Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus (Review)

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[Intervention review]

Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

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ABSTRACT

Background

Epidemiological and basic science evidence suggests that magnesium sulphate before birth may be neuroprotective for the fetus.

Objectives

To assess the effectiveness and safety of magnesium sulphate as a neuroprotective agent when given to women considered at risk of preterm birth.

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (October 2006), CENTRAL (*The Cochrane Library* 2006, Issue 3*)*, MEDLINE (1966 to October 2006), EMBASE (1980 to October 2006), Current Contents (1992 to October 2006), references of retrieved articles, and abstracts submitted to the Society for Pediatric Research (1996 to 2006).

Selection criteria

Randomised controlled trials of antenatal magnesium sulphate therapy given to women threatening or likely to give birth at less than 37 weeks' gestational age.

Data collection and analysis

We independently extracted data regarding clinical outcomes including paediatric mortality, neurologic outcome of survivors (including blindness, deafness, cerebral palsy and major neurosensory disability), and maternal complications and side-effects. At least two authors assessed trial eligibility and quality, and extracted data.

Main results

Four trials (3701 babies) were eligible for this review. No statistically significant effect of antenatal magnesium sulphate therapy was detected on any major paediatric outcome, including mortality (e.g., paediatric mortality relative risk (RR) 0.97; 95% confidence

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interval (CI) 0.74 to 1.28; four trials; 3701 infants), and neurological outcomes in the first few years of life, including cerebral palsy (RR 0.77; 95% CI 0.56 to 1.06; four trials; 3701 infants), neurological impairments or disabilities. There were also no significant effects of antenatal magnesium therapy on combined rates of mortality with neurologic outcomes. There was a significant reduction in the rate of substantial gross motor dysfunction (RR 0.56; 95% CI 0.33 to 0.97; two trials; 2848 infants). There were higher rates of minor maternal side-effects in the magnesium groups, but no significant effects on major maternal complications.

Authors' conclusions

The role for antenatal magnesium sulphate therapy as a neuroprotective agent for the preterm fetus is not yet established. Given the possible beneficial effects of magnesium sulphate on gross motor function in early childhood, outcomes later in childhood should be evaluated to determine the presence or absence of later potentially important neurologic effects, particularly on motor or cognitive function. Further information will be available from one of the studies where outcomes are being evaluated again at eight to nine years of age, and from another trial currently in progress.

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PLAIN LANGUAGE SUMMARY

Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Currently there is not enough evidence to show if magnesium sulphate given to women at risk of preterm birth might help to protect the baby's brain and improve long-term outcomes.

Babies born too early (preterm) have a higher risk of dying in the first weeks of life than babies born at term, and those who survive often have damage to their nerves in the form of cerebral palsy, blindness, deafness or physical disabilities. This can cause huge distress for parents. Magnesium is an important element essential for normal body functions. Magnesium sulphate is used to reduce the risk of fits, i.e., it is an anticonvulsant drug, in women with very high blood pressure in pregnancy. So, theoretically, it may help to reduce the effect of damaging events to a preterm baby's brain. However, it has adverse effects in the mother of flushing, sweating, nausea, vomiting, headaches and a rapid heartbeat (palpitations). This review identified four studies involving 3701 infants, but it cannot conclusively confirm if magnesium sulphate therapy protects the unborn baby's brain. Further research (yet to be published) is needed to show if magnesium can provide these benefits.

BACKGROUND

Preterm birth and neurological outcome

Infants born preterm have a higher risk of dying in the first weeks of life. If they survive, they have a greater risk of neurologic impairments, such as cerebral palsy, blindness, deafness, or cognitive dysfunction (either developmental delay, or intellectual impairment), and a greater risk of substantial disability as a result of these neurologic impairments (Doyle 2001; VICS 1997). Moreover, as the rate of preterm birth is rising, up to 12.7% in the United States in 2005 (Hamilton 2006), more babies are at risk of death and adverse neurological outcomes. Cerebral palsy and cognitive dysfunction are the most frequent neurologic impairments, and any therapy that can reduce their prevalence should have a substantial effect on reducing overall neurologic impairments and disabilities in surviving preterm infants.

Cerebral palsy is a term which includes a number of different diseases or conditions that can arise at any time during brain development that involves a disorder of movement or posture, or both, and a disorder of motor function which is permanent but may change over time (Oxford Register 2001; SCPE 2000). The cerebral palsies remain the most frequent cause of severe motor disability in childhood with a background prevalence of two per thousand live births (Oxford Register 2001; Stanley 1994). The life expectancy shows 92% of affected children surviving to 20 years (Hutton 1994), contributing substantially to the burden of illness into adulthood.

Very preterm birth (less than 34 weeks) and very low birthweight (less than 1500 g) are principal risk factors for cerebral palsy (Drummond 2002; Lorenz 1998; Pharoah 1998) making up between 17% to 28% of all cases of cerebral palsy. Over 10% of all preterm births are from a multiple pregnancy with higher rates of cerebral palsy than singleton pregnancies. Twins have seven times and triplets 47 times the risk of cerebral palsy compared with singletons (Petterson 1993).

Evidence from population-based registries shows that the prevalence of cerebral palsy in low and very low birthweight infants is rising (Drummond 2002; Hagberg 2001; Oxford Register 2001; Stanley 1992). However, not all population-based registries have reported an increase in cerebral palsy in very low birthweight survivors; some have reported a decrease (Himmelmann 2005; Surman 2003). Although suspected from earlier birthweight analyses, Drummond's registry study confirms that the increasing prevalence of cerebral palsy is from higher rates in preterm, not term, infants (Drummond 2002). Intraventricular haemorrhage (IVH) is a known risk factor for the later development of cerebral palsy (Kuban 1994) with the risk of IVH increasing the earlier the gestational age at birth (Vermeulen 2001).

In order to reduce the impact of cerebral palsy from very preterm birth, efforts must be focussed on primary prevention.

A possible role for magnesium

The first report that prenatal magnesium sulphate was associated with a reduction in risk of IVH, from 18.9% to 4.4%, in babies born with a birthweight less than 1500 g was by Kuban and colleagues in 1992 (Kuban 1992). A case-control analysis from the California Cerebral Palsy project investigated whether in utero exposure to magnesium sulphate was associated with a lower prevalence of cerebral palsy in infants born weighing less than 1500 g (Nelson 1995). Cases were children with cerebral palsy who were singletons and whose birthweight had been less than 1500 g. Controls were randomly sampled from live births of less than 1500 g from the same birth populations. Magnesium sulphate given to the mother during labour was associated with a marked reduction in the risk of cerebral palsy (odds ratio 0.14; 95% confidence interval 0.05 to 0.51).

Other observational studies have supported a reduction in cerebral palsy in preterm infants by maternal administration of magnesium sulphate (Hauth 1995; Schendel 1996; Wiswell 1996) and some have found a reduction in the risk of IVH (Finesmith 1997;

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Perlman 1994; Wiswell 1996) and perinatal mortality (Grether 1998). However, not all observational studies have reported benefit for prenatal magnesium sulphate on the risk of IVH (Canterino 1999; Kimberlin 1998; Paneth 1997; Weintraub 2001), cerebral palsy (Grether 2000; O'Shea 1998; Paneth 1997) or perinatal mortality (Kimberlin 1998). However, observational studies alone cannot be the basis for changing clinical practice.

Animal studies have shown that magnesium can provide a neuroprotective effect (McDonald 1990). It can prevent posthypoxic brain injury by blocking the excess release of glutamate in the calcium channel. Fetal and newborn brains seem to be more susceptible to damage from glutamate release. Consequently, blocking glutamate receptors through agents such as magnesium may reduce the risk of injury in the perinatal period (Espinoza 1991).

Magnesium sulphate is widely used in obstetrics as an anticonvulsant for the treatment of eclampsia (Duley 2000; Duley 2003a; Duley 2003b), prevention of eclampsia in women with pre-eclampsia (Duley 2003c; Sibai 2003) and has been used as a tocolytic, although it lacks efficacy for inhibition of preterm labour (Crowther 2002).

Magnesium sulphate, by its peripheral vasodilator effects when infused intravenously, produces flushing, sweating, and a sensation of warmth. Reported maternal side-effects, related to dosage and speed of infusion, include nausea, vomiting, headache, palpitations and rarely pulmonary oedema. Administration to levels above the recommended therapeutic range can lead to respiratory depression, respiratory arrest, cardiac arrest and death. For the neonate, hypermagnesaemia can lead to hyporeflexia, poor sucking, and, rarely, respiratory depression needing mechanical ventilation (Levene 1995; Lipsitz 1971).

This review assesses the effectiveness and safety of magnesium sulphate given to women considered to be at risk of preterm birth, as a neuroprotective agent for their baby.

OBJECTIVES

To assess the effectiveness and safety, using the best available evidence, of magnesium sulphate as a neuroprotective agent when given to women considered to be at risk of preterm birth.

METHODS

Criteria for considering studies for this review

Types of studies

All published, unpublished and ongoing randomised trials with reported data comparing outcomes for women at risk of preterm birth given prenatal magnesium sulphate with outcomes in controls, whether treated or not with placebo. Trials were included if the primary aim of the study was to prevent neurologic abnormalities in the unborn baby, or if the primary aim was otherwise but long-term neurological outcomes were reported for the infants. The trials had to use some form of random allocation and report data on one or more of the prestated outcomes. Quasi-randomised trials were excluded.

Types of participants

Women considered to be at risk of preterm birth. We planned predefined subgroups to examine separately the primary outcomes for women and infants based on the primary intent of the study (neuroprotection or other reason such as tocolysis or preventing or treating eclampsia), the reasons the woman was considered to be at risk for preterm birth, the number of infants in utero (singleton, twin or higher order multiple pregnancy), the presence or absence of ruptured membranes at trial entry, and whether prenatal corticosteroids had been given.

Types of interventions

Magnesium sulphate given to the women at risk of preterm birth, administered intravenously, intramuscularly or orally, compared with either placebo or no placebo. Trials where magnesium sulphate was used with the prime aim of tocolysis (Crowther 2002), prevention and treatment of eclampsia (Duley 2000 ; Duley 2003a; Duley 2003b), maintenance therapy after preterm labour (Crowther 1998) or as a dietary supplement in pregnancy (Makrides 2001) were not included unless they reported long-term neurologic outcomes in the children as those trials are covered in these separate Cochrane reviews.

We planned predefined subgroups that examined separately the primary outcomes for women and infants based on the magnesium preparation given, the dosage given, the mode of administration, and the gestational age at which the treatment was given.

Types of outcome measures

We prespecified clinically relevant outcomes after discussion.

Primary outcomes

We chose primary outcomes to be most representative of the clinically important measures of effectiveness and safety, including serious outcomes, for the women and their infants. We recognised that the list of outcomes was extensive and that data for some may not be available but we wanted to encapsulate the types of outcomes that may be of concern to clinicians caring for both the mother and the baby, both now and in the future. In so doing, we also recognised the increased possibility of type I errors because multiple outcomes would be evaluated. Combined outcomes were used for the main analyses, rather than all their components.

For the infants/children

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- Fetal, neonatal or later death.
- Neurologic impairments (developmental delay or intellectual impairment [developmental quotient or intelligence quotient less than one standard deviation {SD} below the mean], cerebral palsy [abnormality of tone with motor dysfunction], blindness [corrected visual acuity worse than 6/60 in the better eye], or deafness [hearing loss requiring amplification or worse]), or neurologic disabilities [abnormal neurologic function caused by any of the preceding impairments] at follow up later in childhood. Substantial gross motor dysfunction [defined as motor dysfunction such that the child was not walking at age two years or later].
- Major neurologic disability (defined as any of: legal blindness, sensorineural deafness requiring hearing aids, moderate or severe cerebral palsy, or developmental delay/intellectual impairment [defined as developmental quotient or intelligence quotient less than two SD below the mean]).
- Paediatric mortality combined with cerebral palsy, substantial gross motor dysfunction, neurological impairment, or major neurologic disability (these latter outcomes recognise the competing risks of death or survival with neurologic problems).

The major paediatric outcomes were death or neurological (cerebral palsy, impairment or disability), or combinations of death with the neurological outcomes.

For the women

- Serious adverse cardiovascular/respiratory outcome (maternal death, respiratory arrest, cardiac arrest).
- Adverse effects severe enough to stop treatment.

Secondary outcomes

These include other measures of effectiveness, complications, satisfaction with care and health service use.

For the infant

- Any intraventricular haemorrhage (IVH).
- IVH grade 3/4.
- Cystic periventricular leucomalacia.
- Apgar score less than seven at five minutes.
- Need for active resuscitation (assisted ventilation via an endotracheal tube) at birth.
- Neonatal convulsions.
- Neonatal hypotonia.
- Use of respiratory support (mechanical ventilation or continuous positive airways pressure, or both).
- Chronic lung disease (need for continuous, supplemental oxygen at 28 days postnatal age or 36 weeks' postmenstrual age).
- Use of postnatal corticosteroids.

For the child

- Growth assessments at childhood follow up (weight, head circumference, length/height).
- Educational achievements.

For the woman

- Blood pressure changes during infusion.
- Respiratory rate changes during infusion.
- Pulse rate at birth changes during infusion.
- Length of labour.
- Need for augmentation of labour.
- Postpartum haemorrhage.
- Mode of birth.
- Intrapartum fever requiring the use of antibiotics.
- Breastfeeding after hospital discharge.
- Women's satisfaction with the therapy.

Use of health services

- Length of postnatal hospitalisation for the women.
- Admission to intensive care unit for the mother.
- Admission to neonatal intensive care.
- Length of stay in neonatal intensive care unit.
- Length of neonatal hospitalisation.
- Costs of care for mother or baby, or both.

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (October 2006).

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 36 journals plus BioMed Central email alerts.

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.

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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, we searched CENTRAL (*The Cochrane Library* 2006, Issue 3), MEDLINE (1966 to October 2006), EMBASE (1980 to October 2006) and Current Contents (1992 to October 2006), using the terms 'magnesium near pregnan*' and 'magnesium near preterm or pre-term', combined with terms related to the main outcomes, including 'mortality', 'survival', 'cerebral palsy', 'deaf*', blind*', 'intellectual impairment', 'developmental delay', 'impairment', and 'disability'. We performed a manual search of the relevant references from retrieved articles. We searched abstracts submitted to major international congresses, such as the Society for Pediatric Research (1996 to 2006).
We did not apply any language restrictions.

Data collection and analysis

At least two review authors evaluated trials under consideration for inclusion without consideration of their results. We also assessed the methodological quality of trials independently. We resolved differences of opinion by discussion. There was no blinding of authorship. We processed included trial data as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005a). Where one of the authors was a chief investigator in a trial included in the review, at least one other author also extracted data.
In assessing selection bias, we examined the processes involved in the generation of the random sequence and the method of allocation concealment separately. These were then judged as adequate or inadequate using the criteria described in Section VI of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005b): A = adequate, B = unclear, C = inadequate, D = not used. Studies rated as C or D were excluded.
We examined performance bias as to whom was blinded in the trials. We sought details of the feasibility and appropriateness of blinding for participant, caregiver, outcome assessment and data analysis, categorised as below:
(A) not known or not likely to guess the allocated treatment;
(B) side-effects of one or other treatment, so that it is likely that for a significant proportion (more than 20%) of participants the allocation could be correctly identified;
(C) knew (or were likely to guess) the allocated treatment;
(D) unclear.
In addition, we assigned scores to each trial for use of a placebo and the completeness of follow up as follows.

Use of placebo

(A) Placebo used;
(B) attempt at a placebo;
(C) no placebo;
(D) unclear.

Completeness of outcome reporting of randomised mothers

(A) Less than 3% of participants excluded;
(B) 3% to 9.9% of participants excluded;
(C) 10% to 19.9% of participants excluded;
(D) 20% or more excluded;
(E) unclear.

Completeness of follow up of randomised infants

(A) Less than 10% of surviving infants not followed;
(B) 10% to 19.9% of surviving infants not followed;
(C) 20% to 29.9% of surviving infants not followed;
(D) 30% or more surviving infants not followed;
(E) unclear.
We included outcome data in the analyses if they met the prestated criteria in 'Types of outcome measures'. We processed included trial data as described in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005a). We extracted the data independently, which were then double entered. We resolved discrepancies by discussion. There was no blinding of authorship. Whenever possible, we sought unpublished data and information about quality issues that were unclear from investigators.
We performed statistical analyses using the Review Manager software (RevMan 2003) and compared categorical data using relative risks and 95% confidence intervals. We tested for statistical heterogeneity between trials using the I^2 statistic. If substantial heterogeneity was found (I^2 greater than 50%), we used a random-effects model, in addition to exploring subgroup analyses. In addition, statistically significant differences between subgroups for primary outcomes were analysed by chi-squared analysis, where possible.
We analysed data extracted from the trials on an intention-to-treat basis. Where this was not done in the original report, we performed re-analysis where possible. If missing data were such that it might significantly affect the results, we excluded these data from the analysis. This decision rested with the review authors and was clearly documented. If missing data become available subsequently, they will be included in the analyses.
A priori it was decided that all eligible trials would be included in the initial analysis and sensitivity analyses carried out to evaluate the effect of trial quality including aspects of selection, performance and attrition bias. This was done by subgrouping for quality of concealment of treatment allocation using the grading A or B and other sensitivity analyses based on the quality assessments as specified above.
We planned a subgroup analysis for the major paediatric outcomes of mortality and long-term neurologic morbidity according to whether the primary intention of administering magnesium sulphate was for neuroprotection of the fetus, as distinct from other

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indications. We also planned subgroup analyses to examine separately the major paediatric outcomes of mortality and long-term neurologic morbidity based on the reasons the woman was considered to be at risk of preterm birth, the number of babies in utero (singleton or multiple), the presence or absence of ruptured membranes at trial entry, the use of prenatal corticosteroids in more than 50% of those at risk, the type of magnesium preparation given, the dosage of magnesium sulphate given, its mode of administration, and the gestational age at which it was given.

We limited primary analysis to the prespecified outcomes and subgroup analyses. In the event of differences in outcomes not prespecified being found, we clearly identified them as such.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of ongoing studies.

Four trials (3701 babies) qualified for inclusion in this review, one from Australia and New Zealand (Crowther 1998), one from the US (Mittendorf 2002), one from France (Marret 2006), and one that was worldwide, but predominantly from developing countries (Magpie 2006) (*see* 'Characteristics of included studies' table). The first three trials specifically targeted women who were likely to give birth early and magnesium was being used for neuroprotection, although one study (Mittendorf 2002) also had a tocolytic arm to the study. The fourth study, the MAGPIE trial (Magpie 2006) was designed to prevent eclampsia in women with pre-eclampsia and included women at all gestational ages. Data from the MAGPIE study relevant to women less than 37 weeks when randomised have been provided by the authors for inclusion in this review.

Mittendorf 2002 (neuroprotection/other intent - tocolysis) - A total of 149 women in preterm labour 25 to 33 weeks' gestation were enrolled from October 1995 to January 1997 at a single US centre. Women were excluded if there was non-reassuring fetal assessment, or clinical features of infection or pre-eclampsia, or more than twin pregnancy. Stratification was by race (black versus other), gestational age (25 to 28 weeks and 28 to 33 weeks), and, several months into the trial, plurality (singleton versus twin). There were two treatment strategies dependent upon cervical dilatation at entry: those with active labour and cervical dilatation less than 5 cm were considered candidates for tocolysis with magnesium sulphate (the 'tocolytic' arm); they were randomly allocated to receive magnesium sulphate as a 4 g bolus followed by 2 to 3 g/hour maintenance (n = 46 women, 55 babies), or an alternative tocolytic (non-blinded) (n = 46 women, 51 babies). The remainder (with cervical dilatation greater than 4 cm) were considered for the 'neuroprotective' arm of the study and were randomly allocated to either a 4 g magnesium sulphate bolus (n = 29 women, 30 babies) or saline placebo (n = 28 women, 29 babies). For the purposes of this review, the Mittendorf study was considered as two separate trials.

Crowther 1998 (neuroprotection) - A total of 1062 women with babies less than 30 weeks' gestation and in whom birth was anticipated within 24 hours were enrolled from February 1996 to September 2000. Women were excluded if birth was imminent (they were in second stage of labour), if they had already received magnesium sulphate during the pregnancy, or if there were contraindications to magnesium sulphate therapy. There were 16 collaborating centres within Australia and New Zealand. Stratification was by centre and multiple pregnancy (three groups - singleton, twin or higher order multiple). Women were randomly allocated to either intravenous magnesium sulphate (n = 535 women, 629 live babies) or an identical volume of saline placebo (n = 527 women, 626 live babies). The magnesium sulphate dose was 4 g over 20 minutes, followed by 1 g/hour for up to 24 hours or until birth, whichever came first. There were no repeat courses of treatment.

Magpie 2006 (other intent - neuroprotection of the mother) - A total of 10,141 women who were either undelivered or within 24 hours of birth with pre-eclampsia and uncertainty about whether to use magnesium sulphate to prevent eclampsia were enrolled from July 1998 to November 2001 in a randomised controlled trial of either magnesium sulphate or saline placebo. Women were excluded if they had hypersensitivity to magnesium, hepatic coma, or myasthenia gravis. The magnesium sulphate dose was 4 g intravenously over 10 to 15 minutes, followed by either 1 g/hour intravenously for 24 hours, or by 5 g every 4 hours intramuscularly for 24 hours. The major endpoint of the study was neuroprotection of the mother (avoidance of eclampsia). Secondary endpoints included long-term outcome for the children. Unpublished outcome data were provided from the trial investigators on the women who were undelivered when treated with magnesium sulphate and who were less than 37 weeks' gestational age at randomisation, as well as for the subgroups less than 34 and less than 30 weeks' gestational age at randomisation, and for the subgroups of singleton pregnancies versus multiple pregnancies. Outcome data for women from the Magpie study were included if the child was selected for follow up and outcomes for the child were known, even if the only outcome available was death.

Marret 2006 (neuroprotection) - A total of 573 women whose birth was planned or expected within 24 hours with singleton, twin or triplet less than 33 weeks' gestation were enrolled at 18 collaborating centres in France, but data from only 13 centres (564 women) were included in the final report; two of the 18 centres recruited no women and three centres enrolled fewer than five women and were excluded on the basis of a prespecified criterion for exclusion of centres. Women were not eligible when the fetus had severe malformations, chromosomal abnormalities or growth restriction, and with various maternal complications, such as pre-eclampsia, hypotension, cardiac arrhythmias, electrolyte anomalies, renal insufficiency. Women were randomly allocated to either

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intravenous magnesium sulphate 4 g or an equal volume of isotonic saline placebo over 30 minutes. The major endpoint of the study was white matter injury to the infant diagnosed by cranial ultrasound.

Risk of bias in included studies

Mittendorf 2002 - The 'tocolytic' arm was unblinded, whereas the 'neuroprotective' arm was blinded. The method of randomisation was not described. Outcomes were given for all mothers and babies enrolled.

Follow-up component: surviving children were assessed at 4, 8, 12 and 18 months of age, corrected for prematurity, in a special follow-up clinic. There was no statement on blinding of the assessors to the treatment allocation. Neurologic outcomes included cerebral palsy at 18 months, with diagnosis made or confirmed by a developmental paediatrician (criteria not described). Other outcomes were not described. The follow-up rate of survivors was not described.

Crowther 1998 - This was a double-blind trial with randomisation performed centrally by non-clinical staff independent of the chief investigators, with random variation in block sizes of four, six or eight, and separately for singleton, twin, or higher order multiple births. Each study number was placed on a masked treatment pack. Packs were sent to individual hospitals ready for use. No-one at individual study sites had access to the treatment code. Outcomes were given for all mothers and fetuses enrolled.

Follow-up component: surviving children were assessed at 24 months of age, corrected for prematurity, by paediatricians and psychologists at individual study sites who were blinded to treatment group allocation. Neurologic outcomes included cerebral palsy (criteria included abnormalities of tone and motor dysfunction) and gross motor function assessed by the criteria of Palisano 1997 . Substantial gross motor dysfunction comprised children who were not walking independently at two years of corrected age. Other outcomes included blindness (bilateral vision worse than 6/60), deafness requiring hearing aids, and developmental delay (defined as an Mental Developmental Index (MDI) on the Bayley Scales of Infant Development less than 85 [less than -1 SD] Bayley 1993). Major neurologic disability was defined as any of moderate or severe cerebral palsy, blindness, deafness or an MDI less than 70. The follow-up rate of survivors at two years was 99% (1047/1061).

Magpie 2006 - This was a double-blind trial with randomisation performed centrally, independent of the clinical investigators, with balance for severity of pre-eclampsia, gestational age, undelivered or delivered, anticonvulsants prior to entry, multiple pregnancy, and country. Masked treatment packs were provided to individual hospitals ready for use. No-one at individual study sites had access to the treatment code. Outcomes were given for 99.7% of mothers and 98.7% of fetuses enrolled.

Follow-up component: not all surviving children could be followed in this multinational trial for various logistic reasons. In the study overall, approximately 2/3 of surviving children were selected for follow up, and of these children outcomes were determined for 73% (n = 3283), including those who died. Children were assessed by a developmental screening questionnaire at 18 or more months of age, corrected for prematurity where appropriate, and those who failed were invited for a more formal developmental test - usually the Bayley Scales of Infant Development, either the first (Bayley 1969) or the second edition (Bayley 1993), or alternative tests such as the Griffiths scales. In addition, 20% of screen negative children were also assessed formally. It was intended that children would be at least 18 months old, corrected for prematurity where appropriate, but in some instances children had data only at younger ages. Major neurologic disability was defined as any of moderate or severe cerebral palsy, blindness, deafness or a MDI on the Bayley Scales less than 70. Children were not routinely examined by a paediatrician or neurologist for diagnoses such as cerebral palsy. Given the lack of formal assessment of all children it is probable that diagnoses such as developmental delay (defined as a MDI on the Bayley Scales less than 85 [less than -1 SD]), or cerebral palsy were underestimated. For this review, the Magpie investigators provided data for 1593 infants whose mothers were treated at less than 37 weeks' gestational age out of the total of 3283 children with follow-up data.

Marret 2006 - This was a single-blind trial with randomisation performed centrally, with randomisation numbers generated by computer using variable block size from two to 16 depending on expected recruitment. Randomisation was independent of the clinical investigators, with balance for study centre, multiple pregnancy, and gestational age (less than 27, 27 to 29, 30 to 32 weeks). The major endpoint of the study was infant death or white matter injury detected by cranial ultrasound and defined as the presence of periventricular cavitation, intraparenchymal haemorrhage, persisting hyperechogenicity or ventricular dilatation.

Follow-up component: at two years of age physicians caring for the children or the study investigators, who were blinded to treatment allocation, obtained data either by clinical examination or telephone with a standardised questionnaire derived from Amiel-Tison's (Amiel-Tison 2004) and the Denver Developmental Scale. Motor and cognitive developmental scales were scored, ranging from one (normal) to four (severely impaired). The follow-up rate of survivors was 96%.

Effects of interventions

We included four trials with a total of 3701 babies (Crowther 1998; Magpie 2006; Marret 2006; Mittendorf 2002). The Mittendorf trial (Mittendorf 2002) has both tocolytic and neuroprotective arms and hence appears twice. Results are presented on a 'as randomised' basis. (Results were also analysed on the basis of liveborn infants only, and these were very similar to the 'as randomised' analyses.)

Infant mortality - fetal, neonatal and later (Graphs

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1.01 to 1.03)

Antenatal magnesium sulphate treatment had no overall significant effect on total (fetal, neonatal and later) mortality (relative risk (RR) 0.97; 95% confidence interval (CI) 0.74 to 1.28; four trials; 3701 infants). While Crowther 1998, Magpie 2006 and Marret 2006 showed no significant mortality differences between magnesium and no magnesium groups, Mittendorf 2002 showed significantly more deaths in the magnesium group (10/85 versus 1/80). Eight of the 10 deaths in the magnesium group (and no deaths in the no magnesium group) occurred in the 'tocolytic' arms of Mittendorf 2002 compared with two deaths and one death respectively in the 'neuroprotective' arms of the trial.

There were sufficient data to permit subgroup analysis based on the primary intent for giving magnesium sulphate in the study, either specifically for neuroprotection of the infant (the neuroprotective intent subgroup) or for other reasons, such as tocolysis or prevention of eclampsia (other intent subgroup). The RR for the neuroprotective intent subgroup was 0.83; 95% CI 0.66 to 1.03; three trials; 2002 infants; and RR for the other intent subgroup was 2.86; 95% CI 0.23 to 35.82; two trials; 1699 infants). There was significant heterogeneity overall (I^2 = 52.3%) and in the other intent subgroup (I^2 = 71.2%) between studies, largely due to the different results from the other intent (tocolytic) arm of Mittendorf 2002. The difference between the "neuroprotective" and the "other intent" subgroups was statistically significant (chi squared = 4.37, P = 0.037).

For fetal deaths only, little difference was seen between the magnesium and no magnesium groups (RR 0.98; 95% CI 0.78 to 1.24; four trials; 3701 infants), or in the subgroups by intent. Most discrepancy between studies was seen for deaths of liveborn infants to latest age of follow up (neuroprotective intent subgroup: RR 0.83; 95% CI 0.65 to 1.05; three trials; 2002 infants and other intent subgroup: RR 3.02; 95% CI 0.28 to 33.04; two trials; 1699 infants).

Paediatric neurologic outcomes (Graphs 1.04 to 1.10)

There were no significant effects of antenatal magnesium sulphate treatment on cerebral palsy (overall RR 0.77; 95% CI 0.56 to 1.06; four trials; 3701 infants; RR for neuroprotective intent subgroup 0.83; 95% CI 0.60 to 1.15; three trials; 2002 infants; and RR for other intent subgroup 0.29; 95% CI 0.07 to 1.16; two trials; 1699 infants). The difference between the "neuroprotective" and the "other intent" subgroups was not statistically significant (chi squared = 1.65, P = 0.20).

Crowther 1998 (neuroprotective intent: 1255 infants) and Magpie 2006 (other intent: 1593 infants) were the only studies to report on a number of other neurologic outcomes (two trials; 2848 infants). Substantial gross motor dysfunction was the only outcome to show a significant difference between magnesium and placebo overall (RR 0.56; 95% CI 0.33 to 0.97 in favour of magnesium), but the result was largely attributable to the Crowther 1998 study (RR 0.53; 95% CI 0.30 to 0.92 in favour of magnesium).

Combined results for the other neurologic outcomes were:

- any neurologic impairment: RR 1.01; 95% CI 0.86 to 1.19; two trials; 2848 infants;
- blindness: RR 0.66; 95% CI 0.11 to 3.97; two trials; 2848 infants;
- deafness: RR 1.12; 95% CI 0.43 to 2.89; two trials; 2848 infants;
- developmental delay or intellectual impairment: RR 1.02; 95% CI 0.85 to 1.21; two trials; 2848 infants;
- major neurologic disability: RR 1.07; 95% CI 0.82 to 1.40; two trials; 2848 infants.

Combined paediatric mortality and neurologic outcomes (Graphs 1.11 to 1.14)

There was no significant effect of antenatal magnesium sulphate treatment on the combined rate of death or cerebral palsy (RR 0.96; 95% CI 0.75 to 1.24; four trials; 3701 infants). The results for the neuroprotective and other intent groups were RR 0.83; 95% CI 0.64 to 1.07; three trials; 2002 infants, and RR 1.28; 95% CI 0.68 to 2.41; two trials; 1699 infants, respectively. There was a high level of heterogeneity, but only for the trials overall (I^2= 60.6%). The difference between the "neuroprotective" and the "other intent" subgroups was statistically significant (chi squared = 5.72, P = 0.017).

Crowther 1998 and Magpie 2006 were the only studies to report other neurologic outcomes, results for combined death/neurologic outcomes are only available from these two trials for a total of 2848 infants.

Neither death nor any neurological impairment (RR 1.00; 95% CI 0.91 to 1.11), or death or major neurological disability (RR 1.02; 95% CI 0.90 to 1.15) showed statistically significant differences between the magnesium and placebo groups overall. The combined outcome of death or substantial gross motor dysfunction was also not significantly in favour of magnesium (RR 0.91; 95% CI 0.61 to 1.36) overall, but there was substantial heterogeneity in this outcome between the two studies (I^2= 87.3%).

Major maternal outcomes (Graphs 1.15 to 1.17)

There were no substantial differences between treatment groups in maternal deaths (RR 1.25; 95% CI 0.51 to 3.07; three trials; 3170 women), cardiac arrest (RR 0.34; 95% CI 0.04 to 3.26; three trials; 3170 women), or respiratory arrest (RR 1.02; 95% CI 0.06 to 16.25; three trials; 3170 women) in either group in this trial, but few women had these outcomes.

Cessation of maternal therapy (Graph 1.18)

Both Crowther 1998 and Magpie 2006 (total 2606 women) reported on this outcome. In both groups individually, significantly more women in the magnesium group ceased therapy because of side-effects, as well as in both groups overall (RR 3.03; 95% CI 2.02 to 4.54).

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Secondary paediatric outcomes (Graphs 1.19 to 1.24)

There were no significant differences seen in any of the secondary paediatric outcomes in all studies combined:

- intraventricular haemorrhage: RR 1.01; 95% CI 0.87 to 1.18; three trials; 2108 infants;
- cystic periventricular leucomalacia: RR 0.99; 95% CI 0.68 to 1.45; three trials; 2108 infants;
- Apgar score less than seven at five minutes: RR 1.12; 95% CI 0.89 to 1.40; two trials; 1943 infants;
- neonatal convulsions: RR 0.77; 95% CI 0.49 to 1.21; two trials; 1943 infants;
- ongoing respiratory support: RR 0.99; 95% CI 0.89 to 1.11; two trials; 1943 infants;
- chronic lung disease (oxygen at 28 days): RR 1.07; 95% CI 0.94 to 1.22; one trial; 1255 infants;
- chronic lung disease (oxygen at 36 weeks): RR 1.12; 95% CI 0.95 to 1.32; two trials; 1943 infants.

None of the trials reported on need for active resuscitation at birth, hypotonia, how many babies were treated with postnatal steroids, measures of growth such as weight, height or head circumference or failing a grade at school.

Secondary maternal outcomes (Graphs 1.25 to 1.30)

There was significantly more maternal hypotension (RR 1.51; 95% CI 1.09 to 2.09; two trials; 1626 women) and tachycardia (RR 1.53; 95% CI 1.03 to 2.29; one trial; 1062 women) in the magnesium group than in the placebo group.
No significant differences between magnesium and placebo were seen for:

- maternal respiratory depression: RR 1.20; 95% CI 0.74 to 1.94; one trial; 1062 women;
- postpartum haemorrhage: RR 0.87; 95% CI 0.67 to 1.13; two trials; 1626 women;
- caesarean birth: RR 1.06; 95% CI 1.00 to 1.13; three trials; 3170 women.

Crowther 1998 reported that none of the women in the trial were admitted to the intensive care unit. There were no significant differences in the rates of admission to intensive care for the mother in the Magpie trial (Magpie 2006; RR 0.89; 95% CI 0.54 to 1.47; one trial; 1544 women).
None of the trials reported on length of labour, augmentation of labour, use of intrapartum antibiotics, breastfeeding, or maternal satisfaction.

Consumption of health resources (Graphs 1.31, 1.32)

No substantial differences were seen between the magnesium and placebo groups for length of mother's hospital stay (weighted mean difference (WMD) 0.17 days; 95% CI -0.18 to 0.53; two trials; 2606 mothers) or infant's primary stay (WMD -0.52 days; 95% CI -4.15 to 3.11; two trials; 2828 infants), but there was significant heterogeneity in the last comparison (I^2 = 51.5%).
No study reported the number of babies admitted to the neonatal intensive care unit (NICU), duration of any NICU stay or costs of care either for the mother or baby.

Subgroup analyses

Neuroprotective intent only

This subgroup analysis is discussed in the primary analysis above.

Gestational age at randomisation (Graphs 2/01 to 2/07)

Although Mittendorf 2002 reported stratifying by gestational age, their results were not presented by gestational age. In Crowther 1998 , all women at entry had fetuses younger than 30 weeks' gestation. In the study of Marret 2006 all fetuses were less than 33 weeks at randomisation. The Magpie investigators (Magpie 2006) provided data for not only all infants less than 37 weeks at randomisation, but also less than 34 weeks and less than 30 weeks separately. No clear differences were seen between treatment groups within the gestational age subgroups although there was substantial heterogeneity in most outcomes where mortality was considered, either alone or combined with neurological outcomes.

Single or multiple pregnancy (Graphs 3/01 to 3/07)

Data were available only from Crowther 1998 and Magpie 2006 for single and multiple pregnancies separately, with no clear differences seen between any of the primary outcomes, although there was substantial heterogeneity where mortality was considered, either alone or combined with neurological outcomes.

Dose (Graphs 4/01 to 4/07)

Loading doses were all 4 g, while most discrepancy was in the maintenance dose, ranging from nil (Marret 2006 and Mittendorf 2002 neuroprotective), to 1 g per hour (Crowther 1998 and Magpie 2006), to 2 to 3 g per hour (Mittendorf 2002 tocolytic). There were no substantial differences between treatment groups within these various dosing regimens.

Corticosteroids (Graphs 5/01 to 5/07)

Corticosteroids were given to the more than 50% of women in the trials of Crowther 1998 and Marret 2006, and to the tocolytic arm of the Mittendorf study (Mittendorf 2002), but the results were not reported separately for the subgroups. Analyses confined to these three studies revealed no different conclusions.

Type of magnesium

All four trials used magnesium sulphate.

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Preterm labour

In Crowther 1998, 63% of women in each group were in preterm labour at randomisation and 84% in the magnesium group and 88% in the placebo group in the study of Marret 2006 but results were not reported separately.

Preterm prelabour rupture of the membranes (PPROM) at randomisation

In Crowther 1998, 8% of women in the magnesium group and 10% in the placebo group had PPROM at randomisation, but results were not reported separately. In the study of Marret 2006, 54% of the magnesium group and 47% of the placebo group had PPROM at randomisation but the results were not reported separately for the subgroups.

Pre-eclampsia/eclampsia

In Crowther 1998, 16% of women in the magnesium group and 14% in the placebo group had pre-eclampsia or eclampsia at randomisation but results were not presented separately. Mittendorf 2002 and Marret 2006 excluded pre-eclamptic women. In the Magpie trial (Magpie 2006), all women had pre-eclampsia.

Mode of administration of magnesium sulphate

All four trials involved the use of intravenous magnesium, at least for the loading dose. Results for the subgroup of women who received intramuscular magnesium sulphate as maintenance were not reported from the Magpie study (Magpie 2006).

DISCUSSION

In women who are threatening to give birth early, the evidence available to date shows that magnesium sulphate therapy has no substantial effects on the unborn baby's chances of survival, or of surviving free of neurologic problems such as cerebral palsy, neurologic impairment or major neurologic disability. However, the conclusions need to be interpreted cautiously given the substantial heterogeneity between the studies reviewed in outcomes such as paediatric mortality, and the combined outcome of paediatric death or cerebral palsy. There is, however, some evidence of a neuroprotective benefit of antenatal magnesium sulphate therapy on the outcome of substantial gross motor dysfunction, but this is restricted to the results from two studies (Crowther 1998; Magpie 2006) where this was a secondary outcome only in the original trials. Importantly, the initial concern about a higher paediatric mortality that led to the early termination of the Mittendorf study (Mittendorf 2002) was not substantiated in the meta-analysis.

Secondary outcomes were not significantly different between treatment groups, but these were not always reported and there were thus less data to examine for effects of magnesium sulphate on these alternative outcomes. As further data accumulate it is hoped that the effects, if any, of magnesium sulphate therapy on secondary outcomes will become clearer.

The expected higher rate of maternal side-effects with magnesium sulphate was observed, but major maternal complications were rare and not significantly different between treatment groups.

The prespecified subgroup analyses did not identify groups who might benefit more from neuroprotective magnesium sulphate therapy.

There are limitations in this meta-analysis related to long-term neurological outcomes, in part because of methodological limitations of the included studies. Only one study (Crowther 1998) was designed to assess long-term effects of magnesium sulphate as the primary outcome. Details of the diagnosis of cerebral palsy were unclear in the study of Mittendorf 2002. In the studies with the outcome of cerebral palsy, children have been assessed early in childhood, usually at two years of age or earlier, when the diagnosis is not always certain (Stanley 1982). Reassessment of neurological outcomes later in childhood, at least into school-age, in all studies is desirable.

One ongoing randomised controlled trial should report more data within the next few year: the BEAM trial from the USA is expected to report results in 2007. In addition, the children in the Crowther 1998 study are being reassessed at eight to nine years of age; results should be available in 2008.

AUTHORS' CONCLUSIONS

Implications for practice

The role for antenatal magnesium sulphate therapy as a neuroprotective agent for the preterm fetus is not yet established.

Implications for research

Given the possible beneficial effects of magnesium sulphate on substantial gross motor dysfunction in early childhood, the children in any randomised controlled trial (RCT) should be reassessed later in childhood to determine the presence or absence of other potentially important neurologic effects, particularly on motor or cognitive function. Current RCTs in progress should be facilitated to enable the possible benefits or harms of magnesium sulphate to be evaluated more thoroughly.

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to the editorial team), one or more members of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Crowther 2003

Methods	Computer-generated randomisation centrally. Blinding of randomisation: yes. Blinding of intervention: yes. Complete follow-up reporting: yes for outcomes during primary hospitalisation - 99% of surviving infants traced to 2 years of age. Outcome assessment blind: yes.
Participants	1062 women (1255 fetuses) < 30 weeks' gestation likely to deliver within 24 hours. Exclusions: already received magnesium sulphate or magnesium sulphate contraindicated.
Interventions	Active treatment - infusion of 4 g magnesium sulphate over 20 minutes, then 1 g/hour until delivery or for 24 hours, whichever came first. Placebo group - equal volume of 0.9% saline.
Outcomes	Primary outcomes: total paediatric mortality (stillbirths, deaths during the primary hospitalisation and after discharge) up to 2 years of age, cerebral palsy, and combined outcome of death or cerebral palsy. Secondary infant outcomes: major IVH, (grade 3 or 4), cystic periventricular leucomalacia, neurosensory

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Crowther 2003

(*Continued*)

	disability (severe - any of severe cerebral palsy [not likely to walk], blindness, or severe developmental delay [MDI < -3 SD]; moderate - moderate cerebral palsy [not walking at 2 years, but likely to do so], deafness, moderate developmental delay [MDI -3 SD to < -2 SD]; mild - mild cerebral palsy [walking at 2 years] or mild developmental delay [MDI - 2 SD to < -1 SD], substantial gross motor dysfunction [not walking at 2 years of age]. Maternal outcomes: adverse cardiovascular and respiratory effects of infusion, postpartum haemorrhage.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Magpie 2006

Methods	Computer-generated randomisation centrally.
Participants	1544 women (1593 fetuses) < 37 weeks' gestation with severe pre-eclampsia and randomised prior to delivery. Women were excluded if they had hypersensitivity to magnesium, hepatic coma, or myasthenia gravis. Data provided by the Magpie Investigators for a subset of the women who were < 37 weeks' gestational age and undelivered at the time of randomisation.
Interventions	Active treatment - magnesium sulphate dose 4 g intravenously over 10-15 minutes, followed by either 1 g/hour intravenously for 24 hours, or by 5 g every 4 hours intramuscularly for 24 hours.
Outcomes	Primary outcomes: neuroprotection of the mother (avoidance of eclampsia). Secondary endpoints included long-term outcomes for the children.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Marret 2006

Methods	Computer-generated randomisation centrally.
Participants	564 women (688 fetuses) in labour < 33 weeks' gestation. Exclusion criteria included fetal malformations, growth restriction, or chromosomal anomalies, and various maternal reasons.
Interventions	4 g magnesium sulphate over 20 minutes.
Outcomes	Primary outcomes: infant death or white matter injury on cranial ultrasound. Secondary outcomes included follow up of children at 2 years of age.

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Notes		

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

Mittendorf 2002

Methods	Methods of randomisation and allocation concealment not described.
Participants	149 women (165 fetuses) in preterm labour, with or without premature rupture of the membranes. Exclusion criteria: mothers with triplet or higher order gestations.
Interventions	"Tandem" randomisation: 1) eligible for aggressive tocolysis (cervix <= 4 cm dilation), magnesium sulphate tocolysis (n = 46), 'other' tocolysis (n = 46); 2) not eligible for tocolysis (cervix > 4 cm dilation) neuroprotective magnesium sulphate (n = 29), saline control (n = 28).
Outcomes	Primary outcomes: not clearly stated.
Notes	

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

[a] IVH: intraventricular haemorrhage
MDI: Mental Developmental Index
SD: standard deviation

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Characteristics of ongoing studies *[ordered by study ID]*

BEAM

Trial name or title	Beneficial Effects of Magnesium Sulfate (NCT 00014989).
Methods	
Participants	2000 women in labour with a premature fetus (24 to 31 weeks' gestation).
Interventions	Magnesium sulphate (intravenously) versus placebo.
Outcomes	Composite death or moderate to severe cerebral palsy, maternal infection, pulmonary oedema, placental abruption, neonatal stillbirth and death, intraventricular haemorrhage, periventricular leukomalacia, other neonatal morbidities.
Starting date	
Contact information	Catherine Spong; spongc@mail.nih.gov
Notes	Recruitment closed early 2006.

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DATA AND ANALYSES

Comparison 1. Magnesium versus no magnesium

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paediatric mortality (fetal and later)	4	3701	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.74, 1.28]
1.1 Neuroprotective intent	3	2002	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.66, 1.03]
1.2 Other intent	2	1699	Risk Ratio (M-H, Random, 95% CI)	2.86 [0.23, 35.82]
2 Fetal death	4	3701	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.78, 1.24]
2.1 Neuroprotective intent	3	2002	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.40, 1.80]
2.2 Other intent	2	1699	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.78, 1.27]
3 Livebirth deaths			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 To latest age of follow up - neuroprotective intent	3	2002	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.65, 1.05]
3.2 To latest age of follow up - other intent	2	1699	Risk Ratio (M-H, Random, 95% CI)	3.02 [0.28, 33.04]
3.3 Neonatal (< 28 days) - neuroprotective intent	1	1255	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.59, 1.11]
3.4 Neonatal (< 28 days) - other intent	1	1593	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.90, 1.74]
3.5 During primary hospitalisation - neuroprotective intent	2	1943	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.67, 1.08]
3.6 During primary hospitalisation - other intent	1	1593	Risk Ratio (M-H, Random, 95% CI)	1.27 [0.92, 1.73]
4 Cerebral palsy	4	3701	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.56, 1.06]
4.1 Neuroprotective	3	2002	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.60, 1.15]
4.2 Other intent	2	1699	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.07, 1.16]
5 Any neurologic impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.86, 1.19]
5.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.87, 1.21]
5.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.34, 1.74]
6 Substantial gross motor dysfunction	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.33, 0.97]
6.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.30, 0.92]
6.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	2.99 [0.12, 73.26]
7 Blindness	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.11, 3.97]
7.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.06, 15.88]
7.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.05, 5.48]
8 Deafness	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.43, 2.89]
8.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.41, 3.12]
8.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.06, 15.90]
9 Developmental delay or intellectual impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.85, 1.21]
9.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.86, 1.23]
9.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.32, 2.01]
10 Major neurologic disability	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.82, 1.40]
10.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.86, 1.51]

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10.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.30, 1.60]
11 Death or cerebral palsy	4	3701	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.75, 1.24]
11.1 Neuroprotective	3	2002	Risk Ratio (M-H, Random, 95% CI)	0.83 [0.64, 1.07]
11.2 Other intent	2	1699	Risk Ratio (M-H, Random, 95% CI)	1.28 [0.68, 2.41]
12 Death or any neurologic impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.91, 1.11]
12.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.84, 1.07]
12.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.92, 1.28]
13 Death or substantial gross motor dysfunction	2	2848	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.61, 1.36]
13.1 Neuroprotective	1	1255	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.59, 0.93]
13.2 Other intent	1	1593	Risk Ratio (M-H, Random, 95% CI)	1.11 [0.94, 1.32]
14 Death or major neurologic disability	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.90, 1.15]
14.1 Neuroprotective	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.80, 1.13]
14.2 Other intent	1	1593	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.92, 1.27]
15 Maternal mortality	3	3170	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.51, 3.07]
16 Maternal cardiac arrest	3	3170	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.04, 3.26]
17 Maternal respiratory arrest	3	3170	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.06, 16.25]
18 Cessation of maternal therapy	2	2606	Risk Ratio (M-H, Fixed, 95% CI)	3.03 [2.02, 4.54]
19 Intraventricular haemorrhage	3	2108	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.87, 1.18]
20 Cystic periventricular leucomalacia	3	2108	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.68, 1.45]
21 Apgar score < 7 at 5 minutes	2	1943	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.89, 1.40]
22 Neonatal convulsions	2	1943	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.49, 1.21]
23 Ongoing respiratory support	2	1943	Risk Ratio (M-H, Fixed, 95% CI)	0.99 [0.89, 1.11]
24 Chronic lung disease			Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
24.1 Oxygen at 28 days	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.94, 1.22]
24.2 Oxygen at 36 weeks	2	1943	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.95, 1.32]
25 Maternal hypotension	2	1626	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [1.09, 2.09]
26 Maternal tachycardia	1	1062	Risk Ratio (M-H, Fixed, 95% CI)	1.53 [1.03, 2.29]
27 Maternal respiratory depression	1	1062	Risk Ratio (M-H, Fixed, 95% CI)	1.20 [0.74, 1.94]
28 Postpartum haemorrhage	2	1626	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.67, 1.12]
29 Caesarean birth	3	3170	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [1.00, 1.13]
30 Mother admitted to intensive care unit	2	2606	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.54, 1.47]
31 Duration of mother's hospital stay (days)	2	2606	Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.18, 0.53]
32 Duration of primary hospital stay for baby (days)	2	2828	Mean Difference (IV, Random, 95% CI)	-0.52 [-4.15, 3.11]

Comparison 2. Gestational age subgroup

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paediatric mortality (fetal and later)			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.1 < 34 weeks at randomisation	4	2913	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.72, 1.27]

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1.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.67, 1.41]
2 Cerebral palsy			Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 < 34 weeks at randomisation	4	2913	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.57, 1.09]
2.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.56, 1.31]
3 Neurologic impairment			Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 < 34 weeks at randomisation	2	2060	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.86, 1.20]
3.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.87, 1.21]
4 Major neurologic disability			Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 < 34 weeks at randomisation	2	2060	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.83, 1.43]
4.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Fixed, 95% CI)	1.12 [0.85, 1.48]
5 Death or cerebral palsy			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 < 34 weeks at randomisation	4	2913	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.74, 1.21]
5.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.69, 1.38]
6 Death or neurological impairment			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
6.1 < 34 weeks at randomisation	2	2060	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.89, 1.08]
6.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Random, 95% CI)	1.03 [0.86, 1.24]
7 Death or major neurological disability			Risk Ratio (M-H, Random, 95% CI)	Subtotals only
7.1 < 34 weeks at randomisation	2	2060	Risk Ratio (M-H, Random, 95% CI)	0.99 [0.88, 1.11]
7.2 < 30 weeks at randomisation	2	1537	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.86, 1.24]

Comparison 3. Single or multiple pregnancy subgroup

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paediatric mortality (fetal and later)	2	2848	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.76, 1.38]
1.1 Single	2	2321	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.74, 1.21]
1.2 Multiple	2	527	Risk Ratio (M-H, Random, 95% CI)	1.34 [0.48, 3.73]
2 Cerebral palsy	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.53, 1.22]
2.1 Single	2	2321	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.57, 1.49]
2.2 Multiple	2	527	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.21, 1.25]
3 Neurologic impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.85, 1.19]
3.1 Single	2	2321	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.88, 1.28]

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3.2 Multiple	2	527	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.61, 1.21]
4 Major neurologic disability	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.82, 1.40]
4.1 Single	2	2321	Risk Ratio (M-H, Fixed, 95% CI)	1.17 [0.87, 1.59]
4.2 Multiple	2	527	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.44, 1.37]
5 Death or cerebral palsy	2	2848	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.76, 1.24]
5.1 Single	2	2321	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.82, 1.14]
5.2 Multiple	2	527	Risk Ratio (M-H, Random, 95% CI)	1.14 [0.45, 2.92]
6 Death or neurological impairment	2	2848	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.86, 1.16]
6.1 Single	2	2321	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.90, 1.12]
6.2 Multiple	2	527	Risk Ratio (M-H, Random, 95% CI)	1.21 [0.56, 2.65]
7 Death or major neurologic disability	2	2848	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.85, 1.22]
7.1 Single	2	2321	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.89, 1.16]
7.2 Multiple	2	527	Risk Ratio (M-H, Random, 95% CI)	1.20 [0.53, 2.71]

Comparison 4. Dose subgroup

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paediatric mortality (fetal and later)	4	3701	Risk Ratio (M-H, Random, 95% CI)	0.97 [0.74, 1.28]
1.1 Loading dose only (4 g)	2	747	Risk Ratio (M-H, Random, 95% CI)	0.88 [0.57, 1.35]
1.2 Loading (4 g) and lower-dose maintenance (1 g/hour)	2	2848	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.71, 1.31]
1.3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic intent	1	106	Risk Ratio (M-H, Random, 95% CI)	15.79 [0.93, 266.72]
2 Cerebral palsy	4	3701	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.56, 1.06]
2.1 Loading dose only (4 g)	2	747	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.48, 1.33]
2.2 Loading (4 g) and lower-dose maintenance (1 g/hour)	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.53, 1.22]
2.3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic	1	106	Risk Ratio (M-H, Fixed, 95% CI)	0.13 [0.01, 2.51]
3 Neurologic impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.86, 1.19]
3.1 Loading (4 g) and lower-maintenance dose (1 g/hour)	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.86, 1.19]
4 Major neurologic disability	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.82, 1.40]
4.1 Loading (4 g) and lower-maintenance dose (1 g/hour)	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.82, 1.40]
5 Death or cerebral palsy	4	3701	Risk Ratio (M-H, Random, 95% CI)	0.96 [0.75, 1.24]
5.1 Loading dose (4 g) only	2	747	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.27, 7.81]

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5.2 Loading (4 g) and lower-maintenance dose (1 g/hour)	2	2848	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.72, 1.26]
5.3 Loading (4 g) and higher-maintenance dose (2-3 g/hour): tocolytic intent	1	106	Risk Ratio (M-H, Random, 95% CI)	2.47 [0.69, 8.81]
6 Death or neurological impairment	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.91, 1.11]
6.1 Loading (4 g) and lower-maintenance dose (1 g/hour)	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.91, 1.11]
7 Death or major neurological disability	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.90, 1.15]
7.1 Loading (4 g) and lower-maintenance dose (1 g/hour)	2	2848	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.90, 1.15]

Comparison 5. High antenatal corticosteroids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Paediatric mortality (fetal and later)	3	2049	Risk Ratio (M-H, Random, 95% CI)	0.89 [0.57, 1.40]
2 Cerebral palsy	3	2049	Risk Ratio (M-H, Fixed, 95% CI)	0.76 [0.54, 1.05]
3 Neurologic impairment	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.87, 1.21]
4 Major neurologic disability	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.86, 1.51]
5 Death or cerebral palsy	3	2049	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.70, 0.99]
6 Death or neurological impairment	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.84, 1.07]
7 Death or major neurological disability	1	1255	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.80, 1.13]

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Analysis 1.1. Comparison 1 Magnesium versus no magnesium, Outcome 1 Paediatric mortality (fetal and later).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Neuroprotective intent					
Crowther 2003	87/629	107/626		34.3 %	0.81 [0.62, 1.05]
Marret 2006	34/352	38/336		22.0 %	0.85 [0.55, 1.32]
Mittendorf 2002	2/30	1/29		1.3 %	1.93 [0.19, 20.18]
Subtotal (95% CI)	**1011**	**991**		**57.6 %**	**0.83 [0.66, 1.03]**
Total events: 123 (Magnesium), 146 (No magnesium)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.55$, df = 2 (P = 0.76); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.67 (P = 0.095)					
2 Other intent					
Magpie 2006	209/798	188/795		41.5 %	1.11 [0.93, 1.31]
Mittendorf 2002	8/55	0/51		0.9 %	15.79 [0.93, 266.72]
Subtotal (95% CI)	**853**	**846**		**42.4 %**	**2.86 [0.23, 35.82]**
Total events: 217 (Magnesium), 188 (No magnesium)					
Heterogeneity: $Tau^2 = 2.58$; $Chi^2 = 3.47$, df = 1 (P = 0.06); $I^2 = 71\%$					
Test for overall effect: Z = 0.81 (P = 0.42)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.97 [0.74, 1.28]**
Total events: 340 (Magnesium), 334 (No magnesium)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 8.39$, df = 4 (P = 0.08); $I^2 = 52\%$					
Test for overall effect: Z = 0.22 (P = 0.83)					

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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Neuroprotective intent				
Crowther 2003	87/629	107/626		0.81 [0.62, 1.05]
Marret 2006	34/352	38/336		0.85 [0.55, 1.32]
Mittendorf 2002	2/30	1/29		1.93 [0.19, 20.18]
Subtotal (95% CI)	**1011**	**991**		**0.83 [0.66, 1.03]**
Total events: 123 (Magnesium), 146 (No magnesium)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.55, df = 2 (P = 0.76); I^2 =0.0%				
Test for overall effect: Z = 1.67 (P = 0.095)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Other intent				
Magpie 2006	209/798	188/795		1.11 [0.93, 1.31]
Mittendorf 2002	8/55	0/51		15.79 [0.93, 266.72]
Subtotal (95% CI)	**853**	**846**		**2.86 [0.23, 35.82]**
Total events: 217 (Magnesium), 188 (No magnesium)				
Heterogeneity: Tau^2 = 2.58; Chi^2 = 3.47, df = 1 (P = 0.06); I^2 =71%				
Test for overall effect: Z = 0.81 (P = 0.42)				

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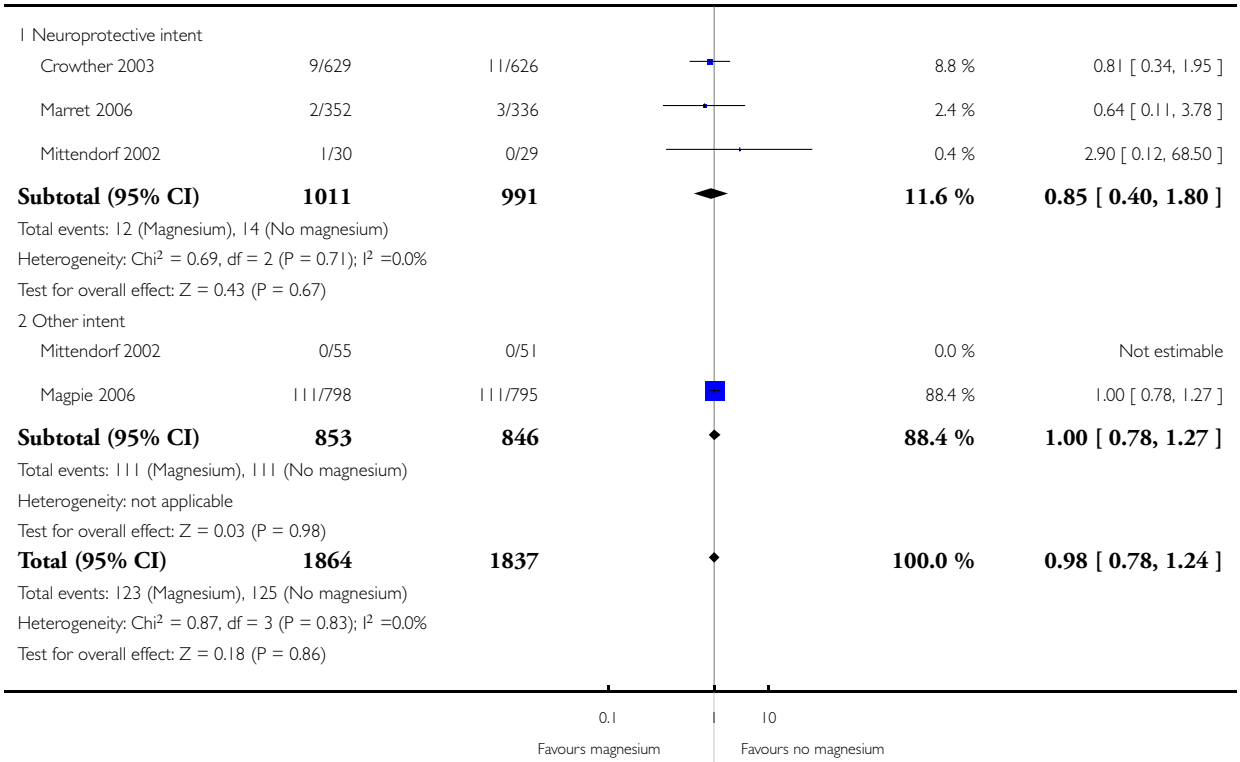
Analysis 1.2. Comparison 1 Magnesium versus no magnesium, Outcome 2 Fetal death.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 2 Fetal death

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective intent					
Crowther 2003	9/629	11/626		8.8 %	0.81 [0.34, 1.95]
Marret 2006	2/352	3/336		2.4 %	0.64 [0.11, 3.78]
Mittendorf 2002	1/30	0/29		0.4 %	2.90 [0.12, 68.50]
Subtotal (95% CI)	**1011**	**991**		**11.6 %**	**0.85 [0.40, 1.80]**
Total events: 12 (Magnesium), 14 (No magnesium)					
Heterogeneity: Chi² = 0.69, df = 2 (P = 0.71); I² =0.0%					
Test for overall effect: Z = 0.43 (P = 0.67)					
2 Other intent					
Mittendorf 2002	0/55	0/51		0.0 %	Not estimable
Magpie 2006	111/798	111/795		88.4 %	1.00 [0.78, 1.27]
Subtotal (95% CI)	**853**	**846**		**88.4 %**	**1.00 [0.78, 1.27]**
Total events: 111 (Magnesium), 111 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.03 (P = 0.98)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.98 [0.78, 1.24]**
Total events: 123 (Magnesium), 125 (No magnesium)					
Heterogeneity: Chi² = 0.87, df = 3 (P = 0.83); I² =0.0%					
Test for overall effect: Z = 0.18 (P = 0.86)					



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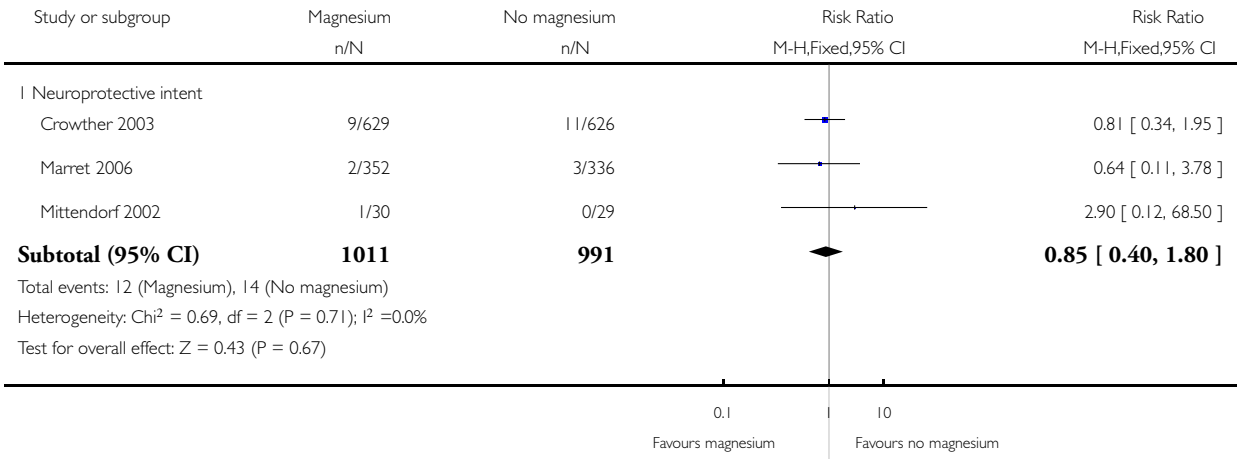
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

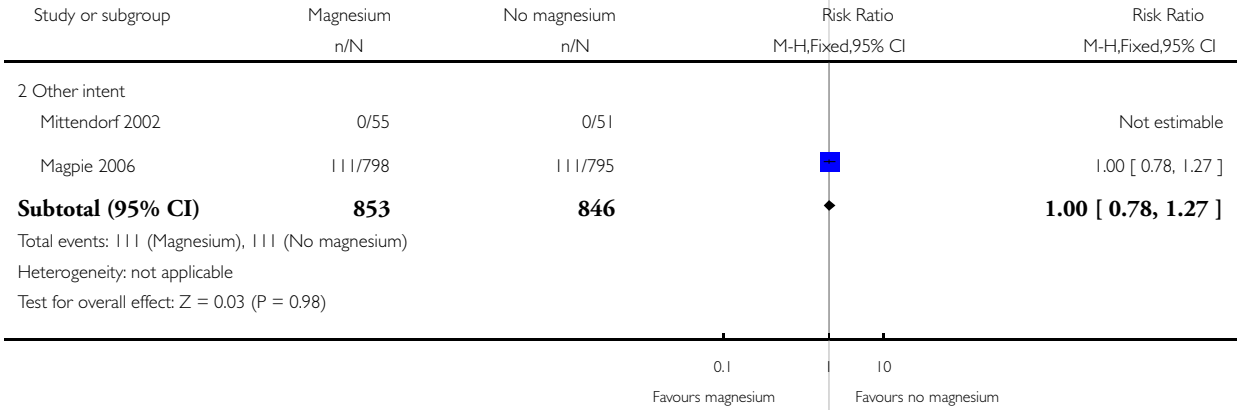
Outcome: 2 Fetal death



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 2 Fetal death



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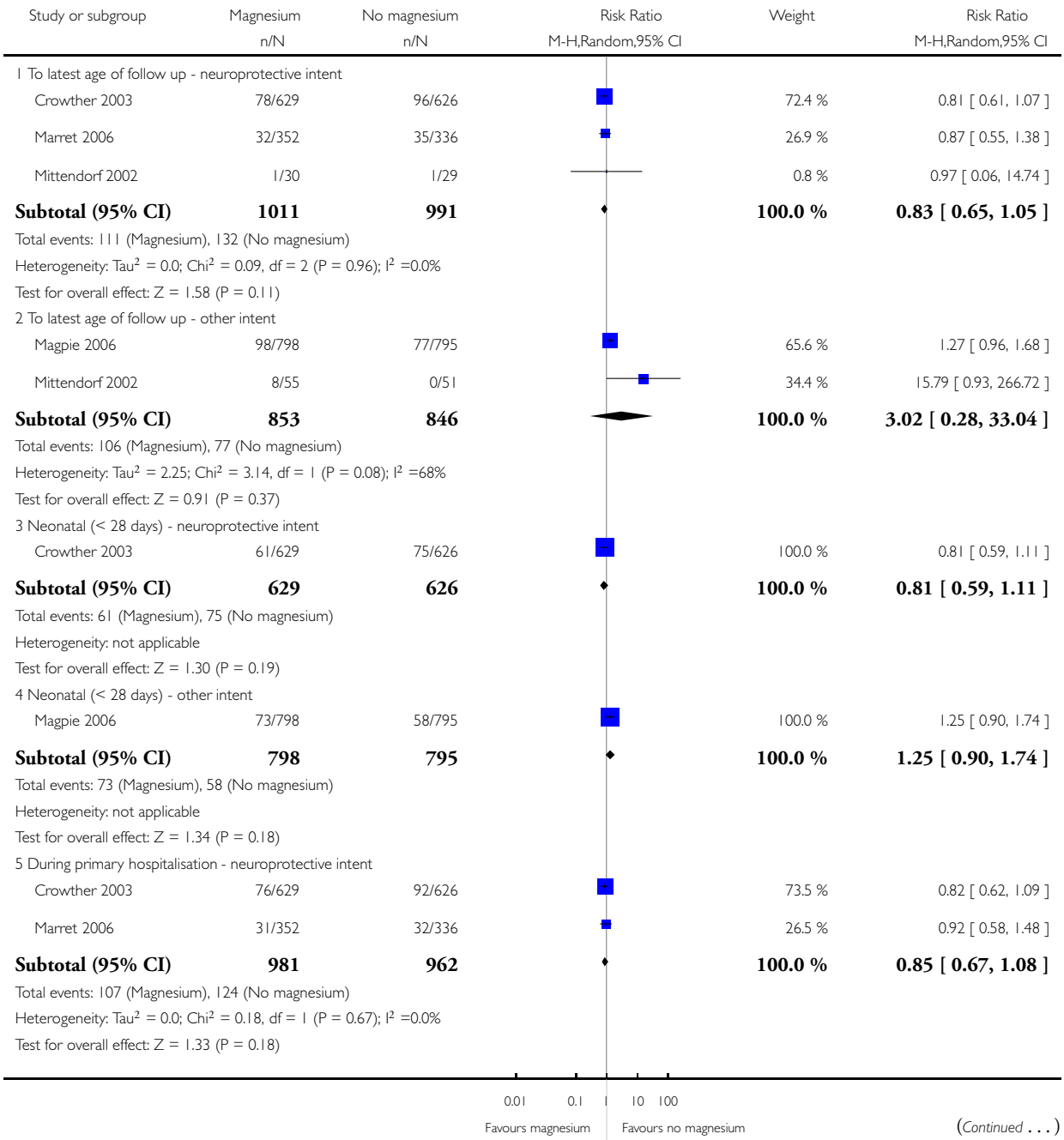
Analysis 1.3. Comparison 1 Magnesium versus no magnesium, Outcome 3 Livebirth deaths.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths



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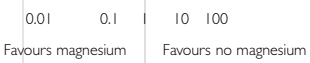
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
6 During primary hospitalisation - other intent					
Magpie 2006	80/798	63/795		100.0 %	1.27 [0.92, 1.73]
Subtotal (95% CI)	**798**	**795**		**100.0 %**	**1.27 [0.92, 1.73]**
Total events: 80 (Magnesium), 63 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.46 (P = 0.14)					

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 To latest age of follow up - neuroprotective intent				
Crowther 2003	78/629	96/626		0.81 [0.61, 1.07]
Marret 2006	32/352	35/336		0.87 [0.55, 1.38]
Mittendorf 2002	1/30	1/29		0.97 [0.06, 14.74]
Subtotal (95% CI)	**1011**	**991**		**0.83 [0.65, 1.05]**
Total events: 111 (Magnesium), 132 (No magnesium)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.09$, df = 2 (P = 0.96); $I^2 = 0.0\%$				
Test for overall effect: Z = 1.58 (P = 0.11)				



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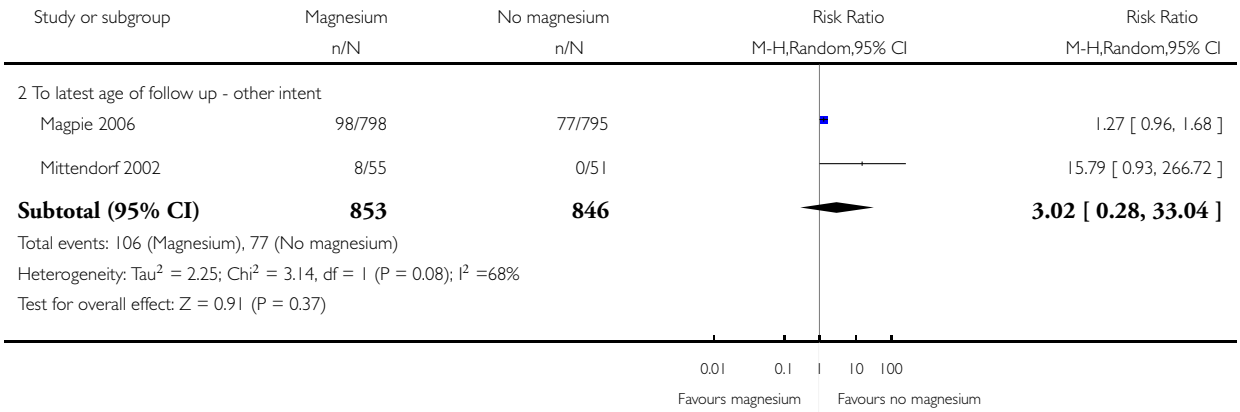
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

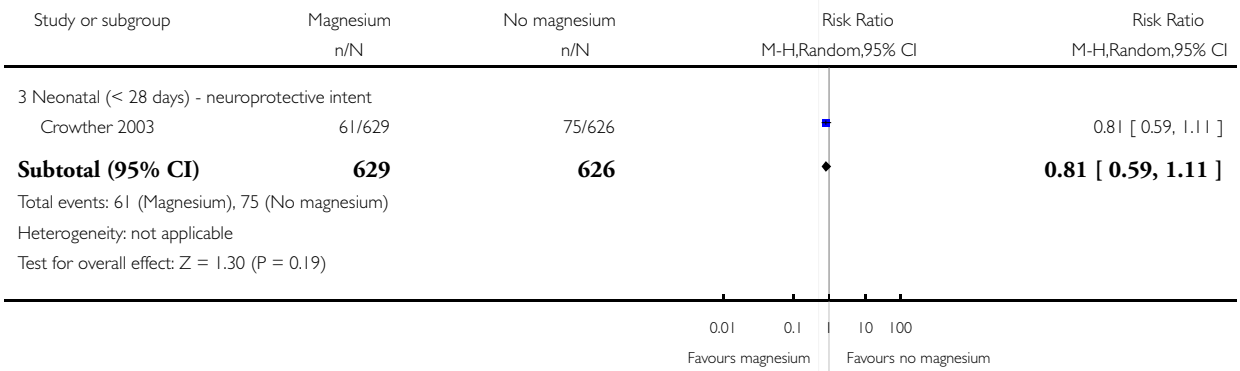
Outcome: 3 Livebirth deaths



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths

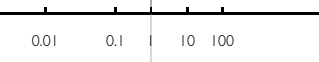
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
4 Neonatal (< 28 days) - other intent				
Magpie 2006	73/798	58/795		1.25 [0.90, 1.74]
Subtotal (95% CI)	**798**	**795**		**1.25 [0.90, 1.74]**
Total events: 73 (Magnesium), 58 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.34 (P = 0.18)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
5 During primary hospitalisation - neuroprotective intent				
Crowther 2003	76/629	92/626		0.82 [0.62, 1.09]
Marret 2006	31/352	32/336		0.92 [0.58, 1.48]
Subtotal (95% CI)	**981**	**962**		**0.85 [0.67, 1.08]**
Total events: 107 (Magnesium), 124 (No magnesium)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.18, df = 1 (P = 0.67); I^2 =0.0%				
Test for overall effect: Z = 1.33 (P = 0.18)				



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 3 Livebirth deaths

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
6 During primary hospitalisation - other intent				
Magpie 2006	80/798	63/795		1.27 [0.92, 1.73]
Subtotal (95% CI)	**798**	**795**		**1.27 [0.92, 1.73]**
Total events: 80 (Magnesium), 63 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.46 (P = 0.14)				

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Analysis 1.4. Comparison 1 Magnesium versus no magnesium, Outcome 4 Cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 4 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective					
Crowther 2003	36/629	42/626		51.4 %	0.85 [0.55, 1.31]
Marret 2006	22/352	30/336		37.5 %	0.70 [0.41, 1.19]
Mittendorf 2002	3/30	0/29		0.6 %	6.77 [0.37, 125.65]
Subtotal (95% CI)	**1011**	**991**		**89.5 %**	**0.83 [0.60, 1.15]**
Total events: 61 (Magnesium), 72 (No magnesium)					
Heterogeneity: Chi² = 2.40, df = 2 (P = 0.30); I² =17%					
Test for overall effect: Z = 1.11 (P = 0.27)					
2 Other intent					
Magpie 2006	2/798	5/795		6.1 %	0.40 [0.08, 2.05]
Mittendorf 2002	0/55	3/51		4.4 %	0.13 [0.01, 2.51]
Subtotal (95% CI)	**853**	**846**		**10.5 %**	**0.29 [0.07, 1.16]**
Total events: 2 (Magnesium), 8 (No magnesium)					
Heterogeneity: Chi² = 0.42, df = 1 (P = 0.52); I² =0.0%					
Test for overall effect: Z = 1.75 (P = 0.080)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.77 [0.56, 1.06]**
Total events: 63 (Magnesium), 80 (No magnesium)					
Heterogeneity: Chi² = 4.47, df = 4 (P = 0.35); I² =10%					
Test for overall effect: Z = 1.59 (P = 0.11)					

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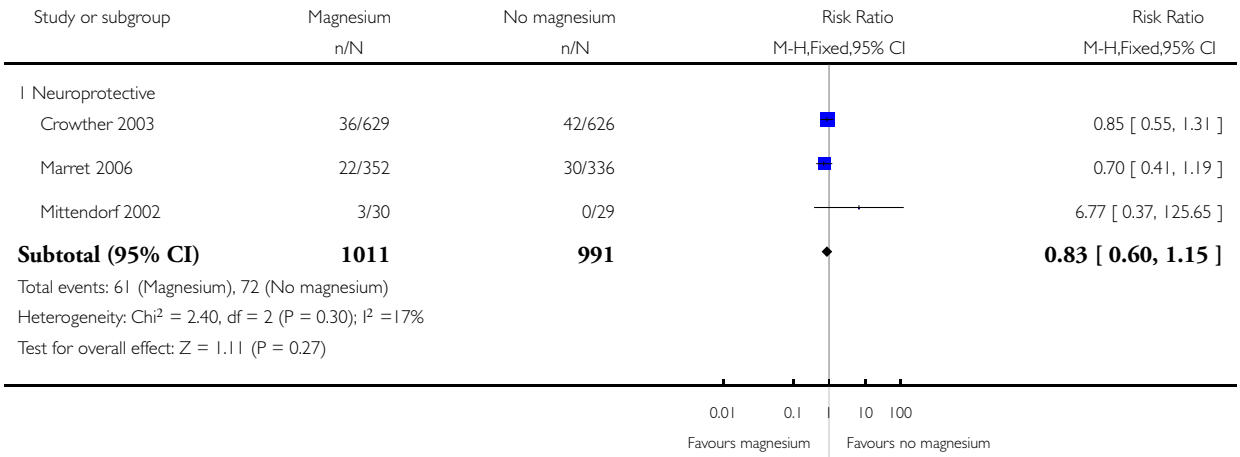
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

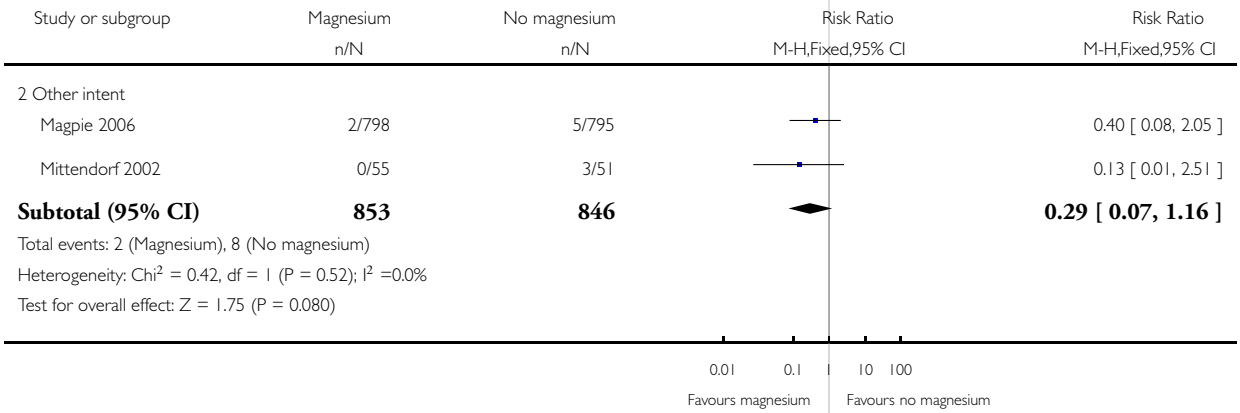
Outcome: 4 Cerebral palsy



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 4 Cerebral palsy



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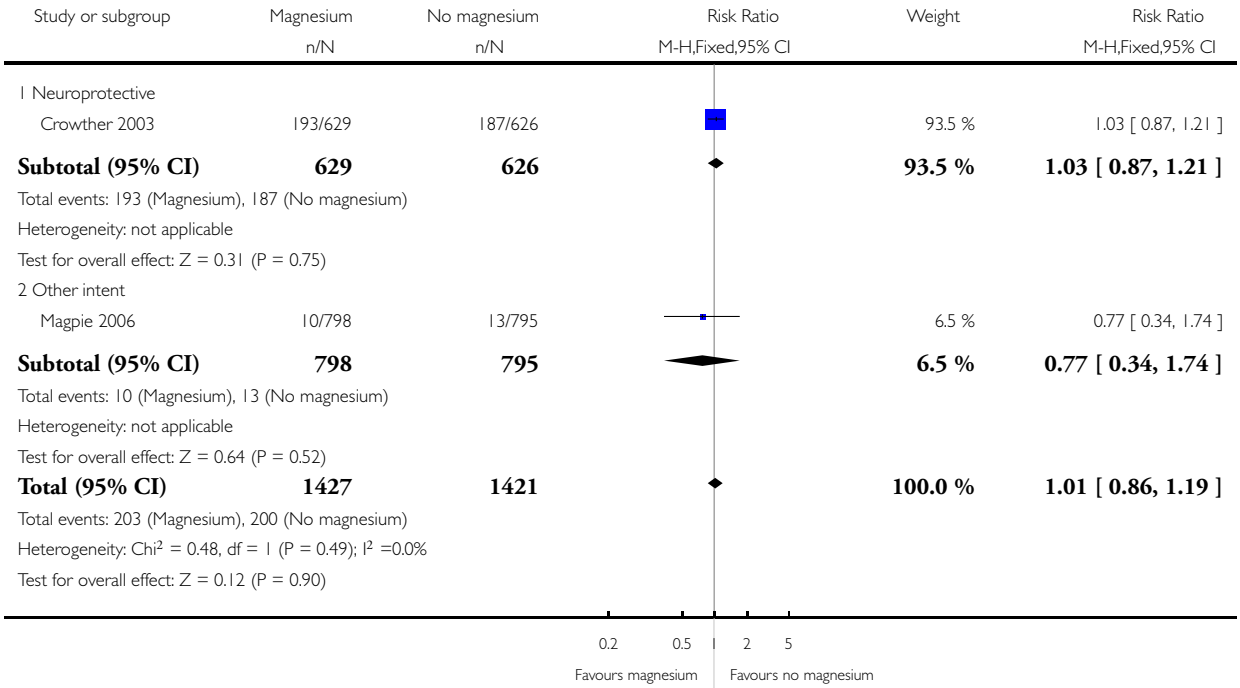
Analysis 1.5. Comparison 1 Magnesium versus no magnesium, Outcome 5 Any neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

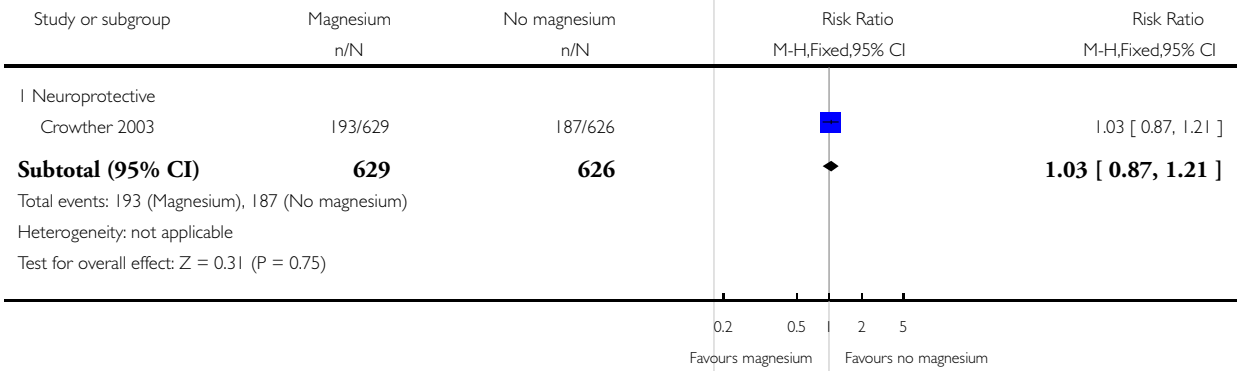
Outcome: 5 Any neurologic impairment



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 5 Any neurologic impairment



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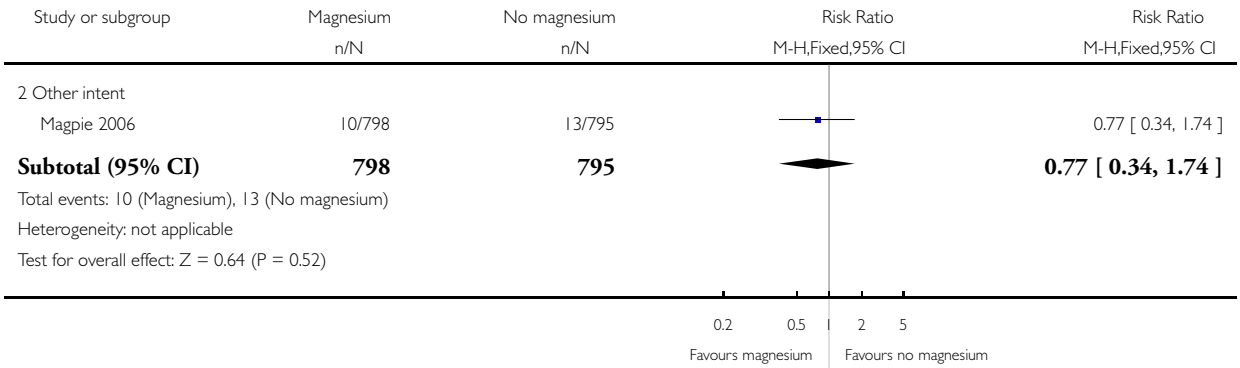
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 5 Any neurologic impairment

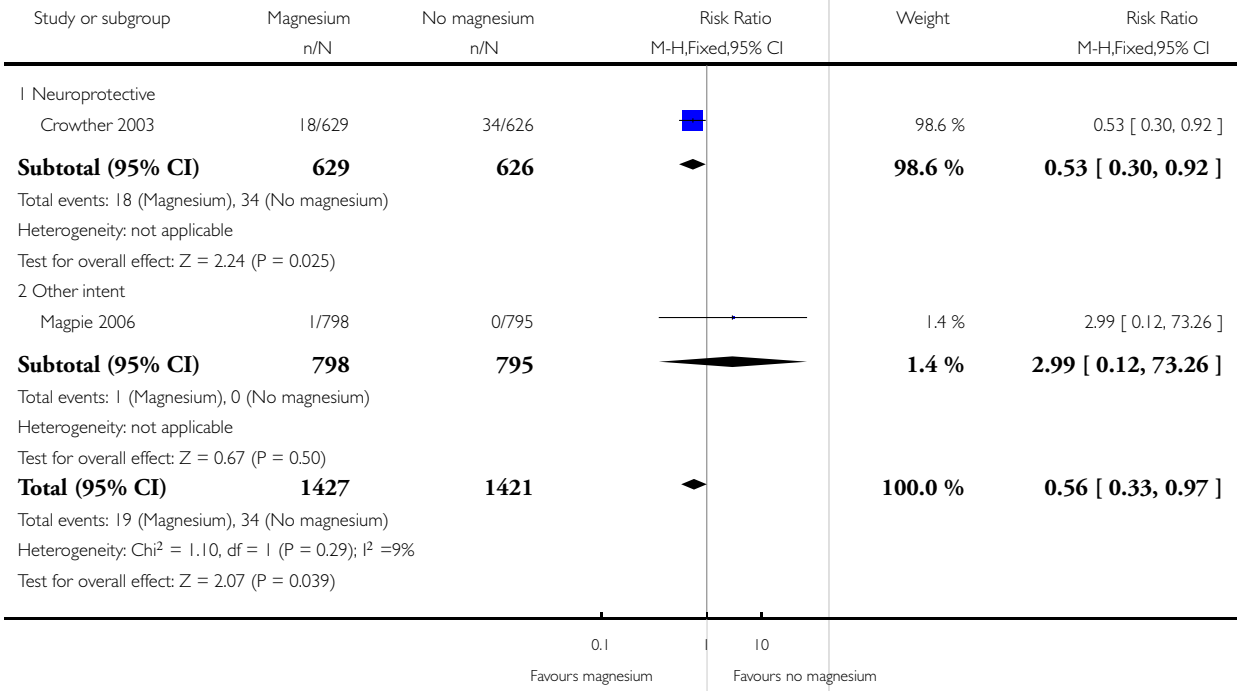


Analysis 1.6. Comparison 1 Magnesium versus no magnesium, Outcome 6 Substantial gross motor dysfunction.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 6 Substantial gross motor dysfunction



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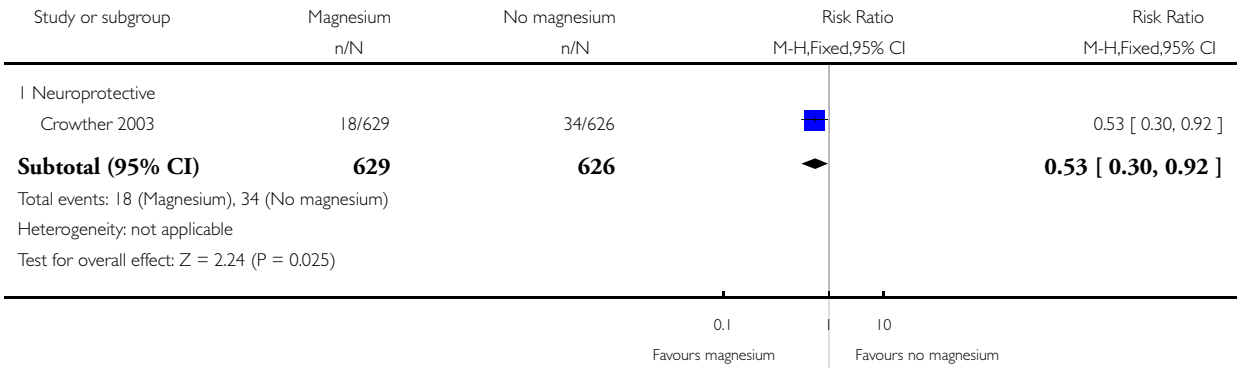
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

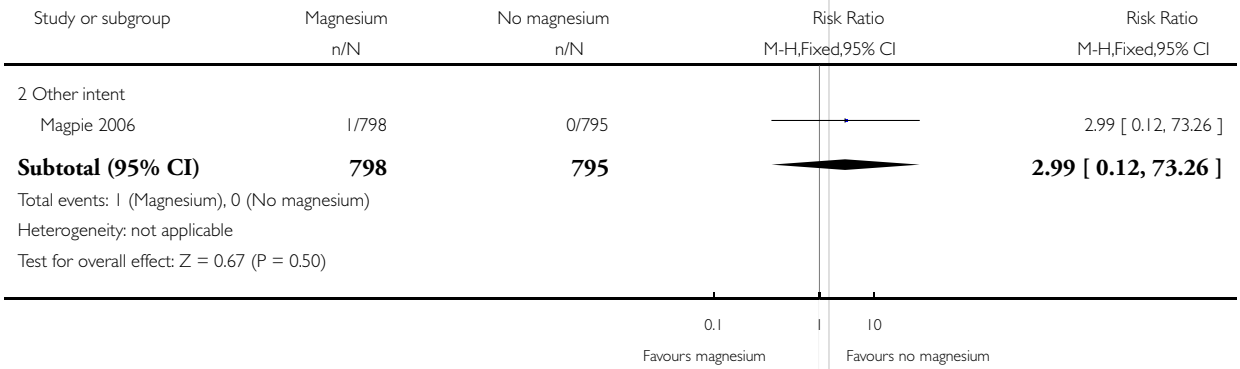
Outcome: 6 Substantial gross motor dysfunction



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 6 Substantial gross motor dysfunction



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Analysis 1.7. Comparison 1 Magnesium versus no magnesium, Outcome 7 Blindness.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 7 Blindness

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective					
Crowther 2003	1/629	1/626		33.3 %	1.00 [0.06, 15.88]
Subtotal (95% CI)	**629**	**626**		**33.3 %**	**1.00 [0.06, 15.88]**
Total events: 1 (Magnesium), 1 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.00 (P = 1.0)					
2 Other intent					
Magpie 2006	1/798	2/795		66.7 %	0.50 [0.05, 5.48]
Subtotal (95% CI)	**798**	**795**		**66.7 %**	**0.50 [0.05, 5.48]**
Total events: 1 (Magnesium), 2 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.57 (P = 0.57)					
Total (95% CI)	**1427**	**1421**		**100.0 %**	**0.66 [0.11, 3.97]**
Total events: 2 (Magnesium), 3 (No magnesium)					
Heterogeneity: Chi^2 = 0.14, df = 1 (P = 0.71); I^2 =0.0%					
Test for overall effect: Z = 0.45 (P = 0.65)					

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 7 Blindness

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective				
Crowther 2003	1/629	1/626		1.00 [0.06, 15.88]
Subtotal (95% CI)	**629**	**626**		**1.00 [0.06, 15.88]**
Total events: 1 (Magnesium), 1 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.00 (P = 1.0)				

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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 7 Blindness

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Other intent				
Magpie 2006	1/798	2/795		0.50 [0.05, 5.48]
Subtotal (95% CI)	**798**	**795**		**0.50 [0.05, 5.48]**
Total events: 1 (Magnesium), 2 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.57 (P = 0.57)				

Analysis 1.8. Comparison 1 Magnesium versus no magnesium, Outcome 8 Deafness.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 8 Deafness

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective					
Crowther 2003	8/629	7/626		87.5 %	1.14 [0.41, 3.12]
Subtotal (95% CI)	**629**	**626**		**87.5 %**	**1.14 [0.41, 3.12]**
Total events: 8 (Magnesium), 7 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.25 (P = 0.80)					
2 Other intent					
Magpie 2006	1/798	1/795		12.5 %	1.00 [0.06, 15.90]
Subtotal (95% CI)	**798**	**795**		**12.5 %**	**1.00 [0.06, 15.90]**
Total events: 1 (Magnesium), 1 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.00 (P = 1.0)					
Total (95% CI)	**1427**	**1421**		**100.0 %**	**1.12 [0.43, 2.89]**
Total events: 9 (Magnesium), 8 (No magnesium)					
Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.93); I^2 =0.0%					
Test for overall effect: Z = 0.23 (P = 0.81)					

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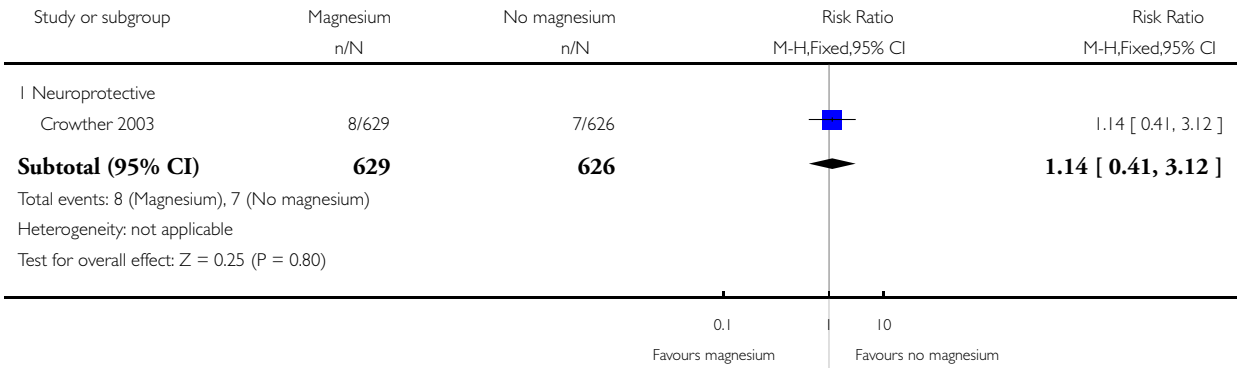
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

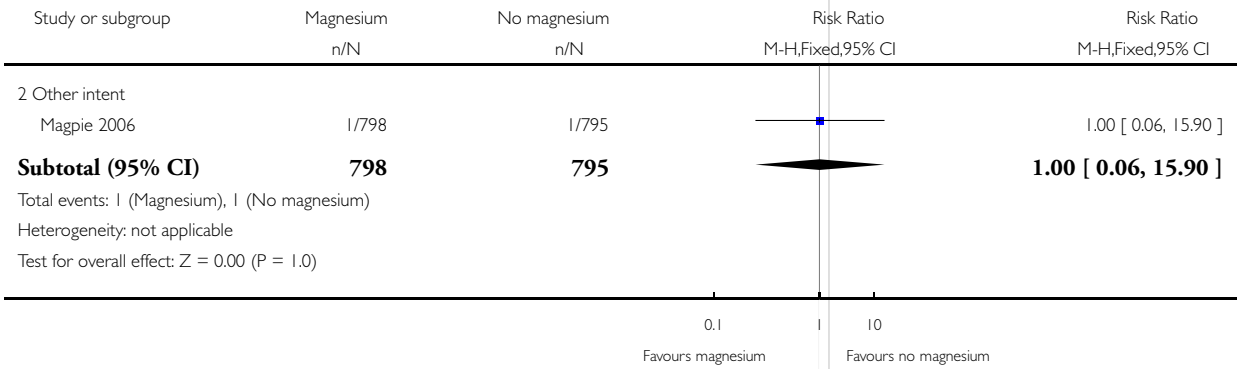
Outcome: 8 Deafness



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 8 Deafness



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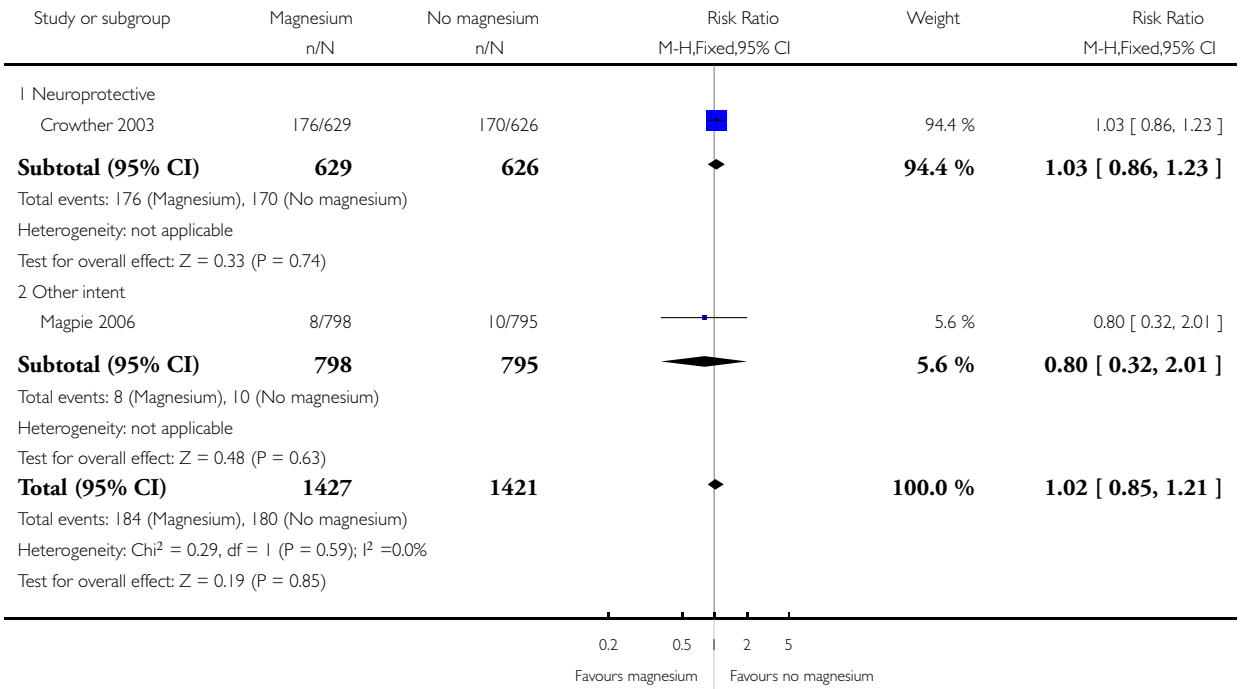
Analysis 1.9. Comparison 1 Magnesium versus no magnesium, Outcome 9 Developmental delay or intellectual impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

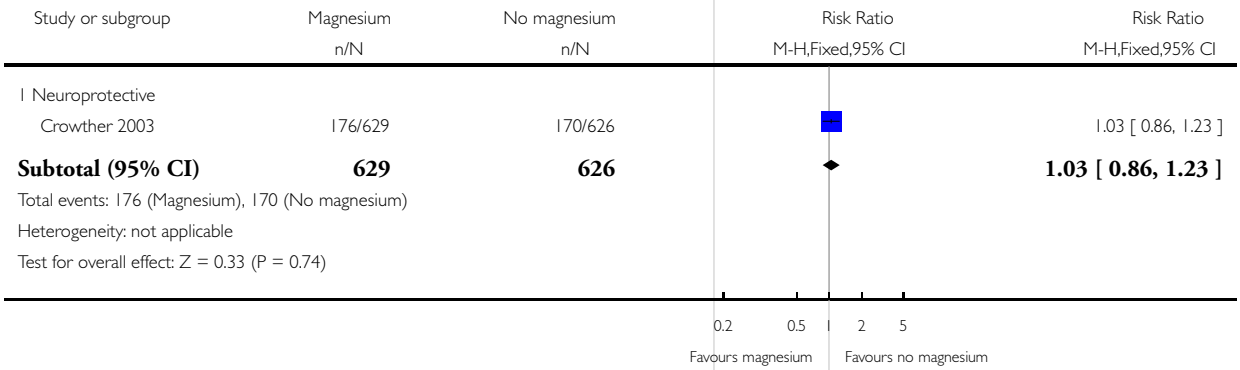
Outcome: 9 Developmental delay or intellectual impairment



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 9 Developmental delay or intellectual impairment



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 9 Developmental delay or intellectual impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Other intent				
Magpie 2006	8/798	10/795		0.80 [0.32, 2.01]
Subtotal (95% CI)	**798**	**795**		**0.80 [0.32, 2.01]**
Total events: 8 (Magnesium), 10 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.48 (P = 0.63)				

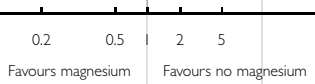
Analysis 1.10. Comparison 1 Magnesium versus no magnesium, Outcome 10 Major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 10 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Neuroprotective					
Crowther 2003	89/629	78/626		85.7 %	1.14 [0.86, 1.51]
Subtotal (95% CI)	**629**	**626**		**85.7 %**	**1.14 [0.86, 1.51]**
Total events: 89 (Magnesium), 78 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.88 (P = 0.38)					
2 Other intent					
Magpie 2006	9/798	13/795		14.3 %	0.69 [0.30, 1.60]
Subtotal (95% CI)	**798**	**795**		**14.3 %**	**0.69 [0.30, 1.60]**
Total events: 9 (Magnesium), 13 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.86 (P = 0.39)					
Total (95% CI)	**1427**	**1421**		**100.0 %**	**1.07 [0.82, 1.40]**
Total events: 98 (Magnesium), 91 (No magnesium)					
Heterogeneity: Chi^2 = 1.21, df = 1 (P = 0.27); I^2 =17%					
Test for overall effect: Z = 0.51 (P = 0.61)					



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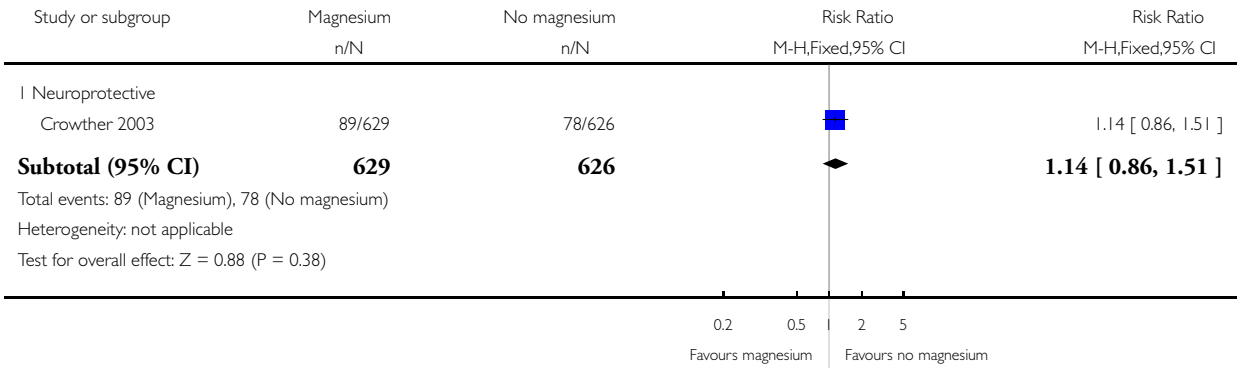
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

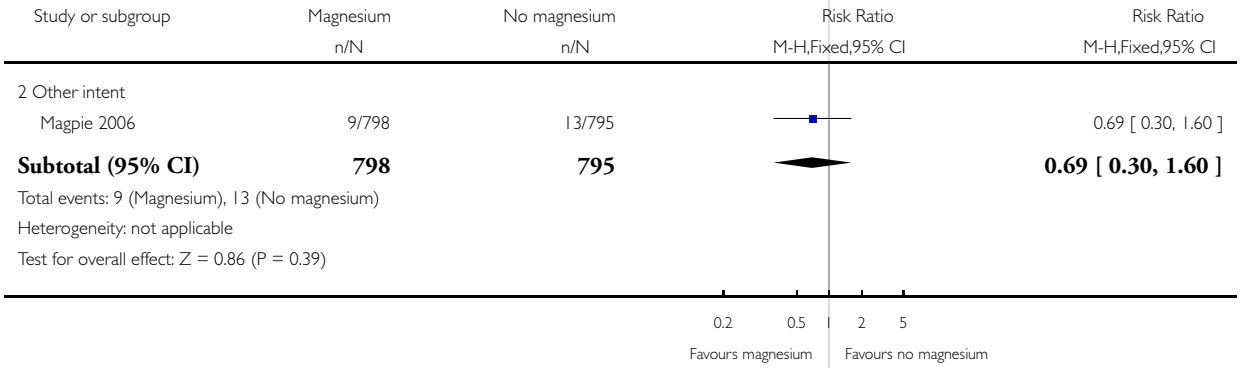
Outcome: 10 Major neurologic disability



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 10 Major neurologic disability



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Analysis 1.11. Comparison 1 Magnesium versus no magnesium, Outcome 11 Death or cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 11 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Neuroprotective					
Crowther 2003	123/629	149/626		33.2 %	0.82 [0.66, 1.02]
Marret 2006	56/352	68/336		25.5 %	0.79 [0.57, 1.08]
Mittendorf 2002	5/30	1/29		1.4 %	4.83 [0.60, 38.90]
Subtotal (95% CI)	**1011**	**991**		**60.1 %**	**0.83 [0.64, 1.07]**
Total events: 184 (Magnesium), 218 (No magnesium)					
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.86$, df = 2 (P = 0.24); $I^2 = 30\%$					
Test for overall effect: Z = 1.46 (P = 0.14)					
2 Other intent					
Magpie 2006	211/798	193/795		36.2 %	1.09 [0.92, 1.29]
Mittendorf 2002	8/55	3/51		3.7 %	2.47 [0.69, 8.81]
Subtotal (95% CI)	**853**	**846**		**39.9 %**	**1.28 [0.68, 2.41]**
Total events: 219 (Magnesium), 196 (No magnesium)					
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 1.58$, df = 1 (P = 0.21); $I^2 = 37\%$					
Test for overall effect: Z = 0.75 (P = 0.45)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.96 [0.75, 1.24]**
Total events: 403 (Magnesium), 414 (No magnesium)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 10.16$, df = 4 (P = 0.04); $I^2 = 61\%$					
Test for overall effect: Z = 0.31 (P = 0.76)					

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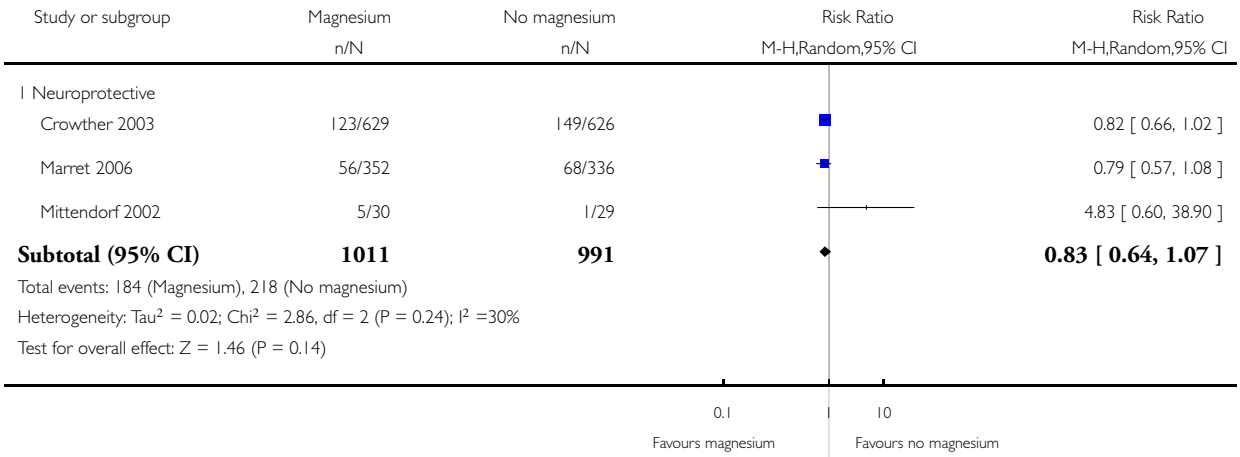
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

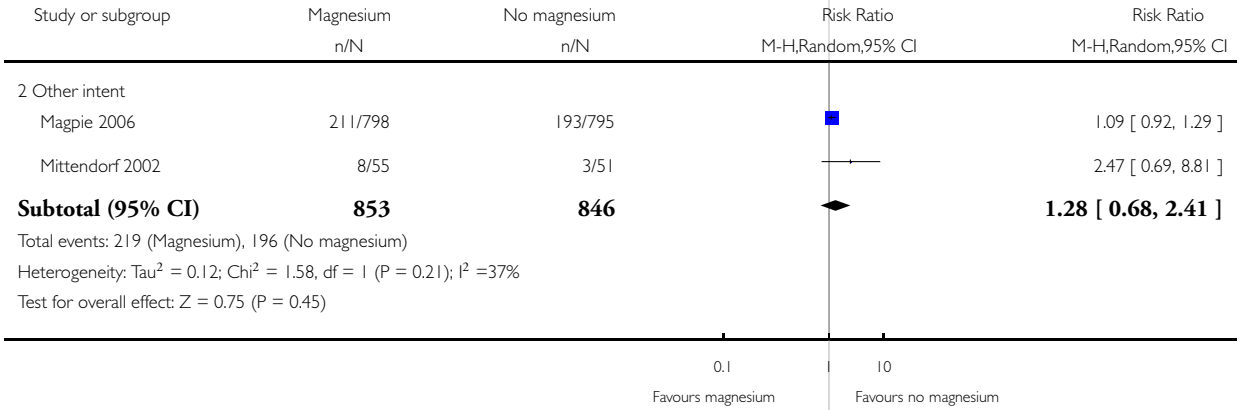
Outcome: 11 Death or cerebral palsy



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 11 Death or cerebral palsy



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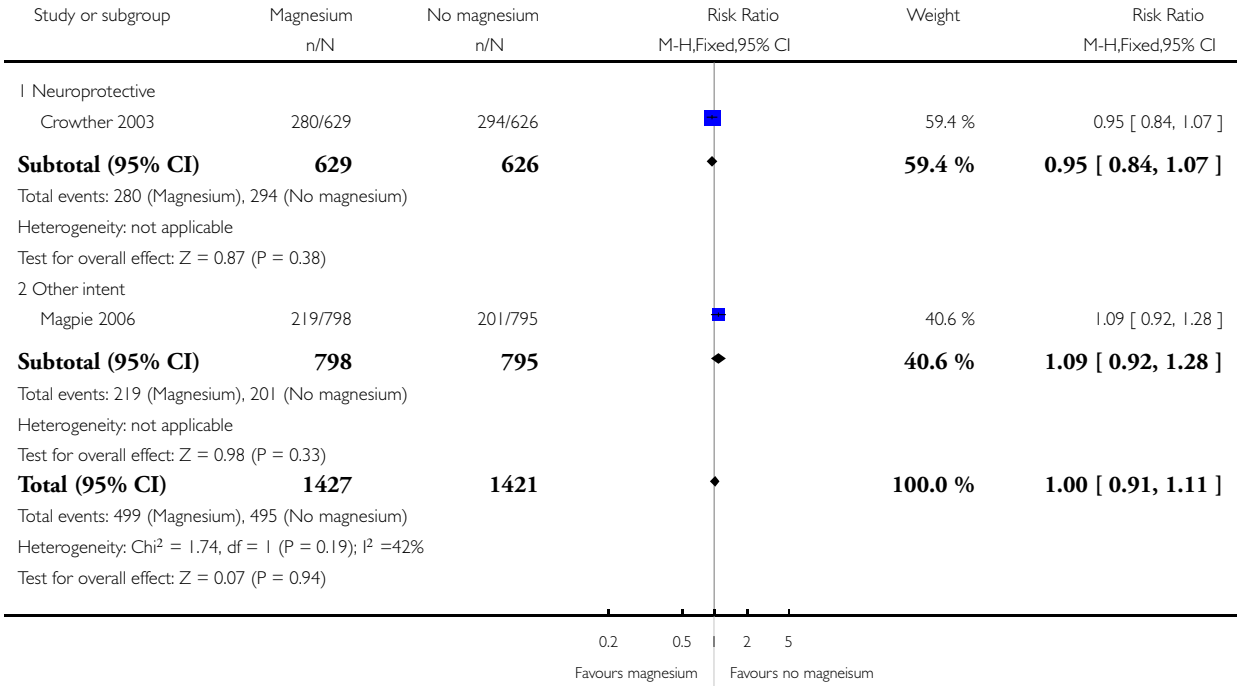
Analysis 1.12. Comparison 1 Magnesium versus no magnesium, Outcome 12 Death or any neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

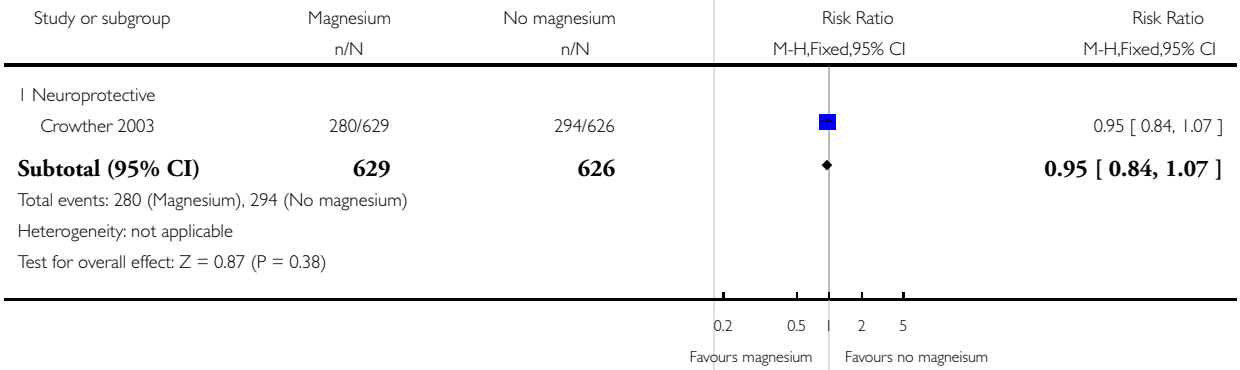
Outcome: 12 Death or any neurologic impairment



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 12 Death or any neurologic impairment



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 12 Death or any neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Other intent				
Magpie 2006	219/798	201/795		1.09 [0.92, 1.28]
Subtotal (95% CI)	**798**	**795**		**1.09 [0.92, 1.28]**
Total events: 219 (Magnesium), 201 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.98 (P = 0.33)				

Analysis 1.13. Comparison 1 Magnesium versus no magnesium, Outcome 13 Death or substantial gross motor dysfunction.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 13 Death or substantial gross motor dysfunction

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Neuroprotective					
Crowther 2003	105/629	141/626		48.2 %	0.74 [0.59, 0.93]
Subtotal (95% CI)	**629**	**626**		**48.2 %**	**0.74 [0.59, 0.93]**
Total events: 105 (Magnesium), 141 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.59 (P = 0.0097)					
2 Other intent					
Magpie 2006	210/798	188/795		51.8 %	1.11 [0.94, 1.32]
Subtotal (95% CI)	**798**	**795**		**51.8 %**	**1.11 [0.94, 1.32]**
Total events: 210 (Magnesium), 188 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.23 (P = 0.22)					
Total (95% CI)	**1427**	**1421**		**100.0 %**	**0.91 [0.61, 1.36]**
Total events: 315 (Magnesium), 329 (No magnesium)					
Heterogeneity: Tau^2 = 0.07; Chi^2 = 7.88, df = 1 (P = 0.005); I^2 =87%					
Test for overall effect: Z = 0.44 (P = 0.66)					

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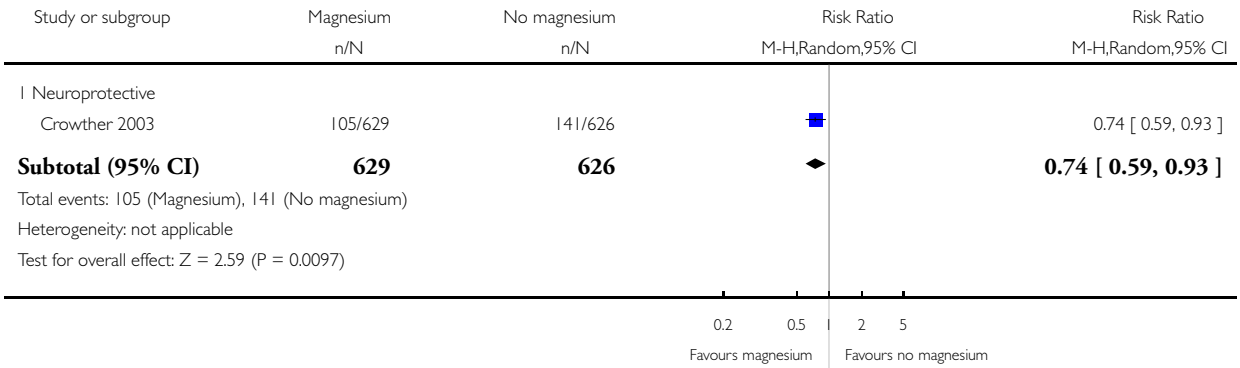
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

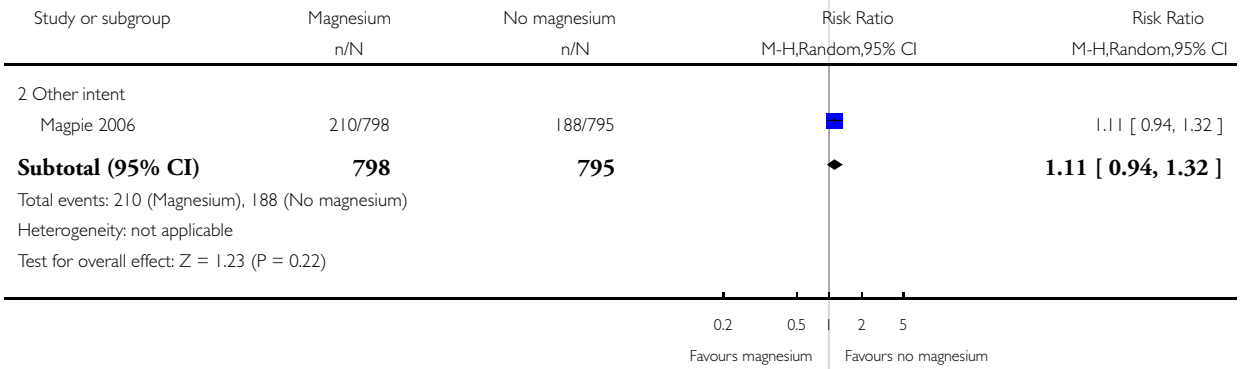
Outcome: 13 Death or substantial gross motor dysfunction



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 13 Death or substantial gross motor dysfunction



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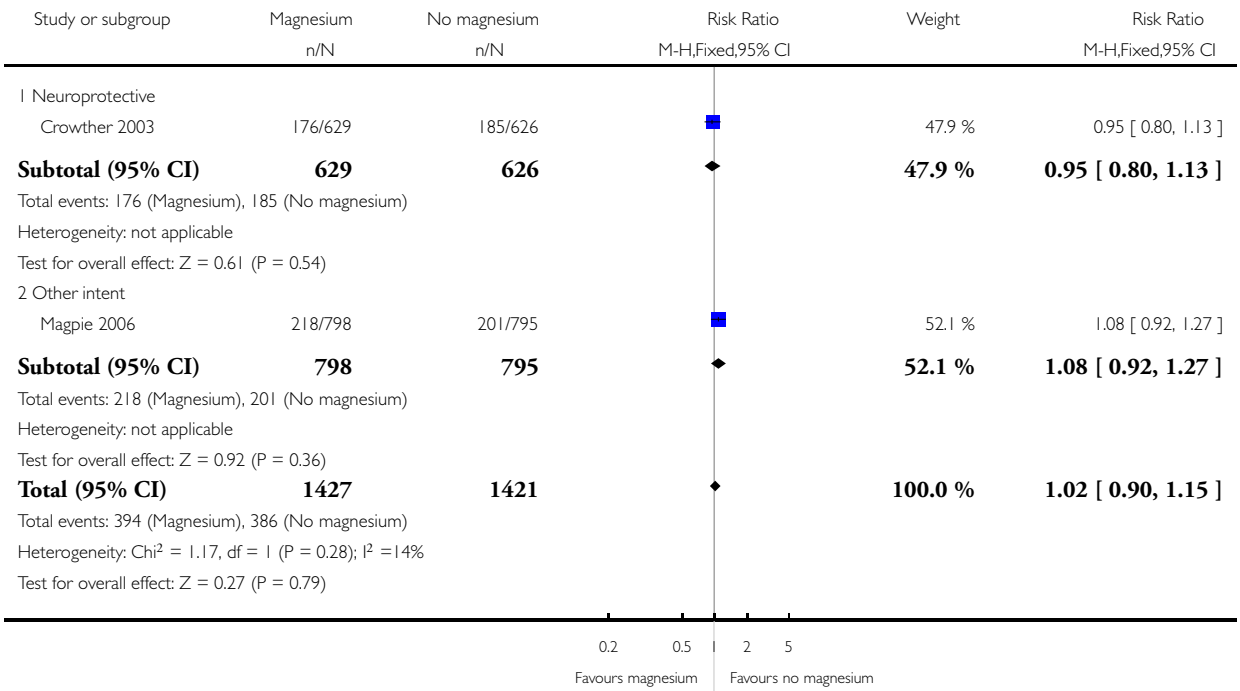
Analysis 1.14. Comparison 1 Magnesium versus no magnesium, Outcome 14 Death or major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

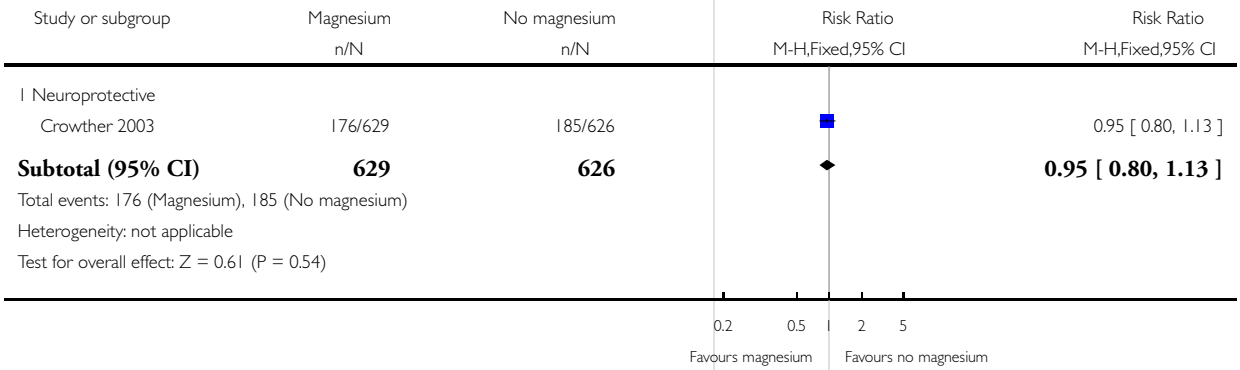
Outcome: 14 Death or major neurologic disability



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 14 Death or major neurologic disability



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 14 Death or major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Other intent				
Magpie 2006	218/798	201/795		1.08 [0.92, 1.27]
Subtotal (95% CI)	**798**	**795**		**1.08 [0.92, 1.27]**
Total events: 218 (Magnesium), 201 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 0.92 (P = 0.36)				

Analysis 1.15. Comparison 1 Magnesium versus no magnesium, Outcome 15 Maternal mortality.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 15 Maternal mortality

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	0/535	0/527		0.0 %	Not estimable
Magpie 2006	10/765	7/779		82.0 %	1.45 [0.56, 3.80]
Marret 2006	0/286	1/278		18.0 %	0.32 [0.01, 7.92]
Total (95% CI)	**1586**	**1584**		**100.0 %**	**1.25 [0.51, 3.07]**
Total events: 10 (Magnesium), 8 (No magnesium)					
Heterogeneity: Chi^2 = 0.78, df = 1 (P = 0.38); I^2 =0.0%					
Test for overall effect: Z = 0.49 (P = 0.62)					

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Analysis 1.16. Comparison 1 Magnesium versus no magnesium, Outcome 16 Maternal cardiac arrest.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 16 Maternal cardiac arrest

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	0/535	0/527		0.0 %	Not estimable
Magpie 2006	1/765	3/779		100.0 %	0.34 [0.04, 3.26]
Marret 2006	0/286	0/278		0.0 %	Not estimable
Total (95% CI)	**1586**	**1584**		**100.0 %**	**0.34 [0.04, 3.26]**

Total events: 1 (Magnesium), 3 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.94 (P = 0.35)

Analysis 1.17. Comparison 1 Magnesium versus no magnesium, Outcome 17 Maternal respiratory arrest.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 17 Maternal respiratory arrest

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	0/535	0/527		0.0 %	Not estimable
Magpie 2006	1/765	1/779		100.0 %	1.02 [0.06, 16.25]
Marret 2006	0/286	0/278		0.0 %	Not estimable
Total (95% CI)	**1586**	**1584**		**100.0 %**	**1.02 [0.06, 16.25]**

Total events: 1 (Magnesium), 1 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.01 (P = 0.99)

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Analysis 1.18. Comparison 1 Magnesium versus no magnesium, Outcome 18 Cessation of maternal therapy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

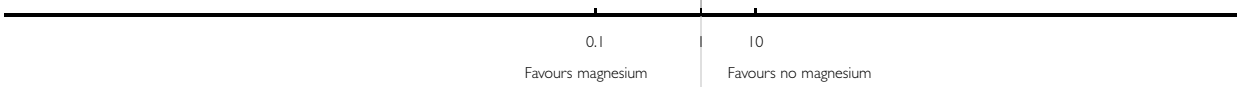
Outcome: 18 Cessation of maternal therapy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	78/535	28/527		96.6 %	2.74 [1.81, 4.15]
Magpie 2006	11/765	1/779		3.4 %	11.20 [1.45, 86.55]
Total (95% CI)	**1300**	**1306**		**100.0 %**	**3.03 [2.02, 4.54]**

Total events: 89 (Magnesium), 29 (No magnesium)

Heterogeneity: Chi^2 = 1.79, df = 1 (P = 0.18); I^2 =44%

Test for overall effect: Z = 5.38 (P < 0.00001)



Analysis 1.19. Comparison 1 Magnesium versus no magnesium, Outcome 19 Intraventricular haemorrhage.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

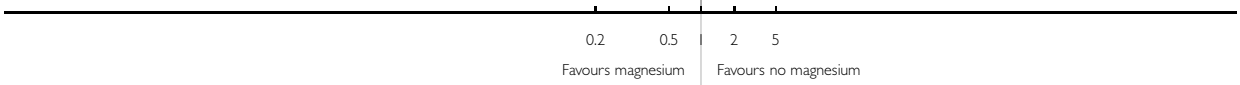
Outcome: 19 Intraventricular haemorrhage

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	165/629	148/626		60.9 %	1.11 [0.92, 1.34]
Marret 2006	71/352	82/336		34.4 %	0.83 [0.62, 1.09]
Mittendorf 2002	13/85	11/80		4.7 %	1.11 [0.53, 2.34]
Total (95% CI)	**1066**	**1042**		**100.0 %**	**1.01 [0.87, 1.18]**

Total events: 249 (Magnesium), 241 (No magnesium)

Heterogeneity: Chi^2 = 2.95, df = 2 (P = 0.23); I^2 =32%

Test for overall effect: Z = 0.15 (P = 0.88)



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Analysis 1.20. Comparison 1 Magnesium versus no magnesium, Outcome 20 Cystic periventricular leucomalacia.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

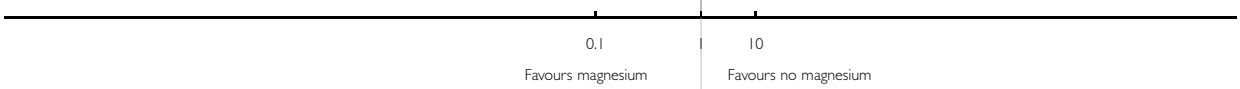
Outcome: 20 Cystic periventricular leucomalacia

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	22/629	21/626		41.9 %	1.04 [0.58, 1.88]
Marret 2006	27/352	28/336		57.1 %	0.92 [0.55, 1.53]
Mittendorf 2002	1/85	0/80		1.0 %	2.83 [0.12, 68.37]
Total (95% CI)	**1066**	**1042**		**100.0 %**	**0.99 [0.68, 1.45]**

Total events: 50 (Magnesium), 49 (No magnesium)

Heterogeneity: Chi² = 0.53, df = 2 (P = 0.77); I² =0.0%

Test for overall effect: Z = 0.05 (P = 0.96)



Analysis 1.21. Comparison 1 Magnesium versus no magnesium, Outcome 21 Apgar score < 7 at 5 minutes.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

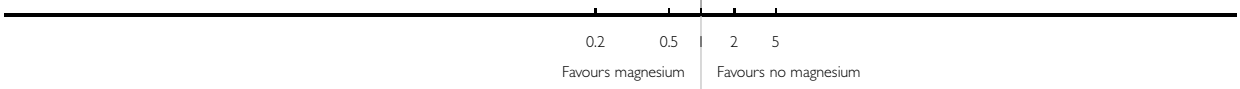
Outcome: 21 Apgar score < 7 at 5 minutes

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	94/629	91/626		74.2 %	1.03 [0.79, 1.34]
Marret 2006	45/352	31/336		25.8 %	1.39 [0.90, 2.14]
Total (95% CI)	**981**	**962**		**100.0 %**	**1.12 [0.89, 1.40]**

Total events: 139 (Magnesium), 122 (No magnesium)

Heterogeneity: Chi² = 1.33, df = 1 (P = 0.25); I² =25%

Test for overall effect: Z = 0.98 (P = 0.33)



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Analysis 1.22. Comparison 1 Magnesium versus no magnesium, Outcome 22 Neonatal convulsions.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 22 Neonatal convulsions

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	25/629	32/626		77.7 %	0.78 [0.47, 1.30]
Marret 2006	7/352	9/336		22.3 %	0.74 [0.28, 1.97]
Total (95% CI)	**981**	**962**		**100.0 %**	**0.77 [0.49, 1.21]**

Total events: 32 (Magnesium), 41 (No magnesium)

Heterogeneity: Chi² = 0.01, df = 1 (P = 0.93); I² =0.0%

Test for overall effect: Z = 1.13 (P = 0.26)

Analysis 1.23. Comparison 1 Magnesium versus no magnesium, Outcome 23 Ongoing respiratory support.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

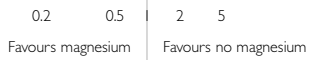
Outcome: 23 Ongoing respiratory support

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	176/629	185/626		50.9 %	0.95 [0.80, 1.13]
Marret 2006	191/352	175/336		49.1 %	1.04 [0.91, 1.20]
Total (95% CI)	**981**	**962**		**100.0 %**	**0.99 [0.89, 1.11]**

Total events: 367 (Magnesium), 360 (No magnesium)

Heterogeneity: Chi² = 0.73, df = 1 (P = 0.39); I² =0.0%

Test for overall effect: Z = 0.11 (P = 0.91)



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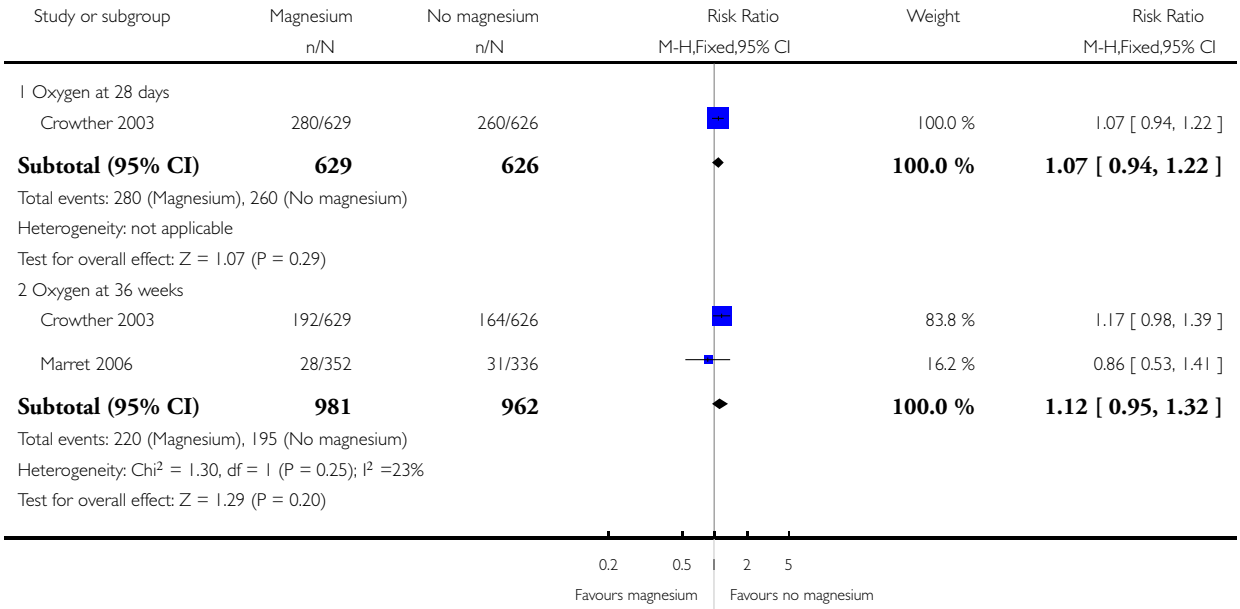
Analysis 1.24. Comparison 1 Magnesium versus no magnesium, Outcome 24 Chronic lung disease.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

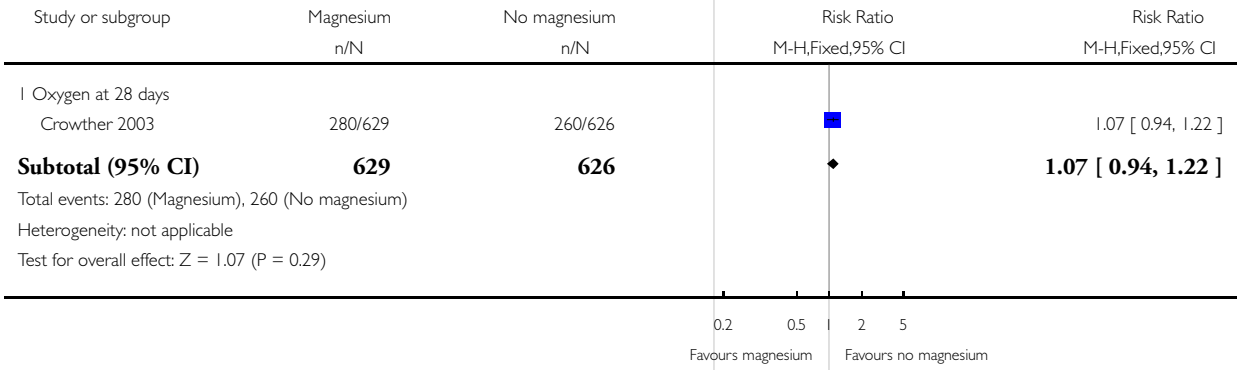
Outcome: 24 Chronic lung disease



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 24 Chronic lung disease



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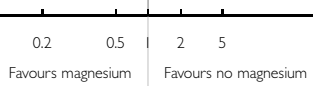
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 24 Chronic lung disease

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Oxygen at 36 weeks				
Crowther 2003	192/629	164/626		1.17 [0.98, 1.39]
Marret 2006	28/352	31/336		0.86 [0.53, 1.41]
Subtotal (95% CI)	**981**	**962**		**1.12 [0.95, 1.32]**
Total events: 220 (Magnesium), 195 (No magnesium)				
Heterogeneity: Chi^2 = 1.30, df = 1 (P = 0.25); I^2 =23%				
Test for overall effect: Z = 1.29 (P = 0.20)				



Analysis 1.25. Comparison 1 Magnesium versus no magnesium, Outcome 25 Maternal hypotension.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 25 Maternal hypotension

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	77/535	52/527		99.0 %	1.46 [1.05, 2.03]
Marret 2006	3/286	0/278		1.0 %	6.80 [0.35, 131.14]
Total (95% CI)	**821**	**805**		**100.0 %**	**1.51 [1.09, 2.09]**
Total events: 80 (Magnesium), 52 (No magnesium)					
Heterogeneity: Chi^2 = 1.04, df = 1 (P = 0.31); I^2 =4%					
Test for overall effect: Z = 2.47 (P = 0.014)					

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Analysis 1.26. Comparison 1 Magnesium versus no magnesium, Outcome 26 Maternal tachycardia.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 26 Maternal tachycardia

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	56/535	36/527		100.0 %	1.53 [1.03, 2.29]
Total (95% CI)	**535**	**527**		**100.0 %**	**1.53 [1.03, 2.29]**

Total events: 56 (Magnesium), 36 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 2.09 (P = 0.037)

Analysis 1.27. Comparison 1 Magnesium versus no magnesium, Outcome 27 Maternal respiratory depression.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 27 Maternal respiratory depression

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	34/535	28/527		100.0 %	1.20 [0.74, 1.94]
Total (95% CI)	**535**	**527**		**100.0 %**	**1.20 [0.74, 1.94]**

Total events: 34 (Magnesium), 28 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.72 (P = 0.47)

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Analysis 1.28. Comparison 1 Magnesium versus no magnesium, Outcome 28 Postpartum haemorrhage.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 28 Postpartum haemorrhage

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	86/535	99/527		99.0 %	0.86 [0.66, 1.11]
Marret 2006	2/286	1/278		1.0 %	1.94 [0.18, 21.32]
Total (95% CI)	**821**	**805**		**100.0 %**	**0.87 [0.67, 1.12]**

Total events: 88 (Magnesium), 100 (No magnesium)

Heterogeneity: Chi^2 = 0.45, df = 1 (P = 0.50); I^2 =0.0%

Test for overall effect: Z = 1.08 (P = 0.28)

Analysis 1.29. Comparison 1 Magnesium versus no magnesium, Outcome 29 Caesarean birth.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 29 Caesarean birth

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	289/535	290/527		34.7 %	0.98 [0.88, 1.10]
Magpie 2006	488/765	456/779		53.7 %	1.09 [1.01, 1.18]
Marret 2006	116/286	96/278		11.6 %	1.17 [0.95, 1.46]
Total (95% CI)	**1586**	**1584**		**100.0 %**	**1.06 [1.00, 1.13]**

Total events: 893 (Magnesium), 842 (No magnesium)

Heterogeneity: Chi^2 = 3.22, df = 2 (P = 0.20); I^2 =38%

Test for overall effect: Z = 1.89 (P = 0.059)

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Analysis 1.30. Comparison 1 Magnesium versus no magnesium, Outcome 30 Mother admitted to intensive care unit.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 30 Mother admitted to intensive care unit

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	0/535	0/527		0.0 %	Not estimable
Magpie 2006	28/765	32/779		100.0 %	0.89 [0.54, 1.47]
Total (95% CI)	**1300**	**1306**		**100.0 %**	**0.89 [0.54, 1.47]**

Total events: 28 (Magnesium), 32 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.45 (P = 0.65)

Analysis 1.31. Comparison 1 Magnesium versus no magnesium, Outcome 31 Duration of mother's hospital stay (days).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 31 Duration of mother's hospital stay (days)

Study or subgroup	Magnesium N	Mean(SD)	No magnesium N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Crowther 2003	535	5.2 (3.6)	527	5 (2.6)		87.5 %	0.20 [-0.18, 0.58]
Magpie 2006	765	11 (10)	779	11 (10)		12.5 %	0.0 [-1.00, 1.00]
Total (95% CI)	**1300**		**1306**			**100.0 %**	**0.17 [-0.18, 0.53]**

Heterogeneity: Chi^2 = 0.14, df = 1 (P = 0.71); I^2 =0.0%

Test for overall effect: Z = 0.97 (P = 0.33)

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Analysis 1.32. Comparison 1 Magnesium versus no magnesium, Outcome 32 Duration of primary hospital stay for baby (days).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 1 Magnesium versus no magnesium

Outcome: 32 Duration of primary hospital stay for baby (days)

Study or subgroup	Magnesium N	Mean(SD)	No magnesium N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Crowther 2003	620	72.9 (36.7)	615	71.1 (42.4)		39.0 %	1.80 [-2.62, 6.22]
Magpie 2006	798	17 (19)	795	19 (34)		61.0 %	-2.00 [-4.71, 0.71]
Total (95% CI)	**1418**		**1410**			**100.0 %**	**-0.52 [-4.15, 3.11]**

Heterogeneity: Tau² = 3.72; Chi² = 2.06, df = 1 (P = 0.15); I² =52%

Test for overall effect: Z = 0.28 (P = 0.78)

Analysis 2.1. Comparison 2 Gestational age subgroup, Outcome 1 Paediatric mortality (fetal and later).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	87/629	107/626		34.3 %	0.81 [0.62, 1.05]
Magpie 2006	167/404	158/401		41.3 %	1.05 [0.89, 1.24]
Marret 2006	34/352	38/336		22.5 %	0.85 [0.55, 1.32]
Mittendorf 2002	10/85	1/80		1.9 %	9.41 [1.23, 71.86]
Subtotal (95% CI)	**1470**	**1443**		**100.0 %**	**0.95 [0.72, 1.27]**
Total events: 298 (Magnesium), 304 (No magnesium)					
Heterogeneity: Tau² = 0.04; Chi² = 7.82, df = 3 (P = 0.05); I² =62%					
Test for overall effect: Z = 0.32 (P = 0.75)					
2 < 30 weeks at randomisation					
Crowther 2003	87/629	107/626		46.3 %	0.81 [0.62, 1.05]
Magpie 2006	100/140	89/142		53.7 %	1.14 [0.97, 1.34]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**0.97 [0.67, 1.41]**
Total events: 187 (Magnesium), 196 (No magnesium)					
Heterogeneity: Tau² = 0.06; Chi² = 5.87, df = 1 (P = 0.02); I² =83%					
Test for overall effect: Z = 0.15 (P = 0.88)					

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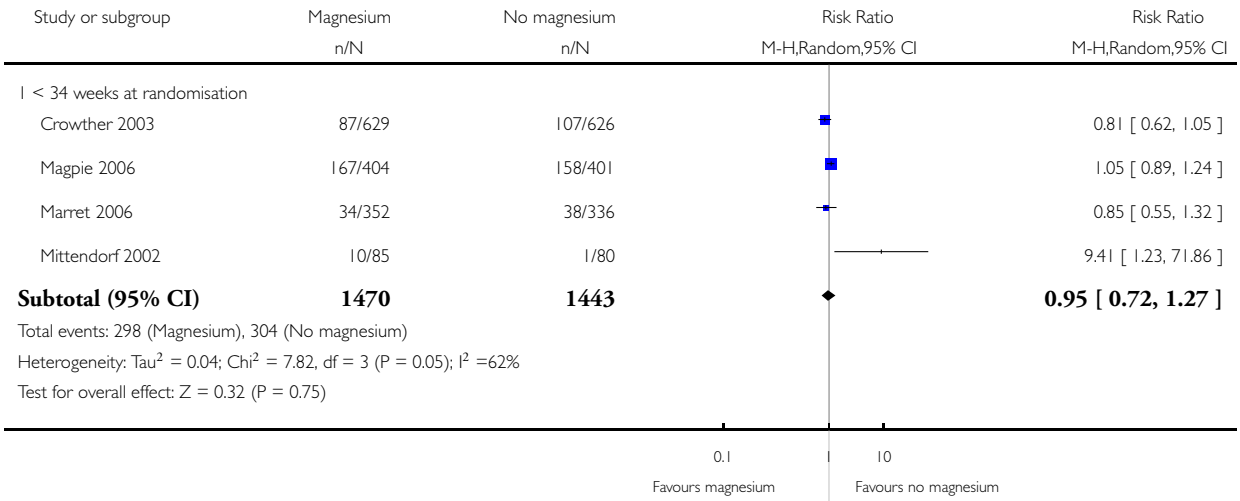
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

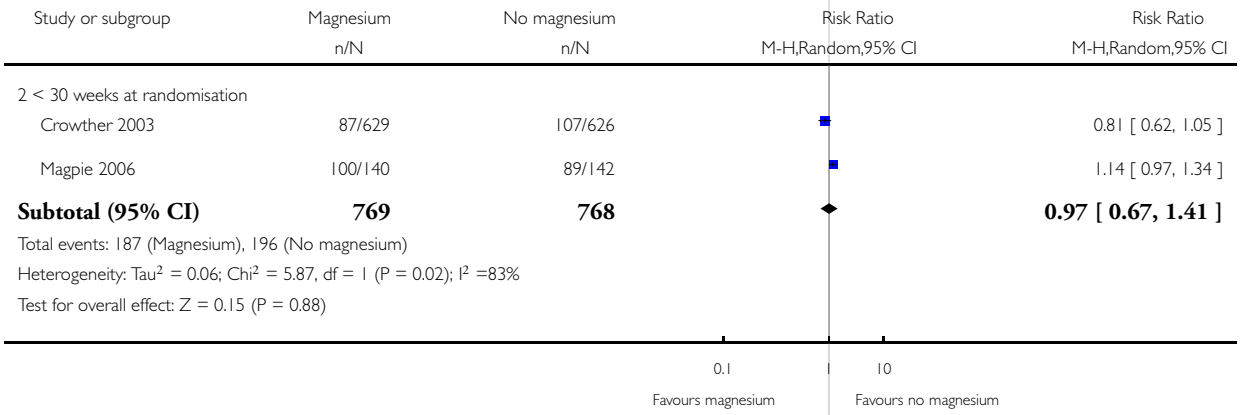
Outcome: 1 Paediatric mortality (fetal and later)



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 1 Paediatric mortality (fetal and later)



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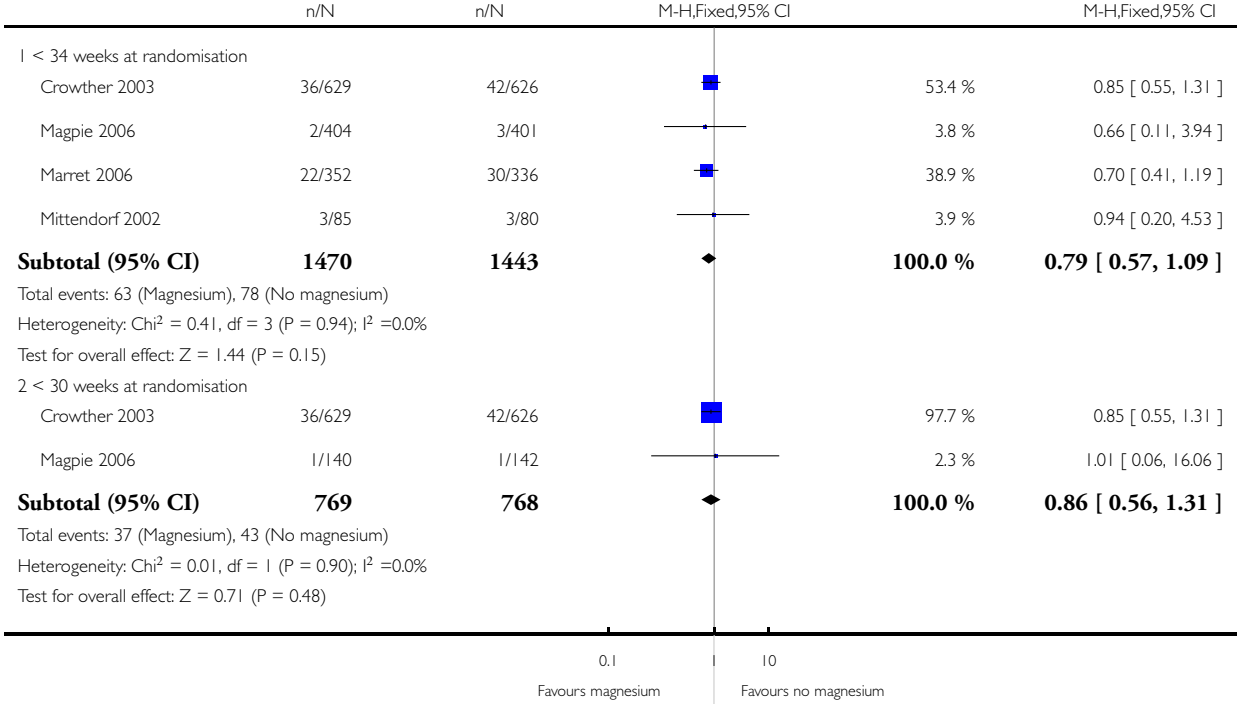
Analysis 2.2. Comparison 2 Gestational age subgroup, Outcome 2 Cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	36/629	42/626		53.4 %	0.85 [0.55, 1.31]
Magpie 2006	2/404	3/401		3.8 %	0.66 [0.11, 3.94]
Marret 2006	22/352	30/336		38.9 %	0.70 [0.41, 1.19]
Mittendorf 2002	3/85	3/80		3.9 %	0.94 [0.20, 4.53]
Subtotal (95% CI)	**1470**	**1443**		**100.0 %**	**0.79 [0.57, 1.09]**
Total events: 63 (Magnesium), 78 (No magnesium)					
Heterogeneity: Chi^2 = 0.41, df = 3 (P = 0.94); I^2 =0.0%					
Test for overall effect: Z = 1.44 (P = 0.15)					
2 < 30 weeks at randomisation					
Crowther 2003	36/629	42/626		97.7 %	0.85 [0.55, 1.31]
Magpie 2006	1/140	1/142		2.3 %	1.01 [0.06, 16.06]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**0.86 [0.56, 1.31]**
Total events: 37 (Magnesium), 43 (No magnesium)					
Heterogeneity: Chi^2 = 0.01, df = 1 (P = 0.90); I^2 =0.0%					
Test for overall effect: Z = 0.71 (P = 0.48)					



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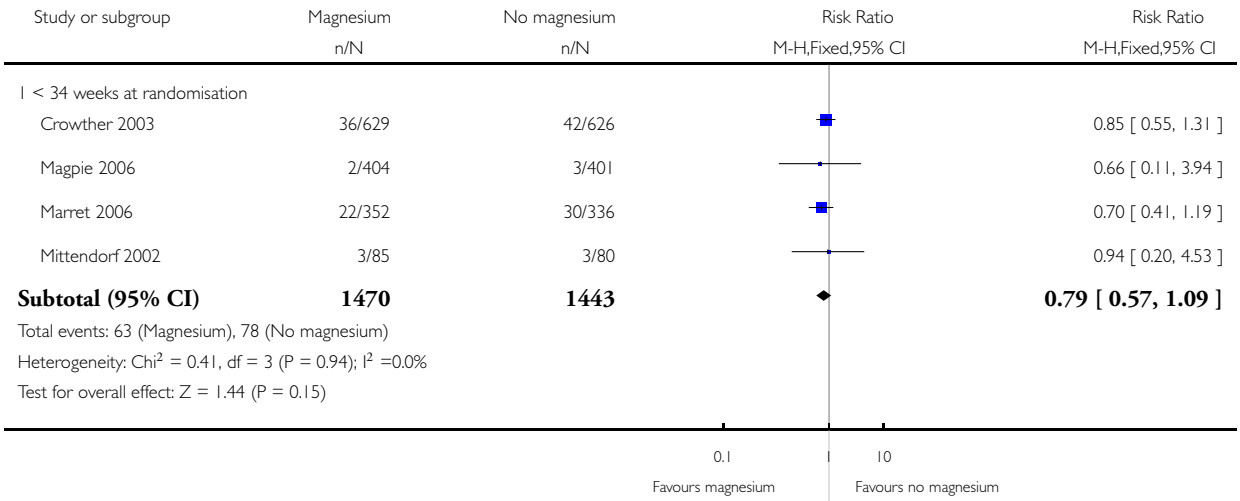
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

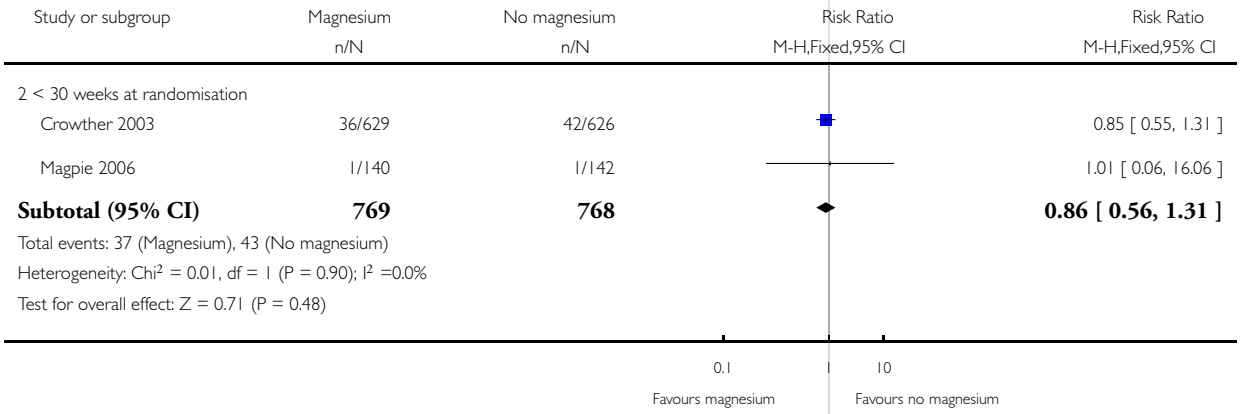
Outcome: 2 Cerebral palsy



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 2 Cerebral palsy



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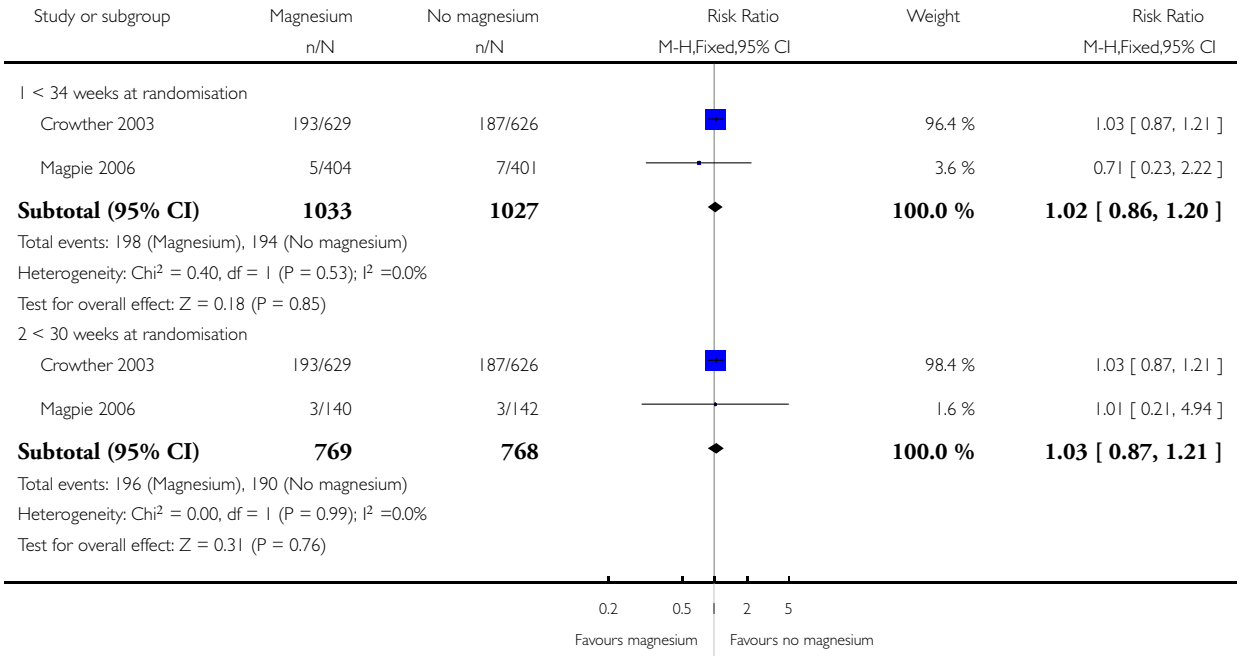
Analysis 2.3. Comparison 2 Gestational age subgroup, Outcome 3 Neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

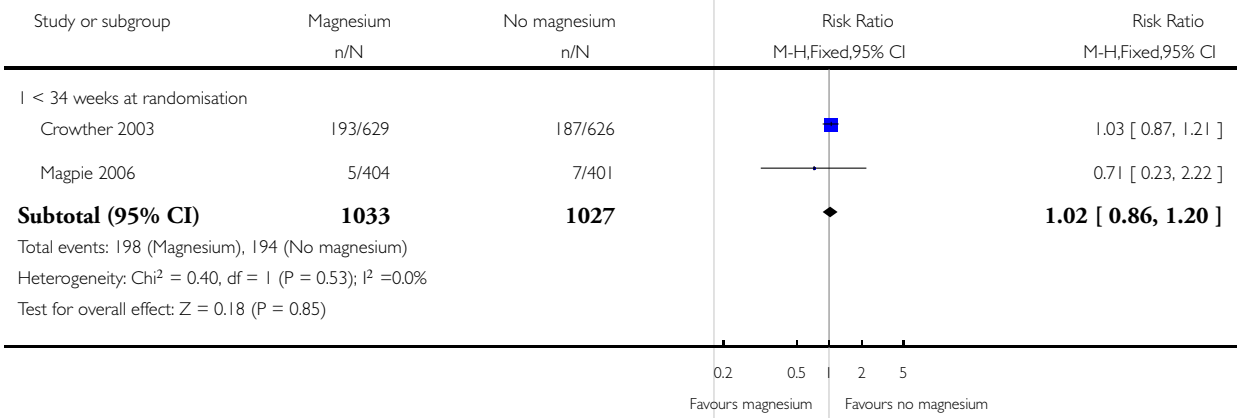
Outcome: 3 Neurologic impairment



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 3 Neurologic impairment



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 3 Neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 < 30 weeks at randomisation				
Crowther 2003	193/629	187/626		1.03 [0.87, 1.21]
Magpie 2006	3/140	3/142		1.01 [0.21, 4.94]
Subtotal (95% CI)	**769**	**768**		**1.03 [0.87, 1.21]**
Total events: 196 (Magnesium), 190 (No magnesium)				
Heterogeneity: Chi^2 = 0.00, df = 1 (P = 0.99); I^2 =0.0%				
Test for overall effect: Z = 0.31 (P = 0.76)				

Analysis 2.4. Comparison 2 Gestational age subgroup, Outcome 4 Major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	89/629	78/626		91.8 %	1.14 [0.86, 1.51]
Magpie 2006	4/404	7/401		8.2 %	0.57 [0.17, 1.92]
Subtotal (95% CI)	**1033**	**1027**		**100.0 %**	**1.09 [0.83, 1.43]**
Total events: 93 (Magnesium), 85 (No magnesium)					
Heterogeneity: Chi^2 = 1.18, df = 1 (P = 0.28); I^2 =15%					
Test for overall effect: Z = 0.61 (P = 0.54)					
2 < 30 weeks at randomisation					
Crowther 2003	89/629	78/626		96.3 %	1.14 [0.86, 1.51]
Magpie 2006	2/140	3/142		3.7 %	0.68 [0.11, 3.99]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**1.12 [0.85, 1.48]**
Total events: 91 (Magnesium), 81 (No magnesium)					
Heterogeneity: Chi^2 = 0.32, df = 1 (P = 0.57); I^2 =0.0%					
Test for overall effect: Z = 0.79 (P = 0.43)					

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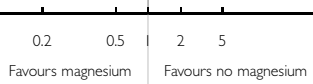
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 < 34 weeks at randomisation				
Crowther 2003	89/629	78/626		1.14 [0.86, 1.51]
Magpie 2006	4/404	7/401		0.57 [0.17, 1.92]
Subtotal (95% CI)	**1033**	**1027**		**1.09 [0.83, 1.43]**
Total events: 93 (Magnesium), 85 (No magnesium)				
Heterogeneity: Chi^2 = 1.18, df = 1 (P = 0.28); I^2 =15%				
Test for overall effect: Z = 0.61 (P = 0.54)				

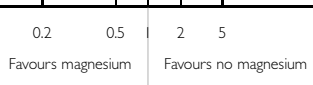


Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 < 30 weeks at randomisation				
Crowther 2003	89/629	78/626		1.14 [0.86, 1.51]
Magpie 2006	2/140	3/142		0.68 [0.11, 3.99]
Subtotal (95% CI)	**769**	**768**		**1.12 [0.85, 1.48]**
Total events: 91 (Magnesium), 81 (No magnesium)				
Heterogeneity: Chi^2 = 0.32, df = 1 (P = 0.57); I^2 =0.0%				
Test for overall effect: Z = 0.79 (P = 0.43)				



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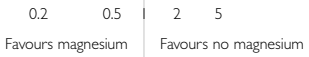
Analysis 2.5. Comparison 2 Gestational age subgroup, Outcome 5 Death or cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	123/629	149/626		33.3 %	0.82 [0.66, 1.02]
Magpie 2006	169/404	161/401		36.7 %	1.04 [0.88, 1.23]
Marret 2006	56/352	68/336		25.3 %	0.79 [0.57, 1.08]
Mittendorf 2002	13/85	4/80		4.7 %	3.06 [1.04, 8.99]
Subtotal (95% CI)	**1470**	**1443**		**100.0 %**	**0.94 [0.74, 1.21]**
Total events: 361 (Magnesium), 382 (No magnesium)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 8.85$, df = 3 (P = 0.03); $I^2 = 66\%$					
Test for overall effect: Z = 0.46 (P = 0.64)					
2 < 30 weeks at randomisation					
Crowther 2003	123/629	149/626		48.1 %	0.82 [0.66, 1.02]
Magpie 2006	101/140	90/142		51.9 %	1.14 [0.97, 1.34]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**0.97 [0.69, 1.38]**
Total events: 224 (Magnesium), 239 (No magnesium)					
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 6.92$, df = 1 (P = 0.01); $I^2 = 86\%$					
Test for overall effect: Z = 0.15 (P = 0.88)					



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 5 Death or cerebral palsy

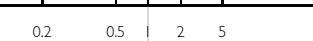
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation				
Crowther 2003	123/629	149/626		0.82 [0.66, 1.02]
Magpie 2006	169/404	161/401		1.04 [0.88, 1.23]
Marret 2006	56/352	68/336		0.79 [0.57, 1.08]
Mittendorf 2002	13/85	4/80		3.06 [1.04, 8.99]
Subtotal (95% CI)	**1470**	**1443**		**0.94 [0.74, 1.21]**
Total events: 361 (Magnesium), 382 (No magnesium)				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 8.85$, df = 3 (P = 0.03); $I^2 = 66\%$				
Test for overall effect: Z = 0.46 (P = 0.64)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 < 30 weeks at randomisation				
Crowther 2003	123/629	149/626		0.82 [0.66, 1.02]
Magpie 2006	101/140	90/142		1.14 [0.97, 1.34]
Subtotal (95% CI)	**769**	**768**		**0.97 [0.69, 1.38]**
Total events: 224 (Magnesium), 239 (No magnesium)				
Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 6.92$, df = 1 (P = 0.01); $I^2 = 86\%$				
Test for overall effect: Z = 0.15 (P = 0.88)				



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Analysis 2.6. Comparison 2 Gestational age subgroup, Outcome 6 Death or neurological impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	280/629	294/626		64.6 %	0.95 [0.84, 1.07]
Magpie 2006	172/404	165/401		35.4 %	1.03 [0.88, 1.22]
Subtotal (95% CI)	**1033**	**1027**		**100.0 %**	**0.98 [0.89, 1.08]**
Total events: 452 (Magnesium), 459 (No magnesium)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.72, df = 1 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 0.46 (P = 0.65)					
2 < 30 weeks at randomisation					
Crowther 2003	280/629	294/626		53.8 %	0.95 [0.84, 1.07]
Magpie 2006	103/140	92/142		46.2 %	1.14 [0.97, 1.33]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**1.03 [0.86, 1.24]**
Total events: 383 (Magnesium), 386 (No magnesium)					
Heterogeneity: Tau^2 = 0.01; Chi^2 = 3.40, df = 1 (P = 0.07); I^2 =71%					
Test for overall effect: Z = 0.32 (P = 0.75)					

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation				
Crowther 2003	280/629	294/626		0.95 [0.84, 1.07]
Magpie 2006	172/404	165/401		1.03 [0.88, 1.22]
Subtotal (95% CI)	**1033**	**1027**		**0.98 [0.89, 1.08]**
Total events: 452 (Magnesium), 459 (No magnesium)				
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.72, df = 1 (P = 0.40); I^2 =0.0%				
Test for overall effect: Z = 0.46 (P = 0.65)				

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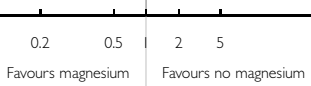
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 < 30 weeks at randomisation				
Crowther 2003	280/629	294/626		0.95 [0.84, 1.07]
Magpie 2006	103/140	92/142		1.14 [0.97, 1.33]
Subtotal (95% CI)	**769**	**768**		**1.03 [0.86, 1.24]**
Total events: 383 (Magnesium), 386 (No magnesium)				
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.40$, df = 1 (P = 0.07); $I^2 = 71\%$				
Test for overall effect: Z = 0.32 (P = 0.75)				



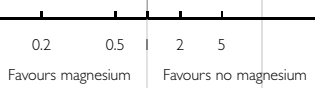
Analysis 2.7. Comparison 2 Gestational age subgroup, Outcome 7 Death or major neurological disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 7 Death or major neurological disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation					
Crowther 2003	176/629	185/626		46.8 %	0.95 [0.80, 1.13]
Magpie 2006	171/404	165/401		53.2 %	1.03 [0.87, 1.21]
Subtotal (95% CI)	**1033**	**1027**		**100.0 %**	**0.99 [0.88, 1.11]**
Total events: 347 (Magnesium), 350 (No magnesium)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.47$, df = 1 (P = 0.49); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.17 (P = 0.86)					
2 < 30 weeks at randomisation					
Crowther 2003	176/629	185/626		47.9 %	0.95 [0.80, 1.13]
Magpie 2006	102/140	92/142		52.1 %	1.12 [0.96, 1.32]
Subtotal (95% CI)	**769**	**768**		**100.0 %**	**1.04 [0.86, 1.24]**
Total events: 278 (Magnesium), 277 (No magnesium)					
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.39$, df = 1 (P = 0.12); $I^2 = 58\%$					
Test for overall effect: Z = 0.38 (P = 0.71)					



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 7 Death or major neurological disability

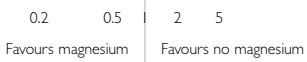
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 < 34 weeks at randomisation				
Crowther 2003	176/629	185/626		0.95 [0.80, 1.13]
Magpie 2006	171/404	165/401		1.03 [0.87, 1.21]
Subtotal (95% CI)	**1033**	**1027**		**0.99 [0.88, 1.11]**
Total events: 347 (Magnesium), 350 (No magnesium)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.47$, df = 1 (P = 0.49); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.17 (P = 0.86)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 2 Gestational age subgroup

Outcome: 7 Death or major neurological disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 < 30 weeks at randomisation				
Crowther 2003	176/629	185/626		0.95 [0.80, 1.13]
Magpie 2006	102/140	92/142		1.12 [0.96, 1.32]
Subtotal (95% CI)	**769**	**768**		**1.04 [0.86, 1.24]**
Total events: 278 (Magnesium), 277 (No magnesium)				
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.39$, df = 1 (P = 0.12); $I^2 = 58\%$				
Test for overall effect: Z = 0.38 (P = 0.71)				



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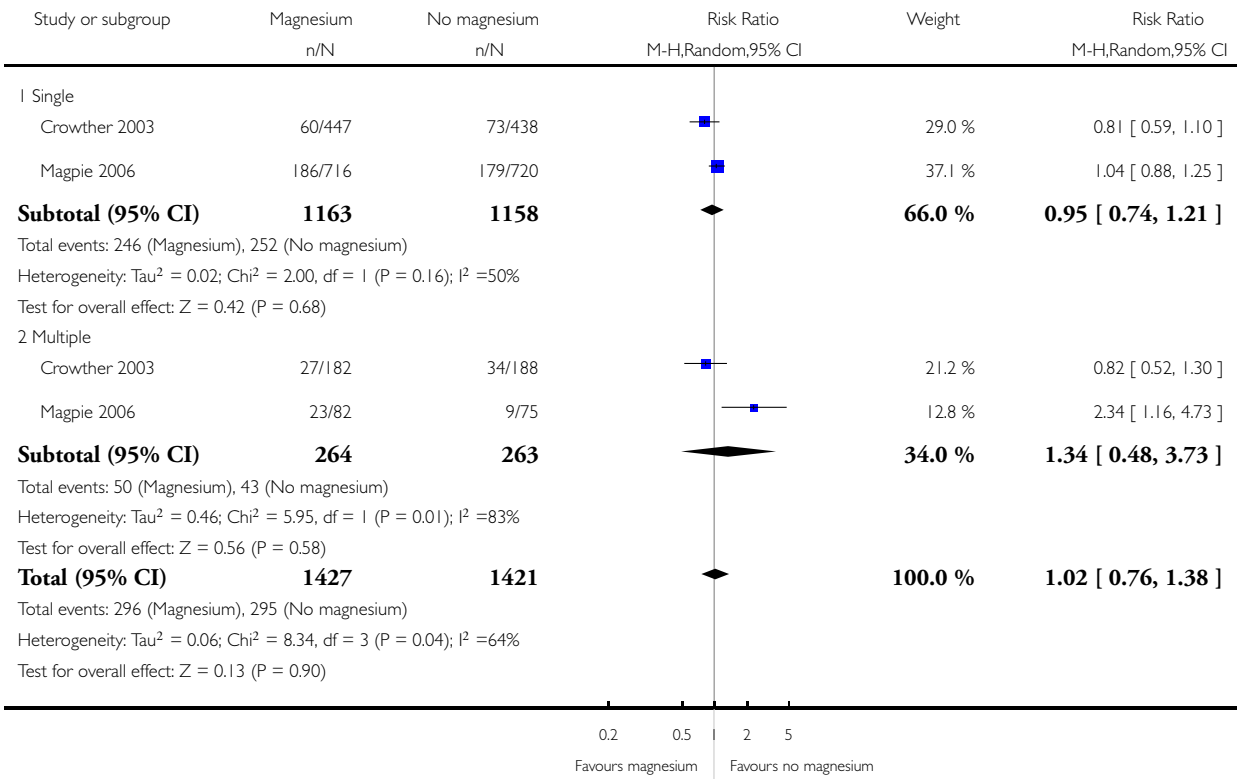
Analysis 3.1. Comparison 3 Single or multiple pregnancy subgroup, Outcome 1 Paediatric mortality (fetal and later).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 1 Paediatric mortality (fetal and later)



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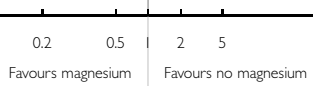
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Single				
Crowther 2003	60/447	73/438		0.81 [0.59, 1.10]
Magpie 2006	186/716	179/720		1.04 [0.88, 1.25]
Subtotal (95% CI)	**1163**	**1158**		**0.95 [0.74, 1.21]**
Total events: 246 (Magnesium), 252 (No magnesium)				
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 2.00$, df = 1 (P = 0.16); $I^2 = 50\%$				
Test for overall effect: Z = 0.42 (P = 0.68)				



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Multiple				
Crowther 2003	27/182	34/188		0.82 [0.52, 1.30]
Magpie 2006	23/82	9/75		2.34 [1.16, 4.73]
Subtotal (95% CI)	**264**	**263**		**1.34 [0.48, 3.73]**
Total events: 50 (Magnesium), 43 (No magnesium)				
Heterogeneity: $Tau^2 = 0.46$; $Chi^2 = 5.95$, df = 1 (P = 0.01); $I^2 = 83\%$				
Test for overall effect: Z = 0.56 (P = 0.58)				

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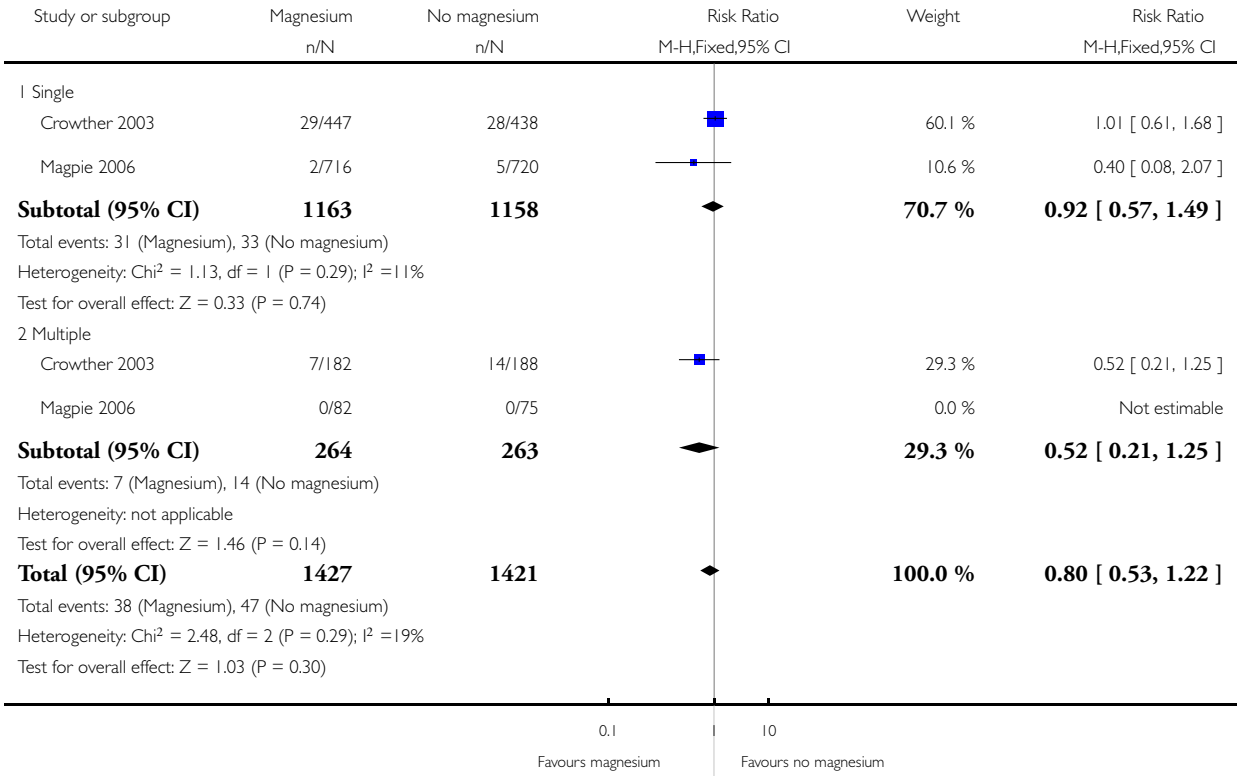
Analysis 3.2. Comparison 3 Single or multiple pregnancy subgroup, Outcome 2 Cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 2 Cerebral palsy



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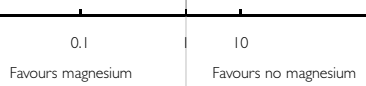
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Single				
Crowther 2003	29/447	28/438		1.01 [0.61, 1.68]
Magpie 2006	2/716	5/720		0.40 [0.08, 2.07]
Subtotal (95% CI)	**1163**	**1158**		**0.92 [0.57, 1.49]**
Total events: 31 (Magnesium), 33 (No magnesium)				
Heterogeneity: Chi^2 = 1.13, df = 1 (P = 0.29); I^2 =11%				
Test for overall effect: Z = 0.33 (P = 0.74)				



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Multiple				
Crowther 2003	7/182	14/188		0.52 [0.21, 1.25]
Magpie 2006	0/82	0/75		Not estimable
Subtotal (95% CI)	**264**	**263**		**0.52 [0.21, 1.25]**
Total events: 7 (Magnesium), 14 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.46 (P = 0.14)				

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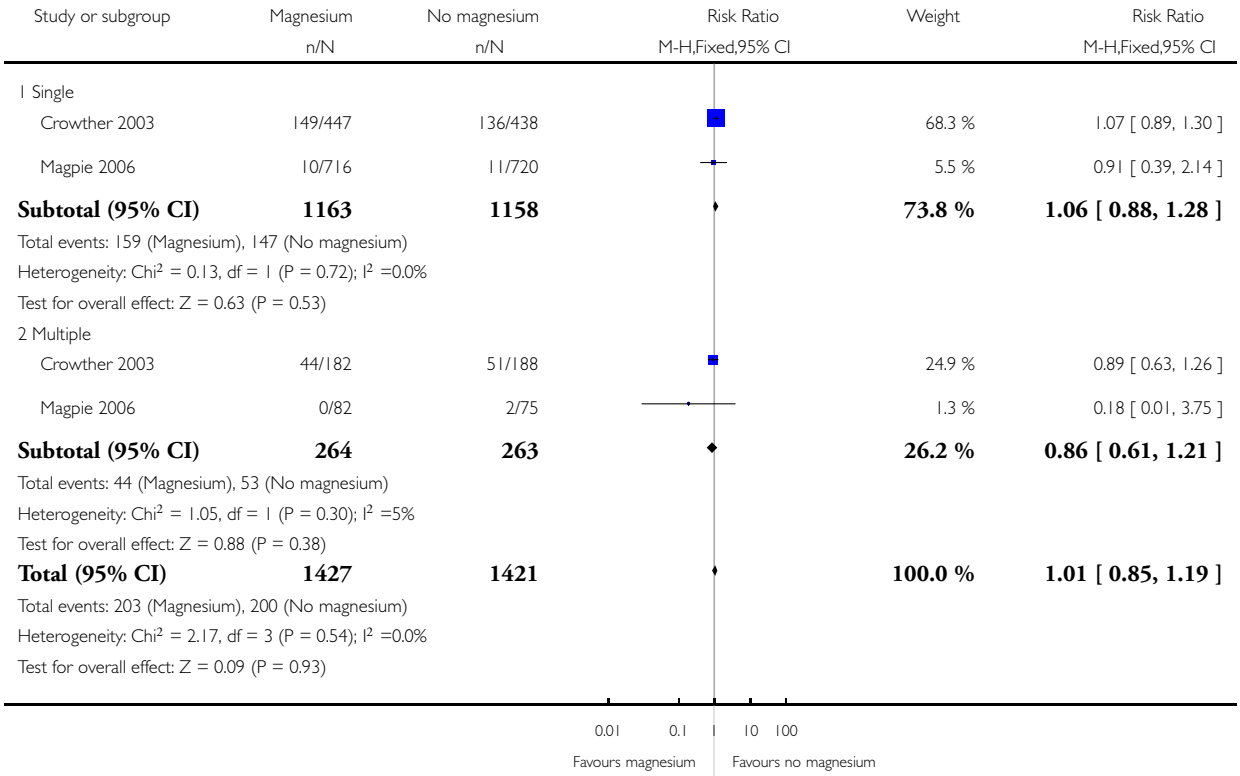
Analysis 3.3. Comparison 3 Single or multiple pregnancy subgroup, Outcome 3 Neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 3 Neurologic impairment



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 3 Neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Single				
Crowther 2003	149/447	136/438		1.07 [0.89, 1.30]
Magpie 2006	10/716	11/720		0.91 [0.39, 2.14]
Subtotal (95% CI)	**1163**	**1158**		**1.06 [0.88, 1.28]**
Total events: 159 (Magnesium), 147 (No magnesium)				
Heterogeneity: Chi^2 = 0.13, df = 1 (P = 0.72); I^2 =0.0%				
Test for overall effect: Z = 0.63 (P = 0.53)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 3 Neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Multiple				
Crowther 2003	44/182	51/188		0.89 [0.63, 1.26]
Magpie 2006	0/82	2/75		0.18 [0.01, 3.75]
Subtotal (95% CI)	**264**	**263**		**0.86 [0.61, 1.21]**
Total events: 44 (Magnesium), 53 (No magnesium)				
Heterogeneity: Chi^2 = 1.05, df = 1 (P = 0.30); I^2 =5%				
Test for overall effect: Z = 0.88 (P = 0.38)				

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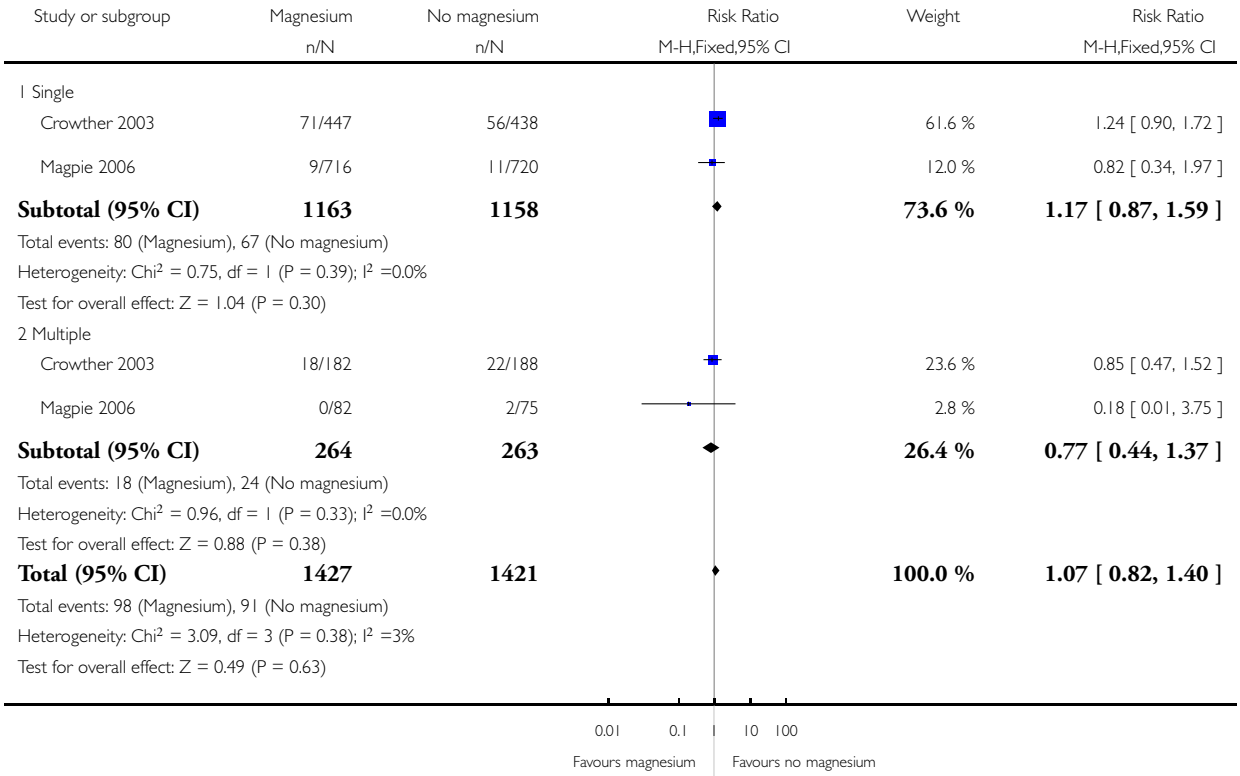
Analysis 3.4. Comparison 3 Single or multiple pregnancy subgroup, Outcome 4 Major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 4 Major neurologic disability



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Single				
Crowther 2003	71/447	56/438		1.24 [0.90, 1.72]
Magpie 2006	9/716	11/720		0.82 [0.34, 1.97]
Subtotal (95% CI)	**1163**	**1158**		**1.17 [0.87, 1.59]**
Total events: 80 (Magnesium), 67 (No magnesium)				
Heterogeneity: Chi^2 = 0.75, df = 1 (P = 0.39); I^2 =0.0%				
Test for overall effect: Z = 1.04 (P = 0.30)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Multiple				
Crowther 2003	18/182	22/188		0.85 [0.47, 1.52]
Magpie 2006	0/82	2/75		0.18 [0.01, 3.75]
Subtotal (95% CI)	**264**	**263**		**0.77 [0.44, 1.37]**
Total events: 18 (Magnesium), 24 (No magnesium)				
Heterogeneity: Chi^2 = 0.96, df = 1 (P = 0.33); I^2 =0.0%				
Test for overall effect: Z = 0.88 (P = 0.38)				

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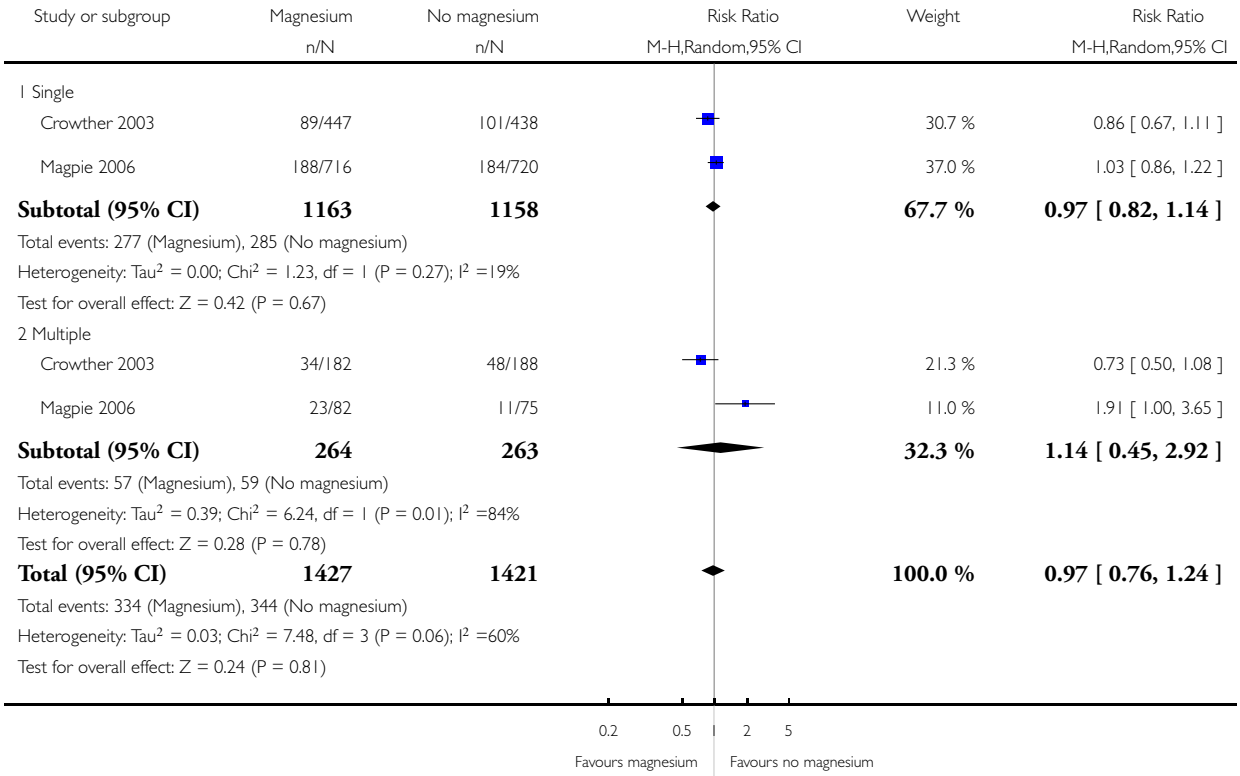
Analysis 3.5. Comparison 3 Single or multiple pregnancy subgroup, Outcome 5 Death or cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 5 Death or cerebral palsy



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

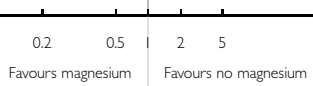
Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Single				
Crowther 2003	89/447	101/438		0.86 [0.67, 1.11]
Magpie 2006	188/716	184/720		1.03 [0.86, 1.22]
Subtotal (95% CI)	**1163**	**1158**		**0.97 [0.82, 1.14]**

Total events: 277 (Magnesium), 285 (No magnesium)

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.23$, df = 1 (P = 0.27); $I^2 = 19\%$

Test for overall effect: Z = 0.42 (P = 0.67)



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

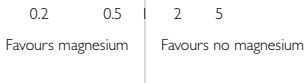
Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Multiple				
Crowther 2003	34/182	48/188		0.73 [0.50, 1.08]
Magpie 2006	23/82	11/75		1.91 [1.00, 3.65]
Subtotal (95% CI)	**264**	**263**		**1.14 [0.45, 2.92]**

Total events: 57 (Magnesium), 59 (No magnesium)

Heterogeneity: $Tau^2 = 0.39$; $Chi^2 = 6.24$, df = 1 (P = 0.01); $I^2 = 84\%$

Test for overall effect: Z = 0.28 (P = 0.78)



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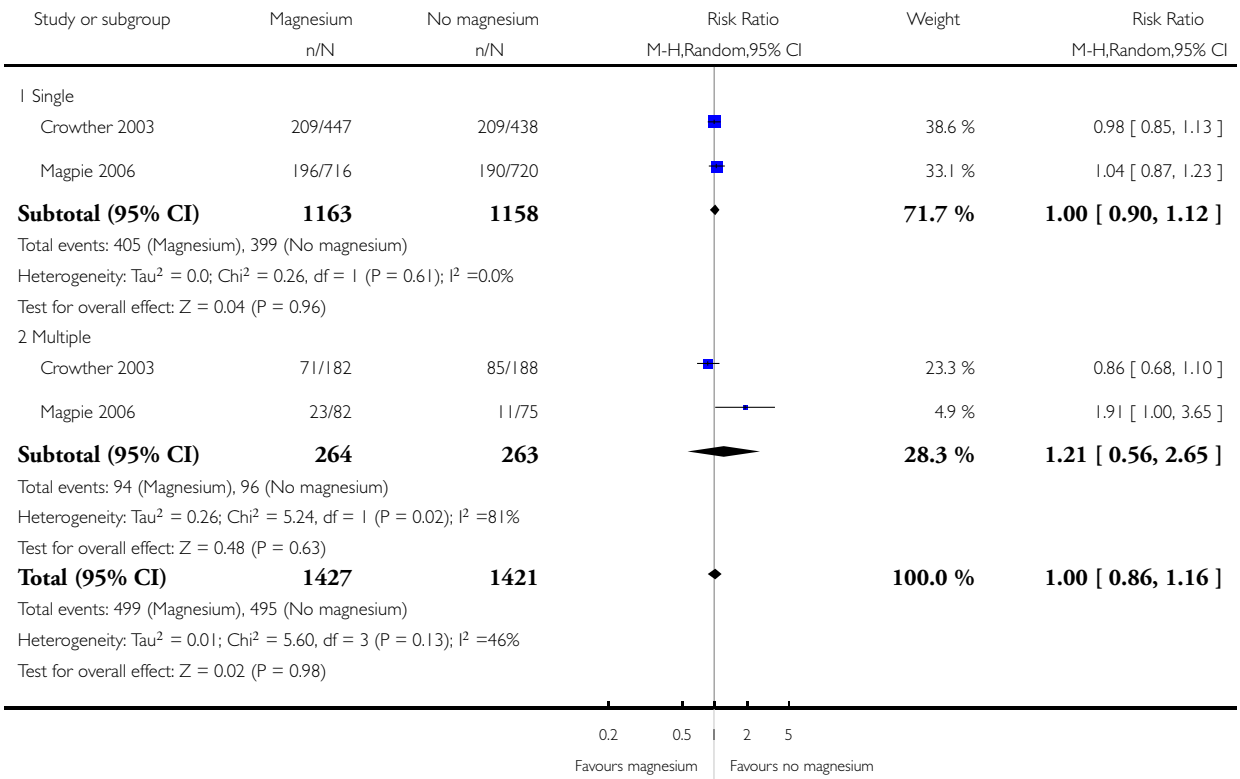
Analysis 3.6. Comparison 3 Single or multiple pregnancy subgroup, Outcome 6 Death or neurological impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 6 Death or neurological impairment



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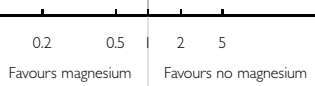
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Single				
Crowther 2003	209/447	209/438		0.98 [0.85, 1.13]
Magpie 2006	196/716	190/720		1.04 [0.87, 1.23]
Subtotal (95% CI)	**1163**	**1158**		**1.00 [0.90, 1.12]**
Total events: 405 (Magnesium), 399 (No magnesium)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.26$, df = 1 (P = 0.61); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.04 (P = 0.96)				

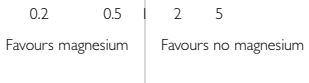


Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Multiple				
Crowther 2003	71/182	85/188		0.86 [0.68, 1.10]
Magpie 2006	23/82	11/75		1.91 [1.00, 3.65]
Subtotal (95% CI)	**264**	**263**		**1.21 [0.56, 2.65]**
Total events: 94 (Magnesium), 96 (No magnesium)				
Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 5.24$, df = 1 (P = 0.02); $I^2 = 81\%$				
Test for overall effect: Z = 0.48 (P = 0.63)				



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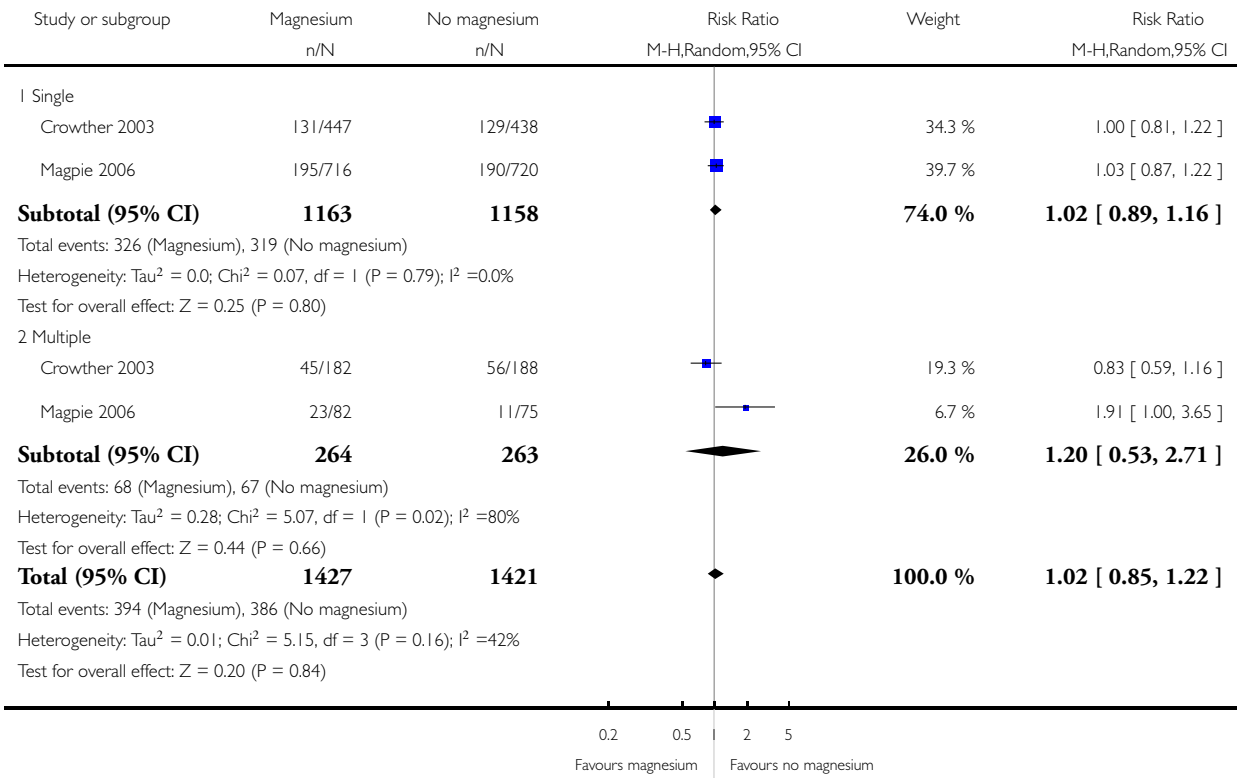
Analysis 3.7. Comparison 3 Single or multiple pregnancy subgroup, Outcome 7 Death or major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 7 Death or major neurologic disability



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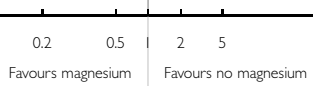
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 7 Death or major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Single				
Crowther 2003	131/447	129/438		1.00 [0.81, 1.22]
Magpie 2006	195/716	190/720		1.03 [0.87, 1.22]
Subtotal (95% CI)	**1163**	**1158**		**1.02 [0.89, 1.16]**
Total events: 326 (Magnesium), 319 (No magnesium)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.07$, df = 1 (P = 0.79); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.25 (P = 0.80)				

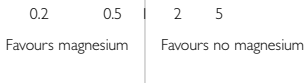


Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 3 Single or multiple pregnancy subgroup

Outcome: 7 Death or major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Multiple				
Crowther 2003	45/182	56/188		0.83 [0.59, 1.16]
Magpie 2006	23/82	11/75		1.91 [1.00, 3.65]
Subtotal (95% CI)	**264**	**263**		**1.20 [0.53, 2.71]**
Total events: 68 (Magnesium), 67 (No magnesium)				
Heterogeneity: $Tau^2 = 0.28$; $Chi^2 = 5.07$, df = 1 (P = 0.02); $I^2 = 80\%$				
Test for overall effect: Z = 0.44 (P = 0.66)				



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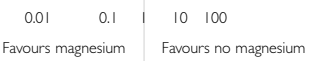
Analysis 4.1. Comparison 4 Dose subgroup, Outcome 1 Paediatric mortality (fetal and later).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
1 Loading dose only (4 g)					
Marret 2006	34/352	38/336		22.0 %	0.85 [0.55, 1.32]
Mittendorf 2002	2/30	1/29		1.3 %	1.93 [0.19, 20.18]
Subtotal (95% CI)	**382**	**365**		**23.3 %**	**0.88 [0.57, 1.35]**
Total events: 36 (Magnesium), 39 (No magnesium)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.45$, df = 1 (P = 0.50); $I^2 = 0.0\%$					
Test for overall effect: Z = 0.59 (P = 0.55)					
2 Loading (4 g) and lower-dose maintenance (1 g/hour)					
Crowther 2003	87/629	107/626		34.3 %	0.81 [0.62, 1.05]
Magpie 2006	209/798	188/795		41.5 %	1.11 [0.93, 1.31]
Subtotal (95% CI)	**1427**	**1421**		**75.8 %**	**0.96 [0.71, 1.31]**
Total events: 296 (Magnesium), 295 (No magnesium)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 3.91$, df = 1 (P = 0.05); $I^2 = 74\%$					
Test for overall effect: Z = 0.25 (P = 0.80)					
3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic intent					
Mittendorf 2002	8/55	0/51		0.9 %	15.79 [0.93, 266.72]
Subtotal (95% CI)	**55**	**51**		**0.9 %**	**15.79 [0.93, 266.72]**
Total events: 8 (Magnesium), 0 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.91 (P = 0.056)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.97 [0.74, 1.28]**
Total events: 340 (Magnesium), 334 (No magnesium)					
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 8.39$, df = 4 (P = 0.08); $I^2 = 52\%$					
Test for overall effect: Z = 0.22 (P = 0.83)					



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Loading dose only (4 g)				
Marret 2006	34/352	38/336		0.85 [0.55, 1.32]
Mittendorf 2002	2/30	1/29		1.93 [0.19, 20.18]
Subtotal (95% CI)	**382**	**365**		**0.88 [0.57, 1.35]**
Total events: 36 (Magnesium), 39 (No magnesium)				
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.45$, df = 1 (P = 0.50); $I^2 = 0.0\%$				
Test for overall effect: Z = 0.59 (P = 0.55)				

0.01 0.1 1 10 100

Favours magnesium Favours no magnesium

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Loading (4 g) and lower-dose maintenance (1 g/hour)				
Crowther 2003	87/629	107/626		0.81 [0.62, 1.05]
Magpie 2006	209/798	188/795		1.11 [0.93, 1.31]
Subtotal (95% CI)	**1427**	**1421**		**0.96 [0.71, 1.31]**
Total events: 296 (Magnesium), 295 (No magnesium)				
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 3.91$, df = 1 (P = 0.05); $I^2 = 74\%$				
Test for overall effect: Z = 0.25 (P = 0.80)				

0.01 0.1 1 10 100

Favours magnesium Favours no magnesium

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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic intent				
Mittendorf 2002	8/55	0/51		15.79 [0.93, 266.72]
Subtotal (95% CI)	**55**	**51**		**15.79 [0.93, 266.72]**
Total events: 8 (Magnesium), 0 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.91 (P = 0.056)				

Analysis 4.2. Comparison 4 Dose subgroup, Outcome 2 Cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Loading dose only (4 g)					
Marret 2006	22/352	30/336		37.5 %	0.70 [0.41, 1.19]
Mittendorf 2002	3/30	0/29		0.6 %	6.77 [0.37, 125.65]
Subtotal (95% CI)	**382**	**365**		**38.1 %**	**0.80 [0.48, 1.33]**
Total events: 25 (Magnesium), 30 (No magnesium)					
Heterogeneity: Chi^2 = 2.30, df = 1 (P = 0.13); I^2 =56%					
Test for overall effect: Z = 0.87 (P = 0.39)					
2 Loading (4 g) and lower-dose maintenance (1 g/hour)					
Crowther 2003	36/629	42/626		51.4 %	0.85 [0.55, 1.31]
Magpie 2006	2/798	5/795		6.1 %	0.40 [0.08, 2.05]
Subtotal (95% CI)	**1427**	**1421**		**57.5 %**	**0.80 [0.53, 1.22]**
Total events: 38 (Magnesium), 47 (No magnesium)					
Heterogeneity: Chi^2 = 0.78, df = 1 (P = 0.38); I^2 =0.0%					
Test for overall effect: Z = 1.03 (P = 0.31)					
3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic					
Mittendorf 2002	0/55	3/51		4.4 %	0.13 [0.01, 2.51]

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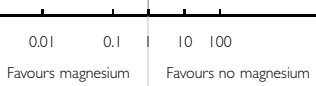
(. . . *Continued*)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Subtotal (95% CI)	**55**	**51**		**4.4 %**	**0.13 [0.01, 2.51]**
Total events: 0 (Magnesium), 3 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.35 (P = 0.18)					
Total (95% CI)	**1864**	**1837**		**100.0 %**	**0.77 [0.56, 1.06]**
Total events: 63 (Magnesium), 80 (No magnesium)					
Heterogeneity: Chi² = 4.47, df = 4 (P = 0.35); I² =10%					
Test for overall effect: Z = 1.59 (P = 0.11)					



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Loading dose only (4 g)				
Marret 2006	22/352	30/336		0.70 [0.41, 1.19]
Mittendorf 2002	3/30	0/29		6.77 [0.37, 125.65]
Subtotal (95% CI)	**382**	**365**		**0.80 [0.48, 1.33]**
Total events: 25 (Magnesium), 30 (No magnesium)				
Heterogeneity: Chi² = 2.30, df = 1 (P = 0.13); I² =56%				
Test for overall effect: Z = 0.87 (P = 0.39)				

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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 2 Cerebral palsy

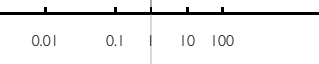
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
2 Loading (4 g) and lower-dose maintenance (1 g/hour)				
Crowther 2003	36/629	42/626		0.85 [0.55, 1.31]
Magpie 2006	2/798	5/795		0.40 [0.08, 2.05]
Subtotal (95% CI)	**1427**	**1421**		**0.80 [0.53, 1.22]**
Total events: 38 (Magnesium), 47 (No magnesium)				
Heterogeneity: Chi^2 = 0.78, df = 1 (P = 0.38); I^2 =0.0%				
Test for overall effect: Z = 1.03 (P = 0.31)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
3 Loading (4 g) and higher-dose maintenance (2-3 g/hour): tocolytic				
Mittendorf 2002	0/55	3/51		0.13 [0.01, 2.51]
Subtotal (95% CI)	**55**	**51**		**0.13 [0.01, 2.51]**
Total events: 0 (Magnesium), 3 (No magnesium)				
Heterogeneity: not applicable				
Test for overall effect: Z = 1.35 (P = 0.18)				



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Analysis 4.3. Comparison 4 Dose subgroup, Outcome 3 Neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 3 Neurologic impairment

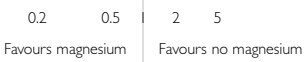
Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Loading (4 g) and lower-maintenance dose (1 g/hour)					
Crowther 2003	193/629	187/626		93.5 %	1.03 [0.87, 1.21]
Magpie 2006	10/798	13/795		6.5 %	0.77 [0.34, 1.74]
Total (95% CI)	**1427**	**1421**		**100.0 %**	**1.01 [0.86, 1.19]**
Total events: 203 (Magnesium), 200 (No magnesium)					
Heterogeneity: Chi^2 = 0.48, df = 1 (P = 0.49); I^2 =0.0%					
Test for overall effect: Z = 0.12 (P = 0.90)					

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 3 Neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Loading (4 g) and lower-maintenance dose (1 g/hour)				
Crowther 2003	193/629	187/626		1.03 [0.87, 1.21]
Magpie 2006	10/798	13/795		0.77 [0.34, 1.74]



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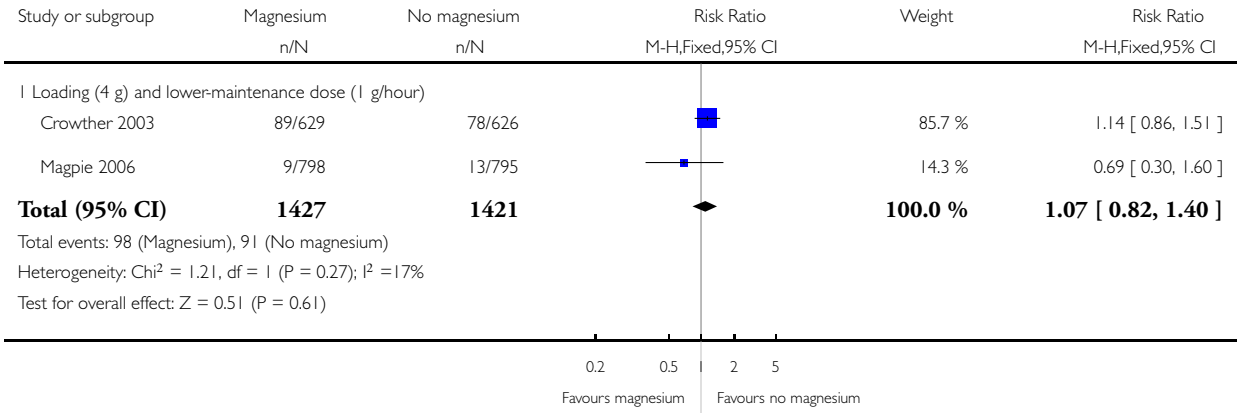
Analysis 4.4. Comparison 4 Dose subgroup, Outcome 4 Major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

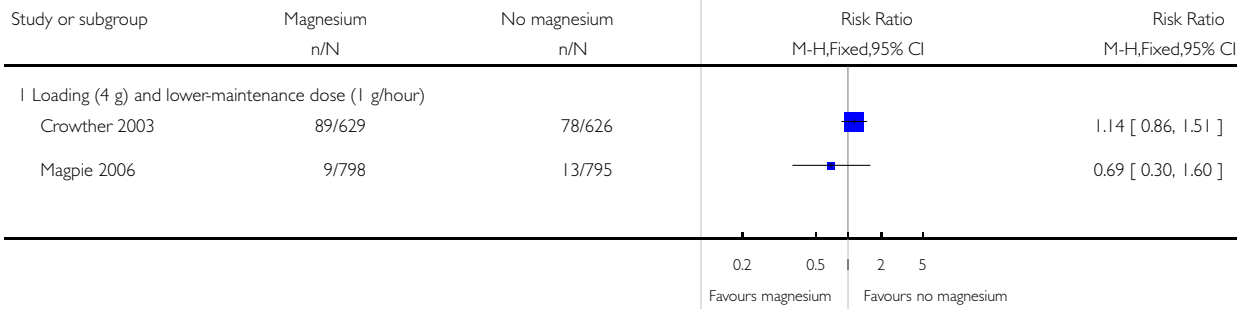
Outcome: 4 Major neurologic disability



Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 4 Major neurologic disability



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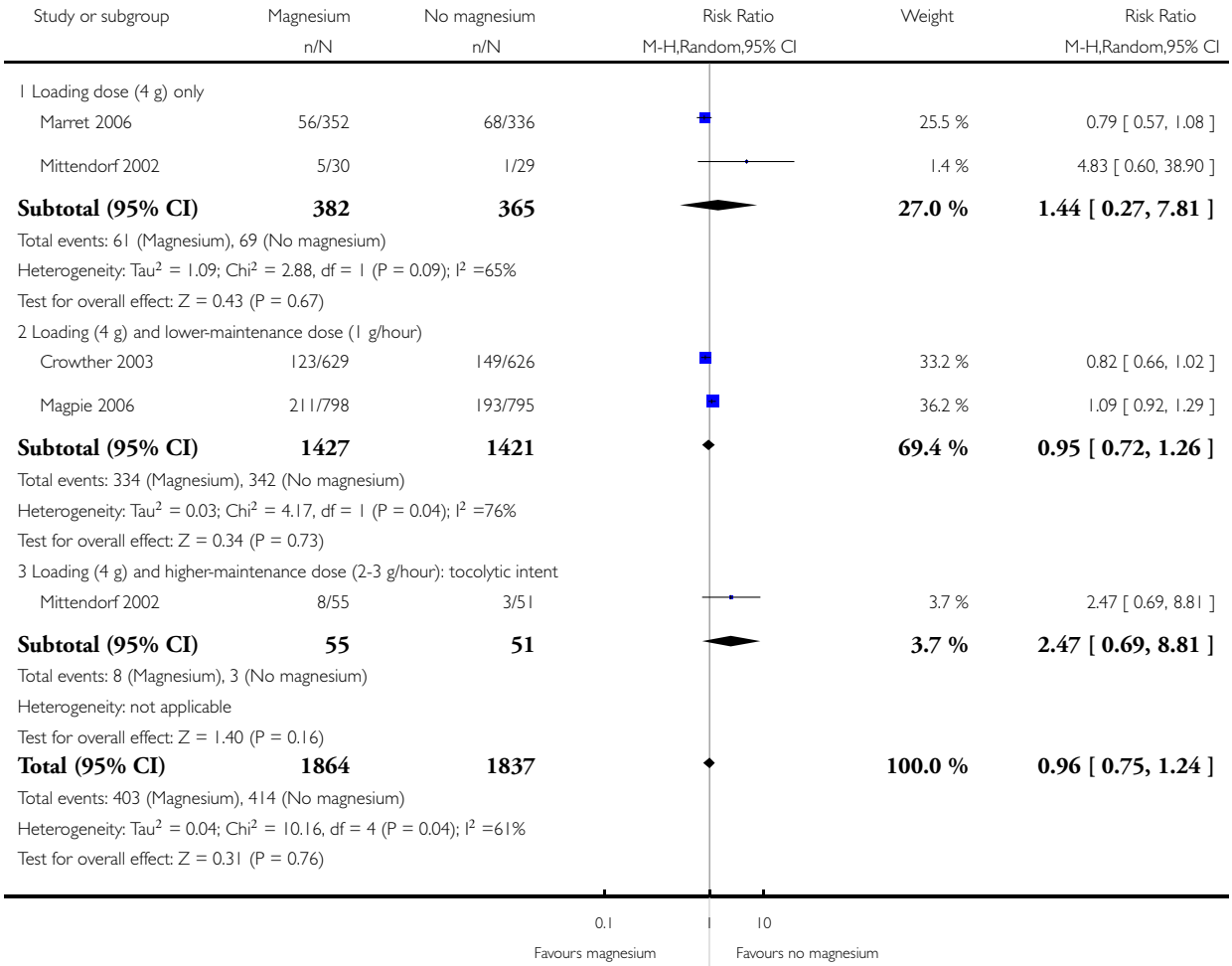
Analysis 4.5. Comparison 4 Dose subgroup, Outcome 5 Death or cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 5 Death or cerebral palsy



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Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
1 Loading dose (4 g) only				
Marret 2006	56/352	68/336		0.79 [0.57, 1.08]
Mittendorf 2002	5/30	1/29		4.83 [0.60, 38.90]
Subtotal (95% CI)	**382**	**365**		**1.44 [0.27, 7.81]**
Total events: 61 (Magnesium), 69 (No magnesium)				
Heterogeneity: Tau^2 = 1.09; Chi^2 = 2.88, df = 1 (P = 0.09); I^2 =65%				
Test for overall effect: Z = 0.43 (P = 0.67)				

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Risk Ratio M-H,Random,95% CI
2 Loading (4 g) and lower-maintenance dose (1 g/hour)				
Crowther 2003	123/629	149/626		0.82 [0.66, 1.02]
Magpie 2006	211/798	193/795		1.09 [0.92, 1.29]
Subtotal (95% CI)	**1427**	**1421**		**0.95 [0.72, 1.26]**
Total events: 334 (Magnesium), 342 (No magnesium)				
Heterogeneity: Tau^2 = 0.03; Chi^2 = 4.17, df = 1 (P = 0.04); I^2 =76%				
Test for overall effect: Z = 0.34 (P = 0.73)				

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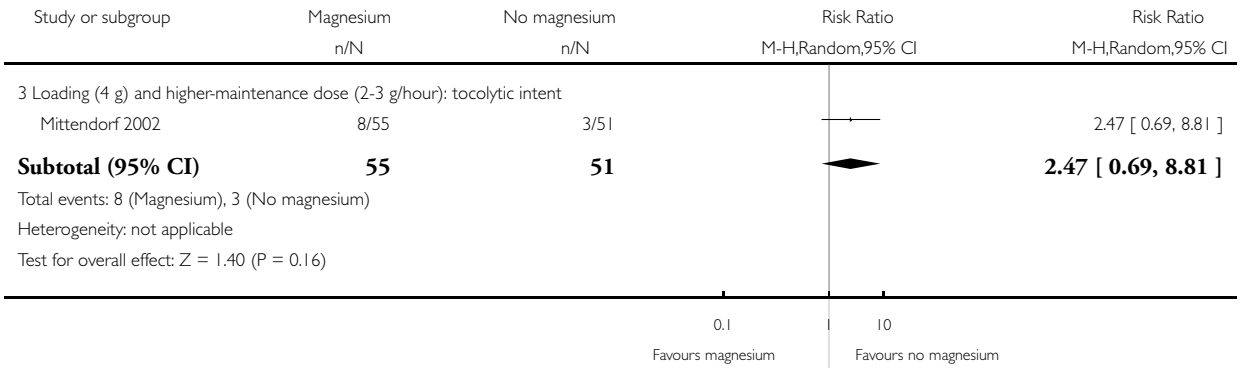
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 5 Death or cerebral palsy

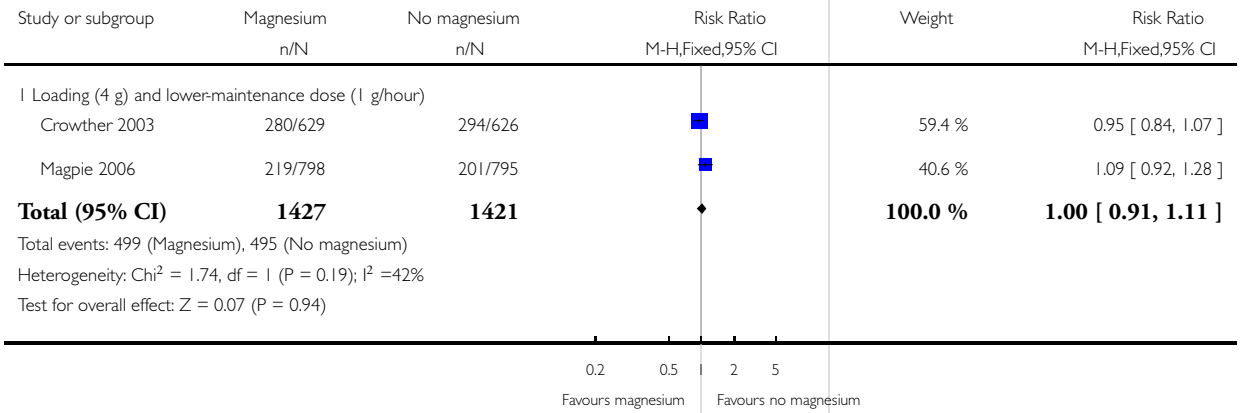


Analysis 4.6. Comparison 4 Dose subgroup, Outcome 6 Death or neurological impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 6 Death or neurological impairment



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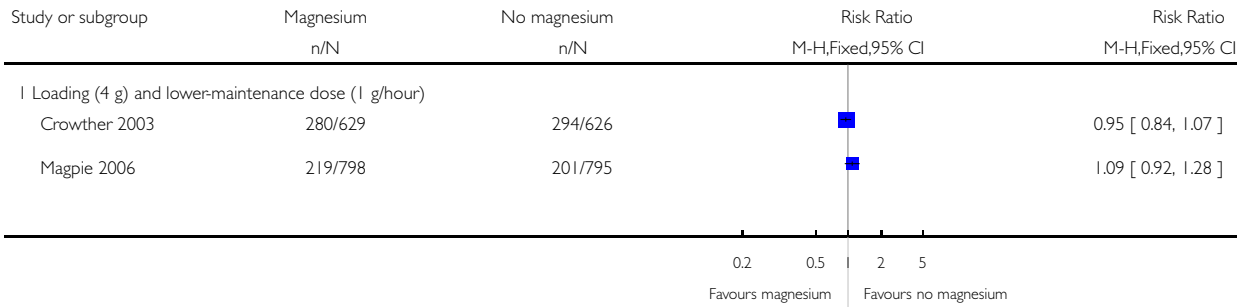
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 6 Death or neurological impairment

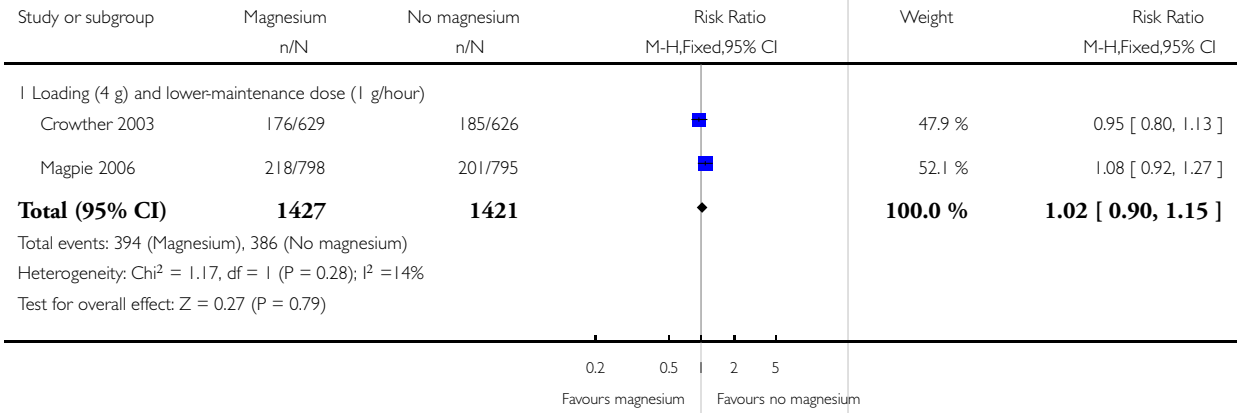


Analysis 4.7. Comparison 4 Dose subgroup, Outcome 7 Death or major neurological disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 7 Death or major neurological disability



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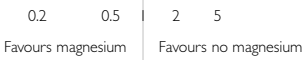
Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 4 Dose subgroup

Outcome: 7 Death or major neurological disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
1 Loading (4 g) and lower-maintenance dose (1 g/hour)				
Crowther 2003	176/629	185/626		0.95 [0.80, 1.13]
Magpie 2006	218/798	201/795		1.08 [0.92, 1.27]



Analysis 5.1. Comparison 5 High antenatal corticosteroids, Outcome 1 Paediatric mortality (fetal and later).

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

Outcome: 1 Paediatric mortality (fetal and later)

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Marret 2006	34/352	38/336		41.7 %	0.85 [0.55, 1.32]
Crowther 2003	87/629	107/626		55.8 %	0.81 [0.62, 1.05]
Mittendorf 2002	8/55	0/51		2.5 %	15.79 [0.93, 266.72]
Total (95% CI)	**1036**	**1013**		**100.0 %**	**0.89 [0.57, 1.40]**
Total events: 129 (Magnesium), 145 (No magnesium)					
Heterogeneity: Tau^2 = 0.08; Chi^2 = 4.37, df = 2 (P = 0.11); I^2 =54%					
Test for overall effect: Z = 0.50 (P = 0.62)					

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Analysis 5.2. Comparison 5 High antenatal corticosteroids, Outcome 2 Cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

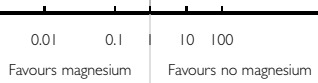
Outcome: 2 Cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	36/629	42/626		55.1 %	0.85 [0.55, 1.31]
Marret 2006	22/352	30/336		40.2 %	0.70 [0.41, 1.19]
Mittendorf 2002	0/55	3/51		4.7 %	0.13 [0.01, 2.51]
Total (95% CI)	**1036**	**1013**		**100.0 %**	**0.76 [0.54, 1.05]**

Total events: 58 (Magnesium), 75 (No magnesium)

Heterogeneity: Chi^2 = 1.73, df = 2 (P = 0.42); I^2 =0.0%

Test for overall effect: Z = 1.65 (P = 0.099)



Analysis 5.3. Comparison 5 High antenatal corticosteroids, Outcome 3 Neurologic impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

Outcome: 3 Neurologic impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	193/629	187/626		100.0 %	1.03 [0.87, 1.21]
Total (95% CI)	**629**	**626**		**100.0 %**	**1.03 [0.87, 1.21]**

Total events: 193 (Magnesium), 187 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.31 (P = 0.75)

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Analysis 5.4. Comparison 5 High antenatal corticosteroids, Outcome 4 Major neurologic disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

Outcome: 4 Major neurologic disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	89/629	78/626		100.0 %	1.14 [0.86, 1.51]
Total (95% CI)	**629**	**626**		**100.0 %**	**1.14 [0.86, 1.51]**

Total events: 89 (Magnesium), 78 (No magnesium)

Heterogeneity: not applicable

Test for overall effect: Z = 0.88 (P = 0.38)

Analysis 5.5. Comparison 5 High antenatal corticosteroids, Outcome 5 Death or cerebral palsy.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

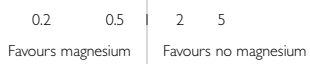
Outcome: 5 Death or cerebral palsy

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	123/629	149/626		67.3 %	0.82 [0.66, 1.02]
Marret 2006	56/352	68/336		31.3 %	0.79 [0.57, 1.08]
Mittendorf 2002	8/55	3/51		1.4 %	2.47 [0.69, 8.81]
Total (95% CI)	**1036**	**1013**		**100.0 %**	**0.83 [0.70, 0.99]**

Total events: 187 (Magnesium), 220 (No magnesium)

Heterogeneity: Chi^2 = 2.96, df = 2 (P = 0.23); I^2 =32%

Test for overall effect: Z = 2.05 (P = 0.041)



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Analysis 5.6. Comparison 5 High antenatal corticosteroids, Outcome 6 Death or neurological impairment.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

Outcome: 6 Death or neurological impairment

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	280/629	294/626		100.0 %	0.95 [0.84, 1.07]
Total (95% CI)	**629**	**626**		**100.0 %**	**0.95 [0.84, 1.07]**
Total events: 280 (Magnesium), 294 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.87 (P = 0.38)					

Analysis 5.7. Comparison 5 High antenatal corticosteroids, Outcome 7 Death or major neurological disability.

Review: Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus

Comparison: 5 High antenatal corticosteroids

Outcome: 7 Death or major neurological disability

Study or subgroup	Magnesium n/N	No magnesium n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Crowther 2003	176/629	185/626		100.0 %	0.95 [0.80, 1.13]
Total (95% CI)	**629**	**626**		**100.0 %**	**0.95 [0.80, 1.13]**
Total events: 176 (Magnesium), 185 (No magnesium)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.61 (P = 0.54)					

WHAT'S NEW

Last assessed as up-to-date: 28 April 2007

Date	Event	Description
24 April 2008	Amended	Converted to new review format.

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HISTORY

Protocol first published: Issue 1, 2004

Review first published: Issue 3, 2007

CONTRIBUTIONS OF AUTHORS

Lex Doyle and Caroline Crowther wrote the protocol. Lex Doyle searched the literature, reviewed all possible trials for inclusion, extracted details of the studies' methods and results, entered the data into Review Manager, wrote the initial synthesis of the results, and contributed to all versions of the review. Caroline Crowther extracted details of the results and contributed to all versions of the review. Philippa Middleton searched the literature, extracted details of the studies' results, and contributed to all versions of the review. Stephane Marret searched the literature, extracted details of the studies' results, and contributed to the final version of the review.

DECLARATIONS OF INTEREST

Two review authors (Lex Doyle and Caroline Crowther) are principal investigators in the Australasian Collaborative Trial of Magnesium Sulphate given as a neuroprotective prior to very preterm birth for the prevention of mortality and cerebral palsy in their babies (ACTOMgSO_4 - Crowther 1998). This trial is funded by the Australian National Health and Medical Research Council. One review author (Stephane Marret) is the principal investigator in the PREMAG study from France (Marret 2006). The results of these trials were assessed for inclusion and quality using the same criteria as all other potential studies.

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Internal sources

- Discipline of Obstetrics and Gynaecology, The University of Adelaide, Australia.
- Department of Obstetrics and Gynaecology, University of Melbourne, Australia.

External sources

- National Health and Medical Research Council, Commonwealth Department of Health and Ageing, Australia.

INDEX TERMS

Medical Subject Headings (MeSH)

Central Nervous System Diseases [*prevention & control]; Cerebral Palsy [mortality; prevention & control]; Fetal Death [*prevention & control]; Infant, Newborn; Infant, Newborn, Diseases [mortality; prevention & control]; Magnesium Sulfate [*therapeutic use]; Neuroprotective Agents [*therapeutic use]; *Premature Birth; Prenatal Care; Randomized Controlled Trials as Topic

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MeSH check words

Female; Humans; Pregnancy

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