvulsant before trial entry					
Magpie Trial 2002	478/4105	491/4055		81.3	0.96 [0.85, 1.08]
South Africa 1994	20/117	25/118		4.1	0.81 [0.48, 1.37]
South Africa 1998	38/348	28/354		4.6	1.38 [0.87, 2.20]
Subtotal (95% CI)	4570	4527		90.0	0.98 [0.87, 1.09]
Total events: 536 (Magnesium), 544 (Control)					
Test for heterogeneity chi-square=2.69 df=2 p=0.26 I^2 =25.7%					
Test for overall effect z=0.43 p=0.7					
Total (95% CI)	4978	4923		100.0	1.03 [0.93, 1.14]
Total events: 628 (Magnesium), 604 (Control)					
Test for heterogeneity chi-square=9.64 df=3 p=0.02 I^2 =68.9%					
Test for overall effect z=0.50 p=0.6					

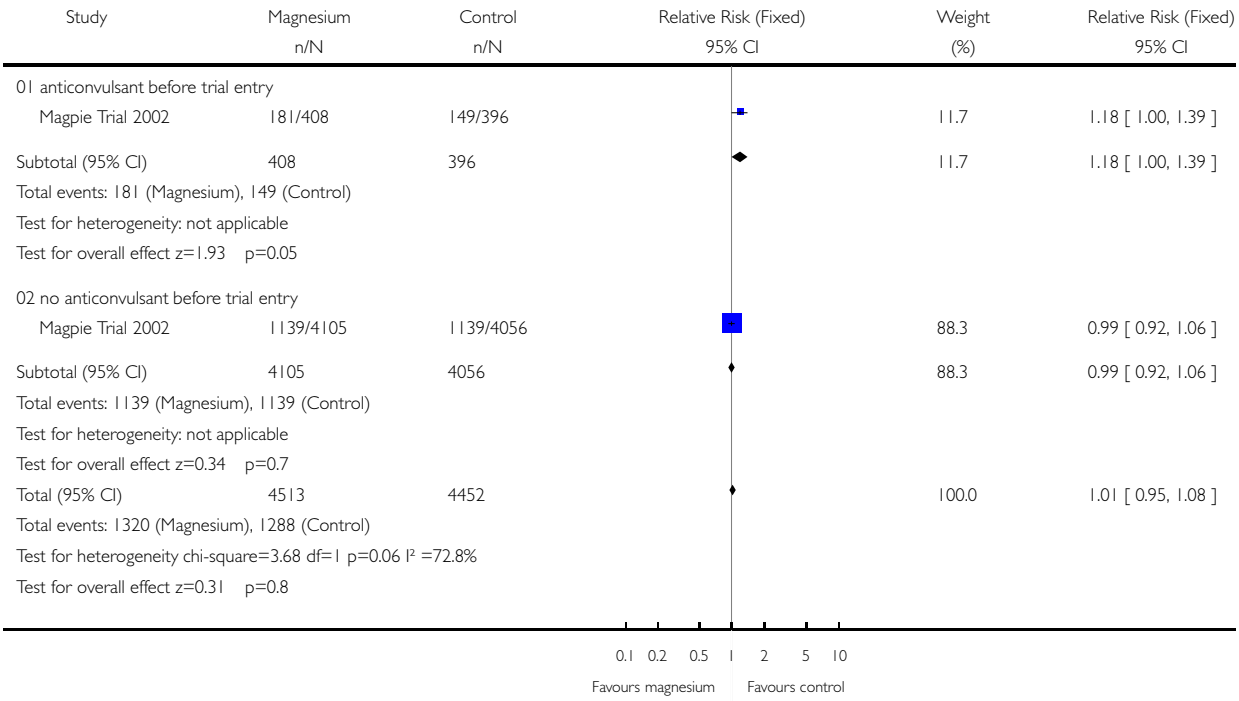


Analysis 04.05. Comparison 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry), Outcome 05 Death or in special care baby unit > 7 days

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 04 Magnesium sulphate versus none/placebo (subgroups by whether anticonvulsant before trial entry)

Outcome: 05 Death or in special care baby unit > 7 days



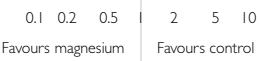
Analysis 05.01. Comparison 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy), Outcome 01 Maternal death

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)

Outcome: 01 Maternal death

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 intramuscular maintenance regimen					
Magpie Trial 2002	8/2301	13/2292		60.5	0.61 [0.25, 1.48]
Subtotal (95% CI)	2301	2292		60.5	0.61 [0.25, 1.48]
Total events: 8 (Magnesium), 13 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.09 p=0.3					
02 intravenous maintenance regimen - 1 g/hour					
Magpie Trial 2002	3/2754	7/2763		32.5	0.43 [0.11, 1.66]
South Africa 1998	0/345	1/340		7.0	0.33 [0.01, 8.04]
Subtotal (95% CI)	3099	3103		39.5	0.41 [0.12, 1.43]
Total events: 3 (Magnesium), 8 (Control)					
Test for heterogeneity chi-square=0.02 df=1 p=0.88 I^2 =0.0%					
Test for overall effect z=1.40 p=0.2					
03 intravenous maintenance regimen - 2 g/hour					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Magnesium), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	5400	5395		100.0	0.53 [0.26, 1.09]
Total events: 11 (Magnesium), 21 (Control)					
Test for heterogeneity chi-square=0.28 df=2 p=0.87 I^2 =0.0%					
Test for overall effect z=1.72 p=0.09					



Analysis 05.02. Comparison 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy), Outcome 02 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)

Outcome: 02 Eclampsia

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 intramuscular maintenance regimen					
Magpie Trial 2002	20/2301	54/2292		50.0	0.37 [0.22, 0.61]
South Africa 1994	1/112	0/116		0.5	3.11 [0.13, 75.46]
Subtotal (95% CI)	2413	2408		50.5	0.39 [0.24, 0.65]
Total events: 21 (Magnesium), 54 (Control)					
Test for heterogeneity chi-square=1.67 df=1 p=0.20 I^2 =40.2%					
Test for overall effect z=3.69 p=0.0002					
02 intravenous maintenance regimen - 1 g/hour					
Magpie Trial 2002	20/2754	42/2763		38.8	0.48 [0.28, 0.81]
South Africa 1998	1/345	11/340		10.2	0.09 [0.01, 0.69]
× Taiwan 1995	0/34	0/30		0.0	Not estimable
Subtotal (95% CI)	3133	3133		49.0	0.40 [0.24, 0.66]
Total events: 21 (Magnesium), 53 (Control)					
Test for heterogeneity chi-square=2.51 df=1 p=0.11 I^2 =60.2%					
Test for overall effect z=3.61 p=0.0003					
03 intravenous maintenance regimen - 2 g/hour					
USA - Memphis 1997	1/67	0/68		0.5	3.04 [0.13, 73.42]
× USA - Tennessee 2001	0/109	0/113		0.0	Not estimable
Subtotal (95% CI)	176	181		0.5	3.04 [0.13, 73.42]
Total events: 1 (Magnesium), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.69 p=0.5					
Total (95% CI)	5722	5722		100.0	0.41 [0.29, 0.58]
Total events: 43 (Magnesium), 107 (Control)					
Test for heterogeneity chi-square=5.70 df=4 p=0.22 I^2 =29.8%					
Test for overall effect z=5.05 p<0.00001					

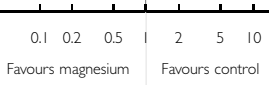
Analysis 05.03. Comparison 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy), Outcome 03 Stillbirths and neonatal deaths

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)

Outcome: 03 Stillbirths and neonatal deaths

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 intramuscular maintenance regimen					
Magpie Trial 2002	380/2171	368/2159		60.2	1.03 [0.90, 1.17]
South Africa 1994	20/117	25/118		4.1	0.81 [0.48, 1.37]
Subtotal (95% CI)	2288	2277		64.2	1.01 [0.89, 1.15]
Total events: 400 (Magnesium), 393 (Control)					
Test for heterogeneity chi-square=0.75 df=1 p=0.39 I^2 =0.0%					
Test for overall effect z=0.20 p=0.8					
02 intravenous maintenance regimen - 1 g/hour					
Magpie Trial 2002	197/2367	190/2327		31.2	1.02 [0.84, 1.23]
South Africa 1998	38/348	28/354		4.5	1.38 [0.87, 2.20]
Subtotal (95% CI)	2715	2681		35.8	1.07 [0.89, 1.27]
Total events: 235 (Magnesium), 218 (Control)					
Test for heterogeneity chi-square=1.40 df=1 p=0.24 I^2 =28.5%					
Test for overall effect z=0.70 p=0.5					
03 intravenous maintenance regimen - 2 g/hour					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Magnesium), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
Total (95% CI)	5003	4958		100.0	1.03 [0.93, 1.14]
Total events: 635 (Magnesium), 611 (Control)					
Test for heterogeneity chi-square=2.35 df=3 p=0.50 I^2 =0.0%					
Test for overall effect z=0.59 p=0.6					



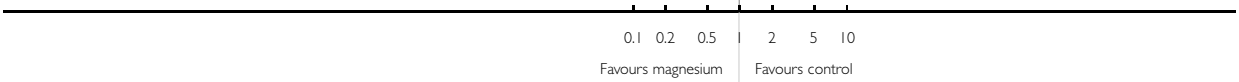
Analysis 05.04. Comparison 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy), Outcome 04 Any reported side effects

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 05 Magnesium sulphate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)

Outcome: 04 Any reported side effects

Study	Magnesium n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 intramuscular maintenance regimen					
Magpie Trial 2002	638/2280	109/2273		45.5	5.84 [4.80, 7.09]
Subtotal (95% CI)	2280	2273		45.5	5.84 [4.80, 7.09]
Total events: 638 (Magnesium), 109 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=17.76 p<0.00001					
02 intravenous maintenance regimen - 1 g/hour					
Magpie Trial 2002	556/2719	119/2720		49.6	4.67 [3.86, 5.66]
Subtotal (95% CI)	2719	2720		49.6	4.67 [3.86, 5.66]
Total events: 556 (Magnesium), 119 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=15.85 p<0.00001					
03 intravenous maintenance regimen - 2 g/hour					
USA - Memphis 1997	45/67	12/68		5.0	3.81 [2.22, 6.53]
Subtotal (95% CI)	67	68		5.0	3.81 [2.22, 6.53]
Total events: 45 (Magnesium), 12 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.85 p<0.00001					
Total (95% CI)	5066	5061		100.0	5.16 [4.52, 5.89]
Total events: 1239 (Magnesium), 240 (Control)					
Test for heterogeneity chi-square=3.79 df=2 p=0.15 I^2 =47.2%					
Test for overall effect z=24.32 p<0.00001					



Analysis 06.01. Comparison 06 Magnesium sulphate versus phenytoin, Outcome 01 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 06 Magnesium sulphate versus phenytoin

Outcome: 01 Eclampsia

Study	Magnesium n/N	Phenytoin n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× USA - Maryland 1993	0/60	0/43		0.0	Not estimable
USA - Texas 1995	0/1049	10/1089		100.0	0.05 [0.00, 0.84]
Total (95% CI)	1109	1132		100.0	0.05 [0.00, 0.84]
Total events: 0 (Magnesium), 10 (Phenytoin)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.08 p=0.04					

Analysis 06.02. Comparison 06 Magnesium sulphate versus phenytoin, Outcome 02 Complications of labour

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 06 Magnesium sulphate versus phenytoin

Outcome: 02 Complications of labour

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 induction of labour					
USA - Texas 1995	317/1049	354/1089		100.0	0.93 [0.82, 1.05]
Subtotal (95% CI)	1049	1089		100.0	0.93 [0.82, 1.05]
Total events: 317 (Treatment), 354 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.14 p=0.3					
02 augmentation of labour					
USA - Texas 1995	352/1049	369/1089		100.0	0.99 [0.88, 1.12]
Subtotal (95% CI)	1049	1089		100.0	0.99 [0.88, 1.12]
Total events: 352 (Treatment), 369 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.16 p=0.9					

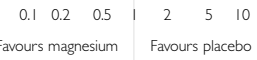
Analysis 06.03. Comparison 06 Magnesium sulphate versus phenytoin, Outcome 03 Caesarean section

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 06 Magnesium sulphate versus phenytoin

Outcome: 03 Caesarean section

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
USA - Alabama 1995	10/27	10/30		3.9	1.11 [0.55, 2.25]
USA - Texas 1995	283/1049	241/1089		96.1	1.22 [1.05, 1.42]
Total (95% CI)	1076	1119		100.0	1.21 [1.05, 1.41]
Total events: 293 (Treatment), 251 (Control)					
Test for heterogeneity chi-square=0.06 df=1 p=0.80 I^2 =0.0%					
Test for overall effect z=2.61 p=0.009					



Analysis 06.04. Comparison 06 Magnesium sulphate versus phenytoin, Outcome 04 Mortality for the fetus or infant

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 06 Magnesium sulphate versus phenytoin

Outcome: 04 Mortality for the fetus or infant

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 stillbirth					
USA - Texas 1995	9/1064	15/1101		100.0	0.62 [0.27, 1.41]
Subtotal (95% CI)	1064	1101		100.0	0.62 [0.27, 1.41]
Total events: 9 (Treatment), 15 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.14 p=0.3					
03 neonatal death					
USA - Texas 1995	13/1064	16/1101		100.0	0.84 [0.41, 1.74]
Subtotal (95% CI)	1064	1101		100.0	0.84 [0.41, 1.74]
Total events: 13 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.47 p=0.6					

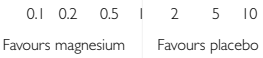
Analysis 06.05. Comparison 06 Magnesium sulphate versus phenytoin, Outcome 05 Infant morbidity

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 06 Magnesium sulphate versus phenytoin

Outcome: 05 Infant morbidity

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 low Apgar at 5 minutes					
USA - Texas 1995	9/1055	16/1086		100.0	0.58 [0.26, 1.30]
Subtotal (95% CI)	1055	1086		100.0	0.58 [0.26, 1.30]
Total events: 9 (Treatment), 16 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.32 p=0.2					
02 admission to special care baby unit					
USA - Texas 1995	34/1055	35/1086		100.0	1.00 [0.63, 1.59]
Subtotal (95% CI)	1055	1086		100.0	1.00 [0.63, 1.59]
Total events: 34 (Treatment), 35 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.00 p=1					



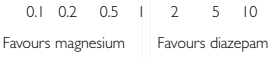
Analysis 07.01. Comparison 07 Magnesium sulphate versus diazepam, Outcome 01 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 07 Magnesium sulphate versus diazepam

Outcome: 01 Eclampsia

Study	Magnesium n/N	Diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Malaysia 1994	0/10	0/18		0.0	Not estimable
Mexico 1992	1/19	0/19		100.0	3.00 [0.13, 69.31]
Total (95% CI)	29	37		100.0	3.00 [0.13, 69.31]
Total events: 1 (Magnesium), 0 (Diazepam)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.69 p=0.5					



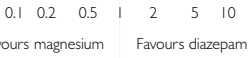
Analysis 07.02. Comparison 07 Magnesium sulphate versus diazepam, Outcome 02 Caesarean section

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 07 Magnesium sulphate versus diazepam

Outcome: 02 Caesarean section

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Malaysia 1994	7/10	9/18		26.3	1.40 [0.76, 2.59]
Mexico 1992	15/19	18/19		73.7	0.83 [0.65, 1.08]
Total (95% CI)	29	37		100.0	0.98 [0.76, 1.27]
Total events: 22 (Treatment), 27 (Control)					
Test for heterogeneity chi-square=2.87 df=1 p=0.09 I^2 =65.2%					
Test for overall effect z=0.13 p=0.9					



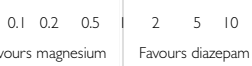
Analysis 07.03. Comparison 07 Magnesium sulphate versus diazepam, Outcome 03 Stillbirths and neonatal deaths

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 07 Magnesium sulphate versus diazepam

Outcome: 03 Stillbirths and neonatal deaths

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 stillbirth					
× Malaysia 1994	0/10	0/18		0.0	Not estimable
Subtotal (95% CI)	10	18		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					
03 perinatal death					
× Malaysia 1994	0/10	0/18		0.0	Not estimable
Subtotal (95% CI)	10	18		0.0	Not estimable
Total events: 0 (Treatment), 0 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					



Analysis 08.01. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 01 Eclampsia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 01 Eclampsia

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	7/831	21/819		100.0	0.33 [0.14, 0.77]
Total (95% CI)	831	819		100.0	0.33 [0.14, 0.77]
Total events: 7 (Magnesium), 21 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.57 p=0.01					

Analysis 08.02. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 02 Stroke

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 02 Stroke

Study	magnesium n/N	nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Nimodipine SG 2003	0/831	0/819		0.0	Not estimable
Total (95% CI)	831	819		0.0	Not estimable
Total events: 0 (magnesium), 0 (nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect: not applicable					

Analysis 08.03. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 03 Coagulopathy

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 03 Coagulopathy

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	3/831	5/819		100.0	0.59 [0.14, 2.47]
Total (95% CI)	831	819		100.0	0.59 [0.14, 2.47]
Total events: 3 (Magnesium), 5 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.72 p=0.5					

Analysis 08.04. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 04 Respiratory problems

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 04 Respiratory problems

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	11/831	3/819		100.0	3.61 [1.01, 12.91]
Total (95% CI)	831	819		100.0	3.61 [1.01, 12.91]
Total events: 11 (Magnesium), 3 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.98 p=0.05					

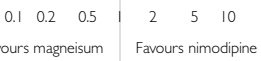
Analysis 08.05. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 05 Cardiac failure

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 05 Cardiac failure

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	2/831	0/819		100.0	4.93 [0.24, 102.49]
Total (95% CI)	831	819		100.0	4.93 [0.24, 102.49]
Total events: 2 (Magnesium), 0 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.03 p=0.3					



Analysis 08.06. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 06 Respiratory depression

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 06 Respiratory depression

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	11/831	3/819		100.0	3.61 [1.01, 12.91]
Total (95% CI)	831	819		100.0	3.61 [1.01, 12.91]
Total events: 11 (Magnesium), 3 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.98 p=0.05					

Analysis 08.07. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 07 Antihypertensive drug

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 07 Antihypertensive drug

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	451/831	374/819		100.0	1.19 [1.08, 1.31]
Total (95% CI)	831	819		100.0	1.19 [1.08, 1.31]
Total events: 451 (Magnesium), 374 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=3.48 p=0.0005					

Analysis 08.08. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 08 Oliguria

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 08 Oliguria

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	55/831	47/819		100.0	1.15 [0.79, 1.68]
Total (95% CI)	831	819		100.0	1.15 [0.79, 1.68]
Total events: 55 (Magneisum), 47 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.74 p=0.5					

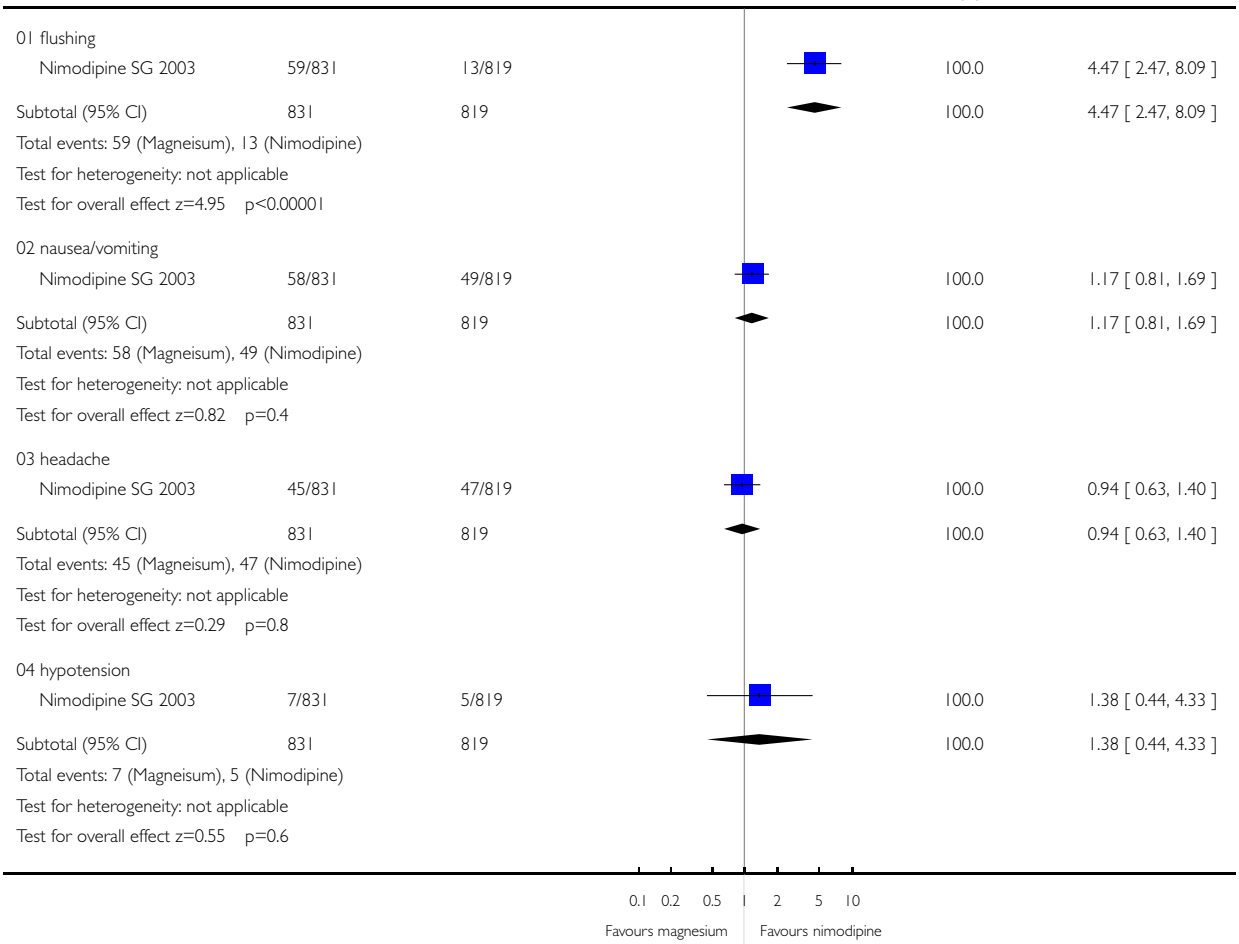
Analysis 08.09. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 09 Side effects

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 09 Side effects

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 flushing					
Nimodipine SG 2003	59/831	13/819		100.0	4.47 [2.47, 8.09]
Subtotal (95% CI)	831	819		100.0	4.47 [2.47, 8.09]
Total events: 59 (Magneisum), 13 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=4.95 p<0.00001					
02 nausea/vomiting					
Nimodipine SG 2003	58/831	49/819		100.0	1.17 [0.81, 1.69]
Subtotal (95% CI)	831	819		100.0	1.17 [0.81, 1.69]
Total events: 58 (Magneisum), 49 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.82 p=0.4					
03 headache					
Nimodipine SG 2003	45/831	47/819		100.0	0.94 [0.63, 1.40]
Subtotal (95% CI)	831	819		100.0	0.94 [0.63, 1.40]
Total events: 45 (Magneisum), 47 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.29 p=0.8					
04 hypotension					
Nimodipine SG 2003	7/831	5/819		100.0	1.38 [0.44, 4.33]
Subtotal (95% CI)	831	819		100.0	1.38 [0.44, 4.33]
Total events: 7 (Magneisum), 5 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.55 p=0.6					



Analysis 08.10. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 10 Placental abruption

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 10 Placental abruption

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	8/831	6/819		100.0	1.31 [0.46, 3.77]
Total (95% CI)	831	819		100.0	1.31 [0.46, 3.77]
Total events: 8 (Magneisum), 6 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.51 p=0.6					

Analysis 08.11. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 11 Caesarean section

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 11 Caesarean section

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	457/831	437/819		100.0	1.03 [0.94, 1.13]
Total (95% CI)	831	819		100.0	1.03 [0.94, 1.13]
Total events: 457 (Magneisum), 437 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.67 p=0.5					

Analysis 08.12. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 12 Postpartum haemorrhage

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 12 Postpartum haemorrhage

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	20/831	8/819		100.0	2.46 [1.09, 5.56]
Total (95% CI)	831	819		100.0	2.46 [1.09, 5.56]
Total events: 20 (Magneisum), 8 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.17 p=0.03					

Analysis 08.13. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 13 Respiratory distress syndrome

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 13 Respiratory distress syndrome

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	55/797	43/767		100.0	1.23 [0.84, 1.81]
Total (95% CI)	797	767		100.0	1.23 [0.84, 1.81]
Total events: 55 (Magnesium), 43 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.05 p=0.3					

Analysis 08.14. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 14 Neonatal hypotonia

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 14 Neonatal hypotonia

Study	Magnesium n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	24/797	13/767		100.0	1.78 [0.91, 3.46]
Total (95% CI)	797	767		100.0	1.78 [0.91, 3.46]
Total events: 24 (Magnesium), 13 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.69 p=0.09					

Analysis 08.15. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 15 Baby intubated

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 15 Baby intubated

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	54/797	38/767		100.0	1.37 [0.91, 2.05]
Total (95% CI)	797	767		100.0	1.37 [0.91, 2.05]
Total events: 54 (Magneisum), 38 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.52 p=0.1					

Analysis 08.16. Comparison 08 Magnesium sulphate versus nimodipine, Outcome 16 Neonatal hypotension

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 08 Magnesium sulphate versus nimodipine

Outcome: 16 Neonatal hypotension

Study	Magneisum n/N	Nimodipine n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Nimodipine SG 2003	2/797	6/767		100.0	0.32 [0.06, 1.58]
Total (95% CI)	797	767		100.0	0.32 [0.06, 1.58]
Total events: 2 (Magneisum), 6 (Nimodipine)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.40 p=0.2					

Analysis 09.01. Comparison 09 Magnesium salts versus methyl dopa, Outcome 01 Other antihypertensive therapy

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 09 Magnesium salts versus methyl dopa

Outcome: 01 Other antihypertensive therapy

Study	Magnesium n/N	alpha blocker n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Denmark 2000	10/14	13/17		100.0	0.93 [0.61, 1.43]
Total (95% CI)	14	17		100.0	0.93 [0.61, 1.43]
Total events: 10 (Magnesium), 13 (alpha blocker)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.32 p=0.8					

Analysis 09.02. Comparison 09 Magnesium salts versus methyl dopa, Outcome 02 Admission to special care baby unit

Review: Magnesium sulphate and other anticonvulsants for women with pre-eclampsia

Comparison: 09 Magnesium salts versus methyl dopa

Outcome: 02 Admission to special care baby unit

Study	Magnesium n/N	Alpha blocker n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Denmark 2000	1/14	1/17		100.0	1.21 [0.08, 17.71]
Total (95% CI)	14	17		100.0	1.21 [0.08, 17.71]
Total events: 1 (Magnesium), 1 (Alpha blocker)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.14 p=0.9