Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review)

Crowther CA, Harding JE



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2007, Issue 4

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This record should be cited as:

Crowther CA, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease. *Cochrane Database of Systematic Reviews* 2007, Issue 3. Art. No.: CD003935. DOI: 10.1002/14651858.CD003935.pub2.

This version first published online: 18 July 2007 in Issue 3, 2007. Date of most recent substantive amendment: 11 May 2007

ABSTRACT

Background

It is not clear whether there is benefit in repeating the dose of prenatal corticosteroids for women who remain at risk of preterm birth after an initial course.

Objectives

To assess the effectiveness and safety of a repeat dose(s) of prenatal corticosteroids.

Search strategy

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (February 2007), the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2006, Issue 4), MEDLINE (1965 to November 2006), EMBASE (1988 to November 2006) and Current Contents (1997 to November 2006).

Selection criteria

Randomised controlled trials of women who have already received a single course of corticosteroids seven or more days previously and are still considered to be at risk of preterm birth; outcomes compared for women randomised to receive a repeat dose(s) of prenatal corticosteroids, with women given no further prenatal corticosteroids.

Data collection and analysis

We assessed trial quality and extracted the data independently.

Main results

Five trials, involving over 2000 women between 23 and 33 weeks' gestation, are included. Treatment with repeat dose(s) of corticosteroid was associated with a reduction in occurrence (relative risk (RR) 0.82, 95% confidence interval (CI) 0.72 to 0.93, four trials, 2155 infants) and severity of any neonatal lung disease (RR 0.60, 95% CI 0.48 to 0.75, three trials, 2139 infants) and serious infant morbidity (RR 0.79, 95% CI 0.67 to 0.93, four trials, 2157 infants).

Mean birthweight was not significantly different between treatment groups (weighted mean difference (WMD) -62.07 g, 95% CI -129.10 to 4.96, four trials, 2273 infants), although in one trial, treatment with repeat dose(s) of corticosteroid was associated with a reduction in birthweight Z score (WMD) -0.13, 95% CI -26 to 0.00, 1 trial, 1144 infants), and in two trials, with an increased risk of being small for gestational age at birth (RR 1.63, 95% CI 1.12 to 2.37, two trials, 602 infants).

No statistically significant differences were seen for any of the other primary outcomes that included other measures of respiratory morbidity, fetal and neonatal mortality, periventricular haemorrhage, periventricular leukomalacia and maternal infectious morbidity. Treatment with repeat dose(s) of corticosteroid was associated with a significantly increased risk of caesarean section (RR 1.11, 95% CI 1.01 to 1.22, four trials, 1523 women).

Authors' conclusions

Repeat dose(s) of prenatal corticosteroids reduce the occurrence and severity of neonatal lung disease and the risk of serious health problems in the first few weeks of life. These short-term benefits for babies support the use of repeat dose(s) of prenatal corticosteroids for women at risk of preterm birth. However, these benefits are associated with a reduction in some measures of weight, and head circumference at birth, and there is still insufficient evidence on the longer-term benefits and risks.

PLAIN LANGUAGE SUMMARY

Repeat dose(s) of prenatal corticosteroids given to women who remain at risk of an early birth helps the baby's lungs and reduces serious health problems in the first few weeks of life

Babies born very early are at risk of breathing difficulties (respiratory distress syndrome). A single course of corticosteroids, given to women who may give birth early, helps develop the baby's lungs. However, this benefit does not last beyond seven days. This review of five trials, involving over 2000 women between 23 and 33 weeks' gestation, shows repeat dose(s) of prenatal corticosteroids, given to women who remain at risk of early birth more than seven days after an initial course of corticosteroids, reduces the risk of the baby having breathing difficulties and the baby is less likely to have serious health problems in the first few weeks of life. However, some trials show the baby may be smaller at birth. Further research is needed on other important health outcomes for the woman and baby, which should include child development.

BACKGROUND

Infants born preterm (before 37 weeks' gestation) are at high risk of neonatal lung disease and its sequelae. The more preterm the baby the greater are the risks, especially when birth occurs before 32 weeks. In Australia, in 2003, 1.6% of all births were before 32 weeks' gestation (Laws 2005). Respiratory distress syndrome (RDS), as a consequence of immature lung development, is the principal cause of early neonatal mortality and morbidity and contributes significantly to the high costs of neonatal intensive care. Preterm babies who survive the early weeks of life are at risk of long-term neurological disability (Johnson 1993). Parents are understandably worried and distressed when their baby is born preterm. Strategies to reduce the risk of neonatal respiratory disease for infants who are born preterm have received considerable attention (Roberts 2006; Soll 2001).

A single course of prenatal corticosteroids reduces the risk of RDS from 26% to 17% (relative risk (RR) 0.66, 95% confidence interval (CI) 0.59 to 0.73, 21 trials, 4038 infants) (Roberts 2006). Other beneficial effects include a reduction in neonatal mortality and a reduced risk of intraventricular haemorrhage (Roberts 2006). Prenatal corticosteroids enhance the benefits of postnatal surfactant therapy (Jobe 1994) and reduce the need for blood pressure support (Moise 1995). Overall, there is a reduction in the cost and duration of neonatal care. Long-term follow up into adulthood of babies in the New Zealand trial (Liggins 1972) exposed to prenatal corticosteroids have shown no adverse clinical outcomes (Dalziel 2005a; Dalziel 2005b). The cost benefit of a single course of antenatal steroids is estimated as USD 3000 (NIH 1995). However, even though prenatal corticosteroids remain the most

effective known strategy for reducing the adverse consequences of preterm birth and despite postnatal intensive care and exogenous surfactant, there is still significant neonatal morbidity (Soll 2001).

Prenatal corticosteroids have not been shown to be effective in babies who are born more than seven days after treatment (Roberts 2006). Specifically no reduction in the incidence of respiratory distress syndrome or neonatal mortality has been demonstrated (McLaughlin 2003; Roberts 2006) and birthweight is significantly reduced (Roberts 2006). There may be benefit in repeating the dose of prenatal corticosteroids to women who remain at risk of preterm birth more than seven days after the initial course. This was suggested by Professor Mont Liggins and Associate Professor Howie in the first reported controlled trial of antenatal glucocorticoid treatment for the prevention of respiratory distress syndrome in premature infants (Liggins 1972). Indeed, in some clinical centres this has been standard practice. However, there has been little formal assessment of such a policy, and the effect of this practice on the women and infants is unclear (NIH 2000).

Animal studies have suggested that repeat treatment with prenatal corticosteroids may be more effective than a single course in reducing the risk of respiratory distress syndrome. In sheep fetuses, there is a dose-dependent improvement in lung function with repeat doses of betamethasone (Ikegami 1997). In human infants, improved cardiovascular responses to preterm birth have been observed (Padbury 1996).

However, these potential benefits of repeat prenatal corticosteroid treatment may be balanced by increased maternal risks such as infection and suppression of hypothalamic-pituitary-adrenal function (Ashworth 2006; McKenna 2000). In addition, experimental

reports raise concerns about the use of repeat doses of prenatal corticosteroids because of potential adverse effects for the offspring.

It is well known that corticosteroids inhibit cell growth and DNA replication. Studies in both small and large animals demonstrate that exogenous steroids inhibit fetal growth and increase fetal blood pressure (Fowden 1996; Jensen 2002). In sheep there is a dose-dependent reduction in birthweight in lambs exposed to up to four doses of betamethasone administered to the ewe (Ikegami 1997), although exogenous steroids administered directly to the fetus do not inhibit fetal growth (Newnham 1999).

Other animal experimental studies have shown that repeat doses of steroids may have harmful effects on neuronal myelination (Dunlop 1997), the development of the alveolar septa leaving 'emphysematous' like alveoli (Tschanz 1995) and hypothalamic-pituitary-adrenal function (Ikegami 1997).

In humans, similar concerns have been raised from non-randomised cohort studies, with adverse effects after repeat doses of steroids on measures of growth at birth (French 1999), risk of neonatal infection, fetal pituitary-adrenal axis function, neonatal blood pressure (Mildenhall 2006), childhood behaviour (French 1998), and high levels of stress in parents (French 1998). Longterm developmental follow-up studies of infants exposed to repeat doses of prenatal steroids are limited to date, have used only nonrandomised designs, and have produced conflicting results. Some studies suggest delayed development (Esplin 2000) and adverse effects on childhood behaviour (French 1998), whilst others have shown no difference between exposed and non-exposed children (French 1999; Hasbargen 2001; Thorp 2002), or possible reduced cerebral palsy (French 2004). Another long-term potential adverse outcome that requires further investigation is the possibility that single or repeat doses could program cardiovascular settings in the fetus and lead to adult hypertension (Benediktsson 1993), and insulin resistance leading to diabetes mellitus (Dalziel 2005a).

This review assesses the effectiveness and safety of a repeat dose(s) of prenatal corticosteroids given to women who remain at risk of preterm birth following an initial course of prenatal corticosteroids.

OBJECTIVES

To assess the effectiveness and safety, using the best available evidence, of a repeat dose(s) of prenatal corticosteroids, given to women who remain at risk of preterm birth seven or more days after an initial course of prenatal corticosteroids with the primary aim of reducing fetal, infant and childhood morbidity and mortality.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All published, unpublished and ongoing randomised trials with reported data that compared outcomes for women at risk of preterm birth randomised to receive a repeat dose(s) of prenatal corticosteroids with outcomes in controls given a single course of prenatal corticosteroids, with or without additional placebo administration. The trials used some form of random allocation and reported 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 who have already received a single course of prenatal corticosteroid seven or more days previously. Predefined subgroups were planned to examine separately the outcomes for women and infants based on the reasons the woman was considered to be at risk for preterm birth at trial entry (eg. presence or absence of ruptured membranes, antepartum haemorrhage, preterm labour, cervical incompetence, pre-eclampsia, growth restriction), and the number of infants in utero (singleton, twin or higher order multiple pregnancy).

Types of intervention

Corticosteroid administered to the women intravenously, intramuscularly or orally, compared with either placebo or no placebo. Trials in which the fetus receives corticosteroids directly were excluded. Predefined subgroups were planned to examine separately the primary outcomes for women and infants based on the type of corticosteroid given, the planned interval between corticosteroid treatments, the number of repeat courses planned, the number of repeat courses actually given, the planned dose of corticosteroid given per repeat treatment, the planned dose of repeat corticosteroid drug exposure per week, the method 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

Primary outcomes were chosen to be most representative of the clinically important measures of effectiveness and safety, including serious outcomes, for the women and their infants.

For the infant

Respiratory distress syndrome;

severity of any lung disease (however defined by the authors);

birthweight;

small-for-gestational age;

fetal and neonatal mortality;

fetal, neonatal or infant death;

chronic lung disease (however defined by authors);

periventricular haemorrhage;

periventricular haemorrhage grade 3/4;

periventricular leukomalacia;

composite serious outcome (however defined by authors);

disability at follow up (developmental delay or intellectual impairment, blindness, deafness, or cerebral palsy);

composite serious outcome (however defined by authors).

For the child

Disability at childhood or adult follow up (developmental delay or intellectual impairment, blindness, deafness, or cerebral palsy after 18 months of age);

composite serious outcome (however defined by authors).

For the child as an adult

Disability at adult follow up (developmental delay or intellectual impairment, blindness, deafness, or cerebral palsy); composite serious outcome (however defined by authors).

For the women

Chorioamnionitis (however defined by authors); puerperal sepsis (however defined by authors).

Secondary outcomes

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

For the infant

Gestational age at birth (preterm birth less than 37 weeks, very preterm birth less than 34 weeks, extremely preterm birth less than 28 weeks);

interval between trial entry and birth;

head circumference at birth;

length at birth;

skin fold thickness at birth;

placental weight;

Apgar score less than seven at five minutes;

use of respiratory support (mechanical ventilation or continuous

positive airways pressure (CPAP), or both;

use of mechanical ventilation;

use of CPAP;

duration of respiratory support; use of oxygen supplementation; duration of oxygen supplementation;

use of surfactant; use of inotropic support; duration of inotropic support;

use of nitric oxide for respiratory support; systemic infection in first 48 hours of life;

proven infection while in the neonatal intensive care unit;

admission to neonatal intensive care unit;

air leak syndrome; necrotising enterocolitis;

patent ductus arteriosus requiring treatment;

retinopathy of prematurity; use of postnatal corticosteroids;

neonatal blood pressure (systolic, diastolic and mean arterial blood pressure);

cardiac hypertrophy;

growth assessments at primary hospital discharge (weight, head circumference, length, skin fold thickness);

growth assessments at infant follow up (weight, head circumference, length, skin fold thickness);

infant temperament;

infant behaviour;

developmental delay at infant follow up;

hypothalamo/pituitary/adrenal (HPA) axis suppression (however defined by the authors).

For the child

Growth assessments at childhood follow up (weight, head circumference, length, skin fold thickness);

major sensorineural disability (defined as any of legal blindness, sensorineural deafness requiring hearing aids, moderate or severe cerebral palsy, or developmental delay or intellectual impairment (defined as developmental quotient or intelligence quotient less than -2 standard deviations below mean));

developmental delay (however defined by the authors);

intellectual impairment; motor impairment;

visual impairment;

blindness; deafness;

hearing impairment;

cerebral palsy; child behaviour; child temperament;

learning difficulties; insulin sensitivity;

dyslipidaemia; blood pressure; HPA axis function; lung function;

For the child as an adult

Age at puberty;

bone density.

growth assessments in later life (weight, head circumference, length, skin fold thickness);

major sensorineural disability (defined as any of legal blindness, sensorineural deafness requiring hearing aids, moderate or severe cerebral palsy, or developmental delay or intellectual impairment (defined as developmental quotient or intelligence quotient less

than -2 standard deviations below mean));

developmental delay (however defined by the authors);

intellectual impairment; motor impairment; visual impairment; blindness; deafness; hearing impairment; cerebral palsy; educational achievements; learning difficulties; insulin sensitivity; dyslipidaemia; blood pressure; HPA axis function; lung function; bone density.

For the woman

Death;

pulmonary oedema;

admission to intensive care unit;

prelabour rupture of the membranes after trial entry;

hypertension (variously defined by the authors);

mode of birth;

length of labour;

pyrexia after trial entry requiring the use of antibiotics;

intrapartum fever requiring the use of antibiotics;

postpartum haemorrhage;

postnatal pyrexia (variously defined by authors);

breastfeeding after hospital discharge;

postnatal depression;

side-effects of therapy (including nausea, vomiting, hypertension, glucose intolerance, osteoporosis, adrenal insufficiency, insomnia, pain at the injection site, bruising at the injection site, haematoma at injection site);

discontinuation of therapy because of maternal side-effects; adverse drug reaction;

satisfaction with the therapy;

quality of life;

parenting stress.

Use of health services

Length of antenatal hospitalisation for the women; length of postnatal hospitalisation for the women; maternal admission to intensive care unit; admission to and length of stay in neonatal intensive care unit; length of neonatal hospitalisation; costs of maternal care; cost of neonatal care.

While we sought all the above outcomes from the included trials, only those with data appear in the analysis tables. Outcomes were included in the analysis if reasonable measures were taken to minimise observer bias and data were available for analysis according to original allocation. We reported additional outcomes that appear in individual trials as not prespecified outcomes when included in the review.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (February 2007).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

- (1) quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
- (2) monthly searches of MEDLINE;
- (3) handsearches of 30 journals and the proceedings of major conferences;
- (4) weekly current awareness search of a further 37 journals.

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

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

In addition, we searched the Cochrane Central Register of Controlled Trials (*The Cochrane Library* 2006, Issue 4), MEDLINE (1965 to November 2006), EMBASE (1988 to November 2006) and Current Contents (1997 to November 2006), using the search terms: 'repeat' or 'multiple' and 'antenatal' or 'prenatal' and 'corticosteroid*' or 'steroid*' or 'glucocorticoid*' or 'betamethason*' or 'dexamethason*' or 'hydrocortison*'. We manually searched the reference lists of all retrieved articles. We sought unpublished trials and abstracts submitted to major international congresses and contacted expert informants.

We did not apply any language restrictions.

METHODS OF THE REVIEW

Selection of studies

We evaluated trials under consideration for inclusion without consideration of their results. We resolved any differences of opinion by discussion. There was no blinding of authorship.

Data extraction and management

Two review authors extracted study data, using a predesigned data form. Philippa Middleton independently extracted data for the ACTORDS trial. We resolved discrepancies through discussion.

When information was unclear, we contacted authors of the original reports to provide further details.

Assessment of methodological quality of included studies

We assessed the validity of each study using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2005). We described methods used for generation of the randomisation sequence for each trial.

(1) Selection bias (randomisation and allocation concealment) We assigned codes, using the following criteria:

- (A) adequate concealment of allocation: such as telephone randomisation, consecutively-numbered, sealed opaque envelopes;
- (B) unclear whether adequate concealment of allocation: such as list or table used, sealed envelopes, or study does not report any concealment approach;
- (C) inadequate concealment of allocation: such as open list of random-number tables, use of case record numbers, dates of birth or days of the week.

(2) Attrition bias (loss of participants, eg withdrawals, dropouts, protocol deviations)

We assessed completeness to follow up using the following criteria:

- (A) less than 5% loss of participants;
- (B) 5% to 9.9% loss of participants;
- (C) 10% to 19.9% loss of participants;
- (D) more than 20% loss of participants.

(3) Performance bias (blinding of participants, researchers and outcome assessment)

We assessed blinding using the following criteria:

- (1) blinding of participants (yes/no/unclear);
- (2) blinding of caregiver (yes/no/unclear);
- (3) blinding of outcome assessment (yes/no/unclear).

Measures of treatment effect

We performed statistical analyses using the Review Manager software (RevMan 2003). We used fixed-effect meta-analysis for combining data in the absence of significant heterogeneity as the trials were sufficiently similar. In the presence of substantial heterogeneity ($I^2 > 40\%$) we used a random-effects model.

Dichotomous data

For dichotomous data, we presented results as relative risks with 95% confidence intervals.

Continuous data

For continuous data, we used the weighted mean difference with 95% confidence intervals.

Dealing with missing data

We extracted data from the trials on an intention-to-treat basis. Where this was not done in the original report, re-analysis was performed where possible. If missing data were such that they 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.

Assessment of heterogeneity

We applied tests of heterogeneity between trials, using the I² statistic. When we identified high levels of heterogeneity among the trials, we explored it by prespecified subgroup analysis and performed sensitivity analysis.

Sensitivity analyses

We planned sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, by excluding studies with clearly inadequate allocation of concealment (rated C).

Subgroup analyses

We planned subgroup analyses to examine separately the outcomes for women exposed to repeat dose(s) of prenatal corticosteroids compared with women receiving no repeat prenatal corticosteroids/placebo based on the reasons the woman was considered to be at risk of preterm birth at trial entry, the number of babies in utero (singleton, twins or higher order multiples), the type of corticosteroid given, the planned interval between corticosteroid treatments, the planned number of repeat courses of corticosteroids actually given postrandomisation, the planned dosage of corticosteroid given per treatment, the planned dose of repeat dose of corticosteroid drug exposure/week, the method of treatment administration, and the gestational age at which the treatment was given.

DESCRIPTION OF STUDIES

Seven trials were identified for consideration for inclusion (Aghajafari 2002; Crowther 2006; Guinn 2002; McEvoy 2002; Mercer 2001; Thorp 2000; Wapner 2006), six trials of repeat dose(s) of prenatal corticosteroids given to women who remain at risk of preterm birth seven or more days after an initial course of prenatal corticosteroids, of which five trials met our inclusion criteria (Aghajafari 2002; Crowther 2006; Guinn 2002; McEvoy 2002; Wapner 2006). Two trials were excluded (Mercer 2001; Thorp 2000). One trial was excluded because women recruited to the trial did not have corticosteroids before entry (Mercer 2001). The objective of the trial was to evaluate the need for and benefits of weekly antenatal corticosteroids in women at risk of preterm birth (Mercer 2001). In the other trial, the randomised treatment was not repeat dose(s) of prenatal corticosteroids (Thorp 2000).

A total of 2028 women were recruited into the five trials that met the prespecified criteria for inclusion in this review (12 women in Aghajafari 2002, 502 women in Guinn 2002, 37 women in McEvoy 2002, 982 in Crowther 2006 and 495 in Wapner 2006). Three of the trials were conducted in the United States of America (Guinn 2002; McEvoy 2002; Wapner 2006) and one each in Canada (Aghajafari 2002) and Australia (Crowther 2006).

The gestational age at trial entry varied between the trials being 24 to 30 weeks (Aghajafari 2002), 25 to less than 33 weeks (Guinn 2002), 25 to 33 weeks (McEvoy 2002), less than 32 weeks (Crowther 2006) and 23 to less than 32 weeks (Wapner 2006). All women were at increased risk of preterm birth (*see* 'Characteristics of included studies' table) and had received a single course of antenatal corticosteroids one week or more before trial entry, defined as two doses of 12 mg/dose intramuscular betamethasone, given at 12 or 24 hourly intervals; or four doses of 5 to 6 mg/dose intramuscular dexamethasone, given at 12 hourly intervals (Aghajafari 2002; Guinn 2002), two doses of 12 mg/dose intramuscular betamethasone (McEvoy 2002) or not defined in Crowther 2006 and Wapner 2006.

The type of corticosteroid given as treatment was betamethasone for all the trials although the gestational age at which treatment could begin or was continued varied slightly between the trials. Four trials gave two doses of 12 mg/dose betamethasone, intramuscularly, at weekly intervals (Aghajafari 2002; Guinn 2002; McEvoy 2002; Wapner 2006). For Aghajafari a weekly course of betamethasone was given (two doses of 12 mg/dose betamethasone (Celestone Soluspan; Schering Canada Inc.) intramuscularly, 24 hours apart) until 33 weeks or birth if the woman remained at increased risk of preterm birth (Aghajafari 2002). Guinn used a weekly course of betamethasone (two doses of 12 mg/dose betamethasone, intramuscularly 24 hours apart) until 34 weeks or birth, whichever came first (Guinn 2002). McEvoy used a weekly course of betamethasone (two doses of 12 mg/dose betamethasone (Celestone Soluspan; Schering Corporation, Kenilworth, New Jersey), intramuscularly, until 34 weeks or birth (McEvoy 2002). Wapner used a weekly course of betamethasone (two doses of 12 mg betamethasone as 6 mg betamethasone sodium phosphate and 6 mg betamethasone acetate, intramuscularly in 24 hours) until birth or 33 weeks and 6 days (Wapner 2006). Crowther used a single intramuscular injection of 11.4 mg Celestone Chronodose (Schering-Plough, Sydney, Australia) containing 7.8 mg betamethasone sodium phosphate and 6 mg betamethasone acetate repeated weekly if the woman remained undelivered and less than 32 weeks' gestation and the responsible clinician regarded her as at continued risk of preterm birth (Crowther 2006).

The primary outcomes for Aghajafari 2002 were the rate of recruitment over a 12 month period, risk of complications requiring discontinuation of study treatment, concentrations of plasma cortisol and adrenocorticotropic hormone in cord blood and in maternal blood immediately following birth, perinatal or neonatal mortality or significant neonatal morbidity. The Guinn 2002 trial had a composite neonatal morbidity primary outcome of any of the following: severe respiratory distress syndrome, bronchopulmonary dysplasia, severe intraventricular haemorrhage, periventricular leukomalacia, necrotising enterocolitis, proven sepsis or death between randomisation and nursery discharge. The primary outcomes for McEvoy 2002 were functional residual capacity and respiratory compliance. For Crowther 2006, the primary out-

comes were occurrence of neonatal respiratory distress syndrome, severity of any respiratory disease present, use and duration of oxygen therapy, use and duration of mechanical ventilation, and weight, length and head circumference at birth and at discharge from hospital. For Wapner 2006 the primary outcome was one of the following: severe respiratory distress syndrome (RDS) (defined as clinical features of RDS with the need for oxygen and respiratory support from 6 to 24 hours or more of age, an abnormal chest x-ray, and either administration of a full course of surfactant or a fraction of inspired oxygen (FiO₂ of at least 60%); grade 3 or 4 intraventricular hemorrhage; periventricular leukomalacia; chronic lung disease (defined as the need for supplemental oxygen at 36 weeks' corrected age in infants born before 34 weeks' gestation); or stillbirth or neonatal death. All the trials had a range of secondary outcomes of clinical relevance.

For details of the included and excluded studies, please refer to the 'Characteristics of included studies' and the 'Characteristics of excluded studies' tables.

METHODOLOGICAL QUALITY

Formal randomisation was reported in all five trials. For Aghajafari 2002, randomisation was computer-generated and was centrally controlled by one pharmacist at each hospital who kept the randomisation code with stratification by gestational age (24 to 27 weeks; 28 to 30 weeks) and by hospital using block sizes of two. Guinn 2002 used computer-generated randomisation logs prepared centrally, stratified by centre, and distributed to the research pharmacist at each clinical site. Participants were assigned by the pharmacy to treatment group. In the McEvoy 2002 trial group, assignment was via the pharmacy using a random-number table. The study medication was prepared by the pharmacy. No stratification was reported. Crowther 2006 used a central telephone randomisation service for study number and then treatment pack allocation. The randomisation numbers were generated by a computer with variable block sizes, stratified by centre, gestational age (two groups: less than 28 weeks and 28 weeks or more) and number of fetuses (three groups; singleton, twin and triplet). For Wapner 2006, randomisation sequences for the treatment kits were generated by the independent data co-ordinating centre with stratification by centre, type of qualifying corticosteroid course and whether an in-patient or out-patient using the urn design. The woman was assigned the next sequentially numbered treatment kit by a centralised research pharmacy.

A placebo was used in all five trials but the preparation used was not stated for Guinn 2002 or Wapner 2006. Aghajafari used normal saline (Aghajafari 2002), McEvoy used 25 mg cortisone acetate, an inactive steroid (McEvoy 2002) and Crowther used normal saline (Crowther 2006).

All five trials attempted to blind participants and caregivers to treatment allocation. In Aghajafari 2002, the pharmacist pre-

pared the study treatments in a syringe covered with yellow tape and the injection of the study treatment was given by a designated research nurse in each hospital, who was not caring for the woman. For Guinn 2002, the placebo syringes were indistinguishable from the syringes containing betamethasone. For McEvoy 2002, the placebo was identical in appearance to betamethasone. For Crowther 2006, the treatment packs looked identical and contained an opaque study-labelled syringe. For Wapner 2006, the placebo was identical in appearance to betamethasone.

No losses to follow up were reported for Aghajafari 2002 or McEvoy 2002. In the Guinn 2002 trial, 16 women and one neonate were lost to follow up. Partial data are available for women who were lost to follow up for the birth date, weight, and health status for the neonate. The denominators presented in the trial report vary slightly from one variable to another because of missing data (Guinn 2002). For Crowther 2006, there were no losses to follow-up up to the time of primary hospital discharge. For Wapner 2006, three women were lost to follow up.

Intention-to-treat analyses were conducted for all five trials.

RESULTS

Five trials involving 2028 women were included.

(1) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment (all included trials)

Primary outcomes for the infant

Data were available for all the primary outcomes for the infant.

- Significantly fewer infants exposed to repeat dose(s) of corticosteroids had respiratory distress syndrome compared with infants exposed to placebo (relative risk (RR) 0.82, 95% confidence interval (CI) 0.72 to 0.93, four trials, 2155 infants).
- Treatment with repeat dose(s) of corticosteroid was associated with a reduction in severe lung disease (RR 0.60, 95% CI 0.48 to 0.75, three trials, 2139 infants).
- Four trials reported a composite outcome for serious infant morbidity. Infants exposed to repeat dose(s) of corticosteroids were significantly less likely to have serious infant morbidity (RR 0.79, 95% CI 0.67 to 0.93, four trials, 2157 infants). The composite outcome of serious infant morbidity was defined by Aghajafari 2002 as one or more of the following: stillborn or neonatal death during the first 28 days of life or before hospital discharge, whichever was sooner; respiratory distress syndrome; bronchopulmonary dysplasia (requiring oxygen at 36 corrected postnatal gestational age); grade 3 or 4 intraventricular haemorrhage and necrotising enterocolitis; Crowther 2006 as one of air leak syndrome, patent ductus arteriosus, need for oxygen at 36 weeks' postmenstrual age, severe intraventricular haemorrhage (grade 3 or 4), periventricular leukomalacia, proven necrotising enterocolitis or retinopathy of prematurity; Guinn 2002 as

the presence of any of the following: severe respiratory distress syndrome, bronchopulmonary dysplasia, severe intraventricular haemorrhage, periventricular leukomalacia, necrotising enterocolitis, proven sepsis or death between randomisation and nursery discharge; Wapner 2006 as any one of the following: severe respiratory distress syndrome, grade 3 or 4 intraventricular haemorrhage; periventricular leukomalacia, chronic lung disease (defined as the need for supplemental oxygen at 36 weeks' corrected age in infants born before 34 weeks' gestation), or stillbirth or neonatal death.

Mean birthweight was not significantly different between treatment groups (weighted mean difference (WMD) -62.07 g, 95% CI -129.10 to 4.96, four trials, 2273 infants), although in one trial, treatment with repeat dose(s) of corticosteroid was associated with a reduction in birthweight Z score (WMD -0.13, 95% CI -0.26 to 0.00, one trial, 1144 infants), and in two trials, with an increased risk of being small-for-gestational age at birth (RR 1.63, 95% CI 1.12 to 2.37, two trials, 602 infants).

No statistically significant differences were seen in infants in the repeat dose(s) of corticosteroids group compared with infants in the placebo group for:

- fetal and neonatal mortality (RR 0.80, 95% CI 0.52 to 1.23, four trials, 2157 infants);
- chronic lung disease (RR 0.95, 95% CI 0.75 to 1.21, four trials, 2155 infants);
- periventricular haemorrhage (RR 0.96, 95% CI 0.71 to 1.29, three trials, 2104 infants);
- periventricular haemorrhage (grade 3 or 4) (RR 1.11, 95% CI 0.24 to 5.24, three trials, 1660 infants);
- periventricular leukomalacia (RR 0.50, 95% CI 0.19 to 1.33, three trials, 1660 infants).

Primary outcomes for the child

No data available for inclusion.

Primary outcomes for the child as an adult

No data available for inclusion.

Primary outcomes for the women

No statistically significant differences were seen for women treated with repeat dose(s) of prenatal corticosteroids compared with women given placebo for the two outcomes of maternal infectious morbidity;

- chorioamnionitis (RR 1.23, 95% CI 0.95 to 1.59, four trials, 1971 women); and
- puerperal sepsis (RR 0.76, 95% CI 0.42 to 1.36, three trials, 989 women).

Secondary outcomes for the infant

In keeping with the reduction in respiratory morbidity seen, treatment with repeat dose(s) of corticosteroid compared with placebo was associated with a reduction in the use of:

- oxygen (RR 0.89, 95% CI 0.81 to 0.98, one trial, 1144 infants);
- surfactant (RR 0.71, 95% CI 0.61 to 0.83, four trials, 2173 infants); and
- patent ductus arteriosus requiring treatment (RR 0.60, 95% CI 0.43 to 0.84, three trials, 1652 infants).

No statistically significant differences were seen in infants exposed to repeat dose(s) of corticosteroids group compared with infants exposed to placebo for the other secondary respiratory outcomes (including mechanical ventilation, duration of respiratory support, duration of oxygen supplementation, use of inotropic support, use of nitric oxide for respiratory support, use of postnatal corticosteroids), infectious morbidity outcomes (systemic infection in first 48 hours of life, proven infection while in the neonatal intensive care unit), and other neonatal morbidity (including air leak syndrome, necrotising enterocolitis and retinopathy of prematurity).

The mean gestational age at birth (WMD -0.07 weeks, 95% CI -0.39 to 0.26, five trials, 2187 infants) were not significantly different between treatment groups, neither was the proportion of infants born before 37 weeks, 34 weeks or 28 weeks' gestation.

Mean head circumference at birth (WMD -0.17 cm, 95% CI -0.46 to 0.12, four trials, 2271 infants) and mean length at birth (WMD -0.21 cm, 95% CI -0.72 to 0.30, two trials, 1734 infants), were not significantly different between treatment groups, although in one trial treatment with repeat dose(s) of corticosteroid was associated with a reduction in head circumference Z score (WMD -0.16, 95% CI -0.30 to -0.02, 1 trial, 1144 infants) and in another trial significantly lower length multiples of the median at birth (WMD -0.01, 95% CI -0.02 to 0.00, one trial, 590 infants).

In the one trial that reported blood pressure and cardiac outcomes in a subgroup of infants (recruited at two of the collaborating hospitals) no significant differences were seen between treatment groups for mean blood pressure on the first day of life or at six weeks' postnatally, or in the risk of neonatal cardiac hypertrophy. In the one trial that reported on hypothalamo/pituitary/adrenal axis suppression in a subgroup of infants (recruited at one of the collaborating hospitals), infants exposed to repeat dose(s) of corticosteroids had significantly lower mean cortisol concentrations at birth (WMD -44.90 nmol/L, 95% CI -78.41 to -11.39, one trial, 67 infants).

In the one trial of that reported infant growth assessments at primary hospital discharge no differences were seen between treatment groups for weight, head circumference or length.

Secondary outcomes for the child

No information is currently available for outcomes following primary discharge from hospital.

Secondary outcomes for the child as an adult

No information is currently available for outcomes for the child when an adult.

Secondary outcomes for the women

No trial reported any maternal deaths. No statistically significant differences were seen between treatment groups where data were available for the following outcomes: risk of prelabour rupture of the membranes after trial entry, hypertension, postpartum haemorrhage or postnatal pyrexia.

Data on mode of birth showed significant heterogeneity for vaginal birth. Using a random-effects model no statistically significant difference was seen between treatment groups (RR 0.90, 95% CI 0.75 to 1.07, four trials, 1523 women). Treatment with repeat dose(s) of corticosteroid was associated with a significantly increased risk of caesarean section (RR 1.11, 95% CI 1.01 to 1.22, four trials, 1523 women).

The two trials that reported on side-effects of therapy showed significant heterogeneity. Crowther 2006 reported a significant increase in side-effects with treatment with repeat dose(s) of corticosteroid compared with placebo (RR 1.97, 95% CI 1.23 to 3.18, one trial, 982 women), whilst Wapner 2006 reported a significant reduction in side-effects with repeat dose(s) corticosteroid treatment (RR 0.49, 95% CI 0.39 to 0.61, one trial, 492 women). Using a random-effects model no statistically significant difference was seen for side-effects of therapy (RR 0.97, 95% CI 0.24 to 3.90, two trials, 1474 women). Similar heterogeneity was seen for pain at the site of the injection; Crowther 2006 reported a non-significant increase in side-effects with treatment with repeat dose(s) of corticosteroid compared with placebo (RR 2.02, 95% CI 0.95 to 4.26, one trial, 982 women), whilst Wapner 2006 a significant reduction (RR 0.28, 95% CI 0.19 to 0.41, one trial, 492 women). Overall no statistically significant difference was seen using a random-effects model (RR 0.73, 95% CI 0.11 to 5.05, two trials, 1474 women). Wapner 2006 reported a significant reduction in bruising at the site of the injection with treatment with repeat dose(s) of corticosteroid (RR 0.38, 95% CI 0.21 to 0.71, one trial, 492 women). No significant differences were seen for any of the other side-effects of therapy outcomes reported (glucose intolerance and insomnia).

No data have been reported on other secondary outcomes for the women including postnatal depression, parenting stress, breastfeeding after discharge from hospital, satisfaction with the therapy or quality of life.

Secondary outcomes on use of health services

Few data were reported that related to health services use. No differences were seen between treatment groups in the one trial that reported on need for admission to the neonatal intensive care unit. Similarly in the one trial with data no differences were seen between treatment groups for length of postnatal hospitalisation for the women.

(2) Sensitivity analyses based on trial quality

All five trials were rated of high quality for allocation concealment, so sensitivity analyses were not performed based on trial quality.

(3) Planned subgroup analyses

(3.1) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by reason for being at risk of preterm birth at trial entry (eg. presence or absence of ruptured membranes, antepartum haemorrhage, preterm labour, cervical incompetence, pre-eclampsia and growth restriction)

Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the presence or absence of ruptured membranes at trial entry

One trial (Guinn 2002) reported data for the 160 women at risk of preterm birth because of preterm prelabour rupture of membranes. For the infants no statistically significant differences were seen for any of the primary outcomes where data were available, namely respiratory distress syndrome, small-for-gestational age, fetal, neonatal, infant death, chronic lung disease, periventricular haemorrhage grade three or four. For the women, treatment with repeat dose(s) of corticosteroid was associated with an increased risk of chorioamnionitis (RR 1.56, 95% 1.05 to 2.31, one trial, 160 women) although no differences were seen in puerperal sepsis between treatment groups (RR 0.65, 95% CI 0.19 to 2.22, one trial, 160 women).

Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the presence or absence at trial entry of antepartum haemorrhage, preterm labour, cervical incompetence, pre-eclampsia and growth restriction

No data have been reported on these subgroups to date.

(3.2) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by number of babies in utero (singleton, twins or higher order multiples)

No data have been reported on these subgroups to date.

(3.3) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by type of corticosteroid given (eg. betamethasone, dexamethasone, hydrocortisone)

All five trials have used betamethasone so subgroup analyses were not able to be performed as to the type of repeat corticosteroid treatment given.

(3.4) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the planned interval between corticosteroid treatments (at a minimum interval of seven days or less, at a minimum interval between 8 and 14 days, at a minimum interval greater than 14 days)

All five trials used a minimum interval of seven days or less between corticosteroid treatments so subgroup analyses were not able to be performed.

(3.5) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the number of repeat courses actually

given postrandomisation (one, two, three, four or more repeat courses of prenatal corticosteroids)

One trial reported data on a subgroup of women given with four or more repeat courses of repeat prenatal corticosteroids (Wapner 2006). Infants exposed to four or more repeat courses of betamethasone had a significantly reduced mean birthweight (WMD -161 g, 95% CI -290.52 to -31.48, one trial, 368 infants), and birthweight multiples of the median (WMD -0.04, 95% CI -0.07 to -0.01, one trial, 368 infants).

(3.6) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the planned dose of betamethasone or equivalent given per treatment (12 mg or less of betamethasone or equivalent, greater than 12 mg to 24 mg or less of betamethasone or equivalent, greater than 24 mg or more of betamethasone or equivalent)

The dose of corticosteroid given per treatment was 12 mg or less of betamethasone for one trial (Crowther 2006) and greater than 12 mg to 24 mg or less of betamethasone for the other four trials (Aghajafari 2002; Guinn 2002; McEvoy 2002; Wapner 2006).

Planned treatment with repeat dose(s) of corticosteroid of 12 mg or less of betamethasone compared with placebo for the infant was associated with a statistically significant reduction in the risk of respiratory distress syndrome (RR 0.79, 95% CI 0.68 to 0.92, one trial, 1144 infants), severe lung disease (RR 0.58, 95% CI 0.44 to 0.77, one trial, 1144 infants), serious neonatal morbidity using a composite outcome (RR 0.77, 95% CI 0.62 to 0.96, one trial, 1144 infants), the use of mechanical ventilation (RR 0.83, 95% CI 0.70 to 0.99, one trial, 1144 infants), the use of oxygen (RR 0.89, 95% CI 0.81 to 0.98, one trial, 1144 infants), use of surfactant (RR 0.76, 95% CI 0.63 to 0.91, one trial, 1144 infants), patent ductus requiring treatment (RR 0.61, 95% CI 0.42 to 0.88, one trial, 1144 infants).

These benefits were associated with a reduction in birthweight Z score (WMD -0.13, 95% CI -0.26 to 0.00, one trial, 1144 infants), reduction in head circumference Z score (WMD -0.16, 95% CI -0.30 to -0.02, one trial, 1144 infants) and significantly lower mean cortisol concentrations at birth in a subgroup of infants (recruited at one of the collaborating hospitals) (WMD -44.90 nmol/L, 95% CI -78.41 to -11.39, one trial, 67 infants).

For the women, treatment with repeat dose(s) of corticosteroid of 12 mg or less of betamethasone compared with placebo was associated with a statistically significant reduction in the chances of having a vaginal birth (RR 0.80, 95% CI 0.68 to 0.94, one trial, 982 women), an increased risk of having a caesarean (RR 1.15, 95% CI 1.04 to 1.26, one trial, 982 women), and a significant increase in having side-effects related to the treatment (RR 1.97, 95% CI 1.23 to 3.18, one trial, 982 women).

No statistically significant differences were seen for any of the other outcomes where data were available.

Planned treatment with repeat dose(s) of corticosteroid of greater than 12 mg to 24 mg or less of betamethasone compared with placebo for

the infant was associated with a statistically significant reduction in the risk of severe lung disease (RR 0.63, 95% CI 0.45 to 0.89, two trials, 995 infants), use of mechanical ventilation (RR 0.58, 95% CI 0.40 to 0.84, one trial, 492 infants) and use of surfactant (RR 0.63, 95% CI 0.48 to 0.83, three trials, 1029 infants).

These benefits were associated with a significantly lower mean birthweight (WMD -113.60, 95% CI -208.14 to -19.05, three trials, 1129 infants), significantly lower length multiples of the median at birth (WMD -0.01, 95% CI -0.02 to 0.00, one trial, 590 infants) and an increased risk of being small-for-gestational age at birth (RR 1.63, 95% CI 1.12 to 2.37, two trials, 602 infants).

For the women treatment with repeat dose(s) of corticosteroid of greater than 12 mg to 24 mg or less of betamethasone compared with placebo was associated with a significant decrease in having any side-effects of treatment (RR 0.49, 95% CI 0.39 to 0.61, one trial, 492 women), a significant reduction in pain at the site of the injection ((RR 0.28, 95% CI 0.19 to 0.41, one trial, 492 women) and a significant reduction in bruising at the site of the injection (RR 0.38, 95% CI 0.21 to 0.71, one trial, 492 women).

No statistically significant differences were seen for any of the other outcomes where data were available.

(3.7). Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the planned repeat drug exposure per week (12 mg/week or less of betamethasone or equivalent, greater than 12 mg/week to 24 mg/week of betamethasone or equivalent, greater than 24 mg/week or more of betamethasone or equivalent)

The planned repeat drug exposure per week was 12 mg/week or less of betamethasone for one trial (Crowther 2006) and greater than 12 mg to 24 mg or less of betamethasone for the other four trials (Aghajafari 2002; Guinn 2002; McEvoy 2002; Wapner 2006).

Planned treatment with repeat dose(s) of corticosteroid of 12 mg/week or less of betamethasone compared with placebo for the infant was associated with a statistically significant reduction in the risk of respiratory distress syndrome (RR 0.79, 95% CI 0.68 to 0.92, one trial, 1144 infants), severe lung disease (RR 0.58, 95% CI 0.44 to 0.77, one trial, 1144 infants), serious neonatal morbidity using a composite outcome (RR 0.77, 95% CI 0.62 to 0.96, one trial, 1144 infants), use of mechanical ventilation (relative risk (RR) 0.83, 95% CI 0.70 to 0.99, one trial, 1144 infants), the use of oxygen (RR 0.89, 95% CI 0.81 to 0.98, one trial, 1144 infants), the use of surfactant (RR 0.76, 95% CI 0.63 to 0.91, one trial, 1144 infants) and patent ductus requiring treatment (RR 0.61, 95% CI 0.42 to 0.88, one trial, 1144 infants). These benefits were associated with a reduction in birthweight Z score (WMD -0.13, 95% CI -0.26 to 0.00, one trial, 1144 infants), reduction in head circumference Z score (WMD -0.16, 95% CI -0.30 to -0.02, one trial, 1144 infants) and significantly lower mean cortisol concentrations at birth in a subgroup of infants (recruited at one of the collaborating hospitals) (WMD -44.90 nmol/L, 95% CI -78.41 to -11.39, one trial, 67 infants).

For the women, treatment with repeat dose(s) of corticosteroid of 12 mg or less of betamethasone compared with placebo was associated with a statistically significant reduction in the chances of having a vaginal birth (RR 0.80, 95% CI 0.68 to 0.94, one trial, 982 women), an increased risk of having a caesarean (RR 1.15, 95% CI 1.04 to 1.26, one trial, 982 women), and a significant increase in having side-effects related to the treatment (RR 1.97, 95% CI 1.23 to 3.18, one trial, 982 women).

No statistically significant differences were seen for any of the other outcomes where data were available.

Planned treatment with repeat dose(s) of corticosteroid of greater than 12 mg/week to 24 mg/week or less of betamethasone compared with placebo for the infant was associated with a statistically significant reduction in the risk of severe lung disease (RR 0.63, 95% CI 0.45 to 0.89, two trials, 995 infants), use of mechanical ventilation (RR 0.58, 95% CI 0.40 to 0.84, one trial, 492 infants) and use of surfactant (RR 0.63, 95% CI 0.48 to 0.83, three trials, 1029 infants). These benefits were associated with a significantly lower mean birthweight (WMD -113.60, 95% CI -208.14 to -19.05, three trials, 1129 infants), significantly lower length multiples of the median at birth (WMD -0.01, 95% CI -0.02 to 0.00, one trial, 590 infants) and an increased risk of being small-for-gestational age at birth (RR 1.63, 95% CI 1.12 to 2.37, two trials, 602 infants).

For the women treatment with repeat dose(s) of corticosteroid of greater than 12 mg to 24 mg or less of betamethasone compared with placebo was associated with a significant decrease in having any side-effects of treatment (RR 0.49, 95% CI 0.39 to 0.61, one trial, 492 women), a significant reduction in pain at the site of the injection (RR 0.28, 95% CI 0.19 to 0.41, one trial, 492 women) and a significant reduction in bruising at the site of the injection (RR 0.38, 95% CI 0.21 to 0.71, one trial, 492 women).

No statistically significant differences were seen for any of the other outcomes where data were available.

(3.8) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the method of administration (intramuscular, intravenous, oral)

No data have been reported on these subgroups to date.

(3.9) Repeat dose(s) of prenatal corticosteroids versus placebo/no treatment by the gestational age at entry to the trial No data have been reported on these subgroups to date.

DISCUSSION

Since the last update of this review, two further trials have been published adding to the evidence base assessing whether repeat does(s) of prenatal corticosteroids improve fetal lung maturation, and thereby reduce infant morbidity and mortality. Of the now five included trials, all are recent publications of good methodological quality. All had adequate allocation concealment, used a placebo, and losses to follow up were nil or minimal.

From the available data, there is evidence that repeat doses(s) of prenatal corticosteroids reduce both the occurrence and severity of neonatal lung disease and reduce overall serious neonatal morbidity, all clinically important beneficial effects. In keeping with these benefits, treatment with repeat dose(s) of corticosteroid is associated with less use of mechanical ventilation, oxygen therapy and surfactant and fewer infants have a patent ductus requiring treatment.

In contrast to these clinical benefits, although no overall differences at birth in mean weight, length and head circumference were seen, some trials have reported a increase in the risk of being born small-for-gestational age and a reduction in measures of growth at birth (Z scores for weight and head circumference, length multiples of the median). The data available to date are insufficient to adequately assess any long-term effects the differences observed at birth may have. Only one trial has reported on weight, length and head circumference following birth, at the time of discharge from hospital after birth, and showed no differences in a range of measures of growth.

The few data available on infant cardiovascular outcomes show no differences with repeat dose(s) corticosteroid treatment. Data on longer-term assessment of blood pressure are required.

There was little evidence of either major benefit or harm to the mother from giving repeat dose(s) of prenatal corticosteroids, although women treated with repeat dose(s) of corticosteroid were more likely to give birth by caesarean section. It is unclear why this should be.

There are still no data published on the neurodevelopmental status of the infant or child at follow up or other longer-term outcomes. Such information is needed to assess overall benefits and risks. Several completed trials have ongoing assessment of their children planned (Wapner 2006 24 month postdelivery, Crowther 2006 two years' corrected age and early school-age follow up, MACS 2001 at five years of age).

Planned subgroup analyses were performed where the published data permitted and remain limited to date. Any additional unpublished data will be sought from the trial authors. Currently the data are too few to adequately assess the benefits and harms of repeat dose(s) of corticosteroid treatment by reason for risk of preterm birth at trial entry, plurality of the pregnancy, number of repeat courses planned or given, interval between corticosteroid treatments, planned dose of corticosteroid given per treatment and dose planned per week.

Further information from trials of repeat dose(s) of prenatal corticosteroids for women at risk of preterm birth for the prevention of neonatal respiratory disease are required. Trials should be of high quality, be large enough to assess serious morbidity and mortality, compare different corticosteroid preparations and mode of administration, varying times between repeat courses, different amounts of corticosteroid given at each course and provide neurodevelopmental status of the child at follow up and other longer-term outcomes including behaviour, educational achievement, cardiovascular status, bone density, hypothalamo/pituitary/adrenal axis function, glucose intolerance and lung function.

One trial from the US is in progress (Obstetrix 2003). The Canadian MACS trial (MACS 2001) has now finished recruitment and data collection to two years of corrected age is continuing. One trial from the UK stopped recruitment and publication is awaited (TEAMS 1999). One trial in women with preterm prelabour rupture of the membranes

has only been published in abstract form with no usable data as yet (Sobhrabvand 2001). Another ongoing study was published just as this update was submitted for publication (Peltoniemi 2007). We have therefore added it to the 'Studies awaiting assessment' and will consider it for inclusion in the next update.

AUTHORS' CONCLUSIONS

Implications for practice

Repeat dose(s) of prenatal corticosteroids reduce the occurrence and severity of neonatal lung disease and the risk of serious health problems in the first few weeks of life. These short term benefits for babies support the use of repeat dose(s) of prenatal corticosteroids for women at risk of preterm birth. However, these benefits are associated with a reduction in some measures of weight, and head circumference at birth. and there is still insufficient evidence on the longer-term benefits and risks.

Implications for research

Further information from high-quality trials is required. The trials should be large enough to assess serious morbidity and mortality, compare different corticosteroid preparations, method of administration, dose and timing regimens, and provide neurodevelopmental status of the child at follow up and other longer-term outcomes. Several such trials are in progress.

POTENTIAL CONFLICT OF INTEREST

Both review authors are investigators in the Australasian Collaborative Trial of Repeat Doses of Corticosteroid for the Prevention of Neonatal Respiratory Disease (Crowther 2006).

ACKNOWLEDGEMENTS

Special thanks to Sonja Henderson, Lynn Hampson and Denise Atherton of the Cochrane Pregnancy and Childbirth Group for their support in the updating of this review. Also special thanks to Philippa Middleton who provided review author support for this update and conducted the initial data extraction for the ACTORDS trial. Philippa is supported by a grant from the Commonwealth Department of Health and Ageing, Australia.

SOURCES OF SUPPORT

External sources of support

• Australian Department of Health and Ageing AUSTRALIA

Internal sources of support

- Discipline of Obstetrics and Gynaecology, The University of Adelaide AUSTRALIA
- Liggins Institute, University of Auckland NEW ZEALAND

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TABLES

Characteristics of included studies

Study	Aghajafari 2002
Methods	Type of study: randomised trial. Method of treatment allocation: randomisation was computer-generated and was centrally controlled by one pharmacist at each hospital who kept the randomisation code. The injection of the study treatment was given by a designated research nurse in each hospital who was not caring for the woman. Stratification: by gestational age (24-27 weeks; 28-30 weeks) and by hospital using block sizes of 2. Placebo: yes, normal saline. The physical appearance of the study solutions had to be kept masked since the betamethasone is opaque, while saline is clear. To minimise unblinding, the pharmacist prepared the study treatments in a syringe covered with yellow tape. Sample-size calculation: no. Small pilot study to determine the feasibility of a larger trial. Intention-to-treat analyses: yes. Losses to follow up: none. Funding: support from Canadian Institutes of Health Research Senior Scientist Award.
Participants	Location: 2 hospitals in Toronto, Canada. Timeframe: September 1999-August 2000. Eligibility criteria: women at 24-30 weeks' gestation at continued increased risk of preterm birth who remained undelivered 7 or more days following a single course of antenatal corticosteroids (defined as 2 doses of 12 mg/dose intramuscular betamethasone, given at 12 or 24 hours intervals; or 4 doses of 5-6 mg/dose intramuscular dexamethasone, given at 12 hour intervals. To be at increased risk of preterm birth, women had to have one or more of the following: regular uterine contractions; a shortened cervical length or cervical dilatation; preterm prelabour rupture of the membranes; antepartum bleeding secondary to placental separation or placenta praevia; history of preterm birth; maternal hypertension; or other medical condition increasing the risk of preterm delivery or intrauterine growth restriction; or other fetal conditions increasing the risk of preterm delivery. Gestational age range: 24-30 weeks. Exclusion criteria: women were excluded if they required chronic doses of corticosteroids secondary to medical conditions, had a contra-indication to corticosteroids, had clinical evidence of chorioamnionitis, or of their fetus(es) had a known lethal congenital anomaly. Total recruited: 12-6 in the multiple course of antenatal corticosteroid group and 6 in the placebo group.
Interventions	Multiple course of antenatal corticosteroid group: a weekly course of betamethasone (2 doses of 12 mg/dose betamethasone (Celestone Soluspan; Schering Canada Inc) intramuscularly, 24 hours apart) until 33 weeks or delivery if the woman remained at increased risk of preterm birth. In the placebo group: a weekly course of placebo consisting of 2 doses of normal saline, intramuscularly 24 hours apart, until 33 weeks or birth if the woman remained at increased risk of preterm birth.
Outcomes	Outcomes: rate of recruitment over 12-month period, risk of complications requiring discontinuation of study treatment, concentrations of plasma cortisol and ACTH in cord blood and in maternal blood immediately following birth.

^{*}Indicates the major publication for the study

Characteristics of included studies (Continued)

Perinatal or neonatal mortality or significant neonatal morbidity, defined as one or more of the following: stillborn or neonatal death during the first 28 days of life or prior to hospital discharge, whichever was sooner; respiratory distress syndrome; bronchopulmonary dysplasia (requiring oxygen at 36 corrected postnatal gestational age); intraventricular haemorrhage (grade 3 or 4; and necrotising enterocolitis.

	gestational age); intraventricular haemorrhage (grade 3 or 4; and necrotising enterocolitis.
Notes	
Allocation concealment	A – Adequate
Study	Crowther 2006
Methods	Type of study: randomised controlled trial. Method of treatment allocation: central telephone randomisation. Random-number sequence generated by computer with variable block sizes and stratification by centre, gestational age and number of fetuses. Placebo: yes, normal saline. Treatment packs and syringes identical appearance. (opaque study-labelled syringe). Sample-size calculation: yes. Intention-to-treat analyses: yes. Losses to follow up: none. Funding: Australian National Health and Medical Research Council, The Channel 7 Research Foundation of South Australia, The Women's and Children's Hospital Research Foundation, Adelaide, and The Department of Obstetrics and Gynaecology, The University of Adelaide, South Australia.
Participants	Location: 23 hospitals in Australia and New Zealand. Timeframe: April 1998 to July 2004. Included: single, twin or triplet pregnancy at less than 32 weeks' gestation if women had received an initial treatment of corticosteroid 7 or more days previously and their responsible clinician regarded them to be at continued risk of preterm birth, and there was no contraindication to further corticosteroid therapy. Exclusion criteria: in second stage of labour, had chorioamnionitis needing urgent delivery, or if further corticosteroid therapy was judged to be essential. Gestational age recruited up to less than 32 weeks. Total recruited 982 women (1146 babies). 489 women in the repeat steroid group and 493 women in the placebo group.
Interventions	Repeat steroids: 11.4 mg Celestone Chronodose (as 7.8 mg betamethasone sodium phosphate and 6 mg betamethasone acetate. Placebo: saline intramuscular injection. Every week, if the woman remained undelivered and less than 32 weeks' gestation, and the responsible clinician regarded her as at continued risk of preterm birth, a further treatment pack from the same treatment group was allocated by the telephone randomisation service.
Outcomes	Primary outcomes: frequency and severity of respiratory distress syndrome, weight, length and head circumference at birth and primary discharge from hospital. Secondary outcomes included clinical chorioamnionitis, maternal postpartum pyrexia, any side-effects of the injection for the mother and other measures of neonatal morbidity.
Notes	
Allocation concealment	A – Adequate
C4 1	Ci 2002
Study	Guinn 2002
Methods	Type of study: randomised controlled trial. Method of treatment allocation: computer-generated randomisation logs prepared centrally and distributed to the research pharmacist at each clinical site. Participants were assigned by the pharmacy to treatment group. Stratification: by centre. Placebo: yes. Type of placebo not stated. The placebo syringes were indistinguishable from the syringes containing betamethasone. Sample-size calculation: yes. Intention-to-treat analyses: yes.

Characteristics of included studies (Continued)

Losses to follow up: 16 women and 1 neonate were lost to follow up. Partial data were available for participants who were lost to follow up. In some cases we were able to ascertain the birth date, weight, and health status for the neonate. The denominators presented very slightly from one variable to another because of missing data.

Funding: March of Dimes grant, the Berlex Foundation, the Wisconsin Perinatal Association, the Perinatal Clinical Research Center at the University of Colorado Health Sciences Center (grant from the General Clinical Research Centers Program, National Centers for Research Resources, National Institutes of Health), and the participating departments.

Participants

Location: 13 academic centres in USA.

Timeframe: February 1996-April 2000.

Eligibility criteria: women at 24 weeks to < 33 weeks' gestation at high risk of preterm birth who remained undelivered 1 week following an initial course of antenatal corticosteroids (defined as 2 doses of 12 mg/dose intramuscular betamethasone, repeated at 24 hours; or 4 doses of 6 mg/dose intramuscular dexamethasone, given at 12 hour intervals. To be at high risk of preterm birth qualifying criteria were: preterm labour with intact membranes (either a history of regular uterine contractions associated with cervical dilatation of >/= 2 cm and effacement >/= 80% in a nulliparous participant or cervical dilatation of >/= 3 cm and >/= 80% effacement in a multiparous participant at the time of presentation: or regular uterine contractions with documented cervical change); preterm premature rupture of the membranes (rupture of the membranes occurring > 1 hour prior to the onset of preterm labour); maternal medical illness (pre-eclampsia, hypertension, diabetes, renal disease, systemic lupus erythematosus, trauma); or suspected fetal jeopardy (intrauterine growth restriction < 10th percentile, oligohydramnios, abnormal antepartum testing, progression of a fetal anomaly compatible with like, twin-twin transfusion syndrome).

Gestational age range: 24 weeks to < 33 weeks' gestation.

Exclusion criteria: women were excluded if they required immediate delivery, there were fetal anomalies incompatible with life, documented fetal lung maturity, and maternal active tuberculosis or human immunodeficiency virus infection.

Total recruited: 502-256 in the weekly-course group and 246 in the single-course group.

Interventions

In the weekly-course group: a weekly course of betamethasone (2 doses of 12 mg/dose betamethasone repeated after 24 hours, intramuscularly), until 34 weeks or birth whichever came first. In the single-course group: a similarly administered placebo.

Outcomes

Primary outcomes: composite neonatal morbidity defined as presence of any of the following: severe respiratory distress syndrome, bronchopulmonary dysplasia, severe intraventricular haemorrhage, periventricular leukomalacia, necrotising enterocolitis, proven sepsis or death between randomisation and nursery discharge. Secondary outcomes: frequency and severity of respiratory distress syndrome; need for and duration of oxygen therapy; need for and duration of ventilatory support; bronchopulmonary dysplasia (defined as need for oxygen > 21% and usually ventilatory therapy for at least 28 days of life; in cases were no additional ventilatory support was needed but oxygen was required, chest radiographs consistent with bronchopulmonary dysplasia were used; in the case of neonatal death, bronchopulmonary dysplasia was diagnosed on autopsy findings); severe intraventricular haemorrhage was defined as intraventricular bleeding with dilatation of the cerebral ventricles (grade 3) or parenchymal haemorrhage (grade 4), as diagnosed with an imaging technique or autopsy, periventricular leukomalacia was defined as the presence of more than 1 obvious hypoechoic cyst in the periventricular white matter; proven necrotising enterocolitis; proven sepsis; perinatal death defined as death of a fetus or neonate at any time between randomisation and nursery discharge.

Notes

Planned sample size was 1000 women. Recruitment was stopped early based on safety concerns.

Allocation concealment

A - Adequate

Study

McEvoy 2002

Methods

Type of study: randomised trial.

Method of treatment allocation: group assignment done through pharmacy using a random-number table. The study medication was prepared by the pharmacy.

Characteristics of included studies (Continued)

Stratification: none stated.

Placebo: 25 mg cortisone acetate, an inactive steroid, identical in appearance to betamethasone.

Sample-size calculation: yes. Based on 37 women the average functional residual capacity in the single course remote group is not > 12% smaller than the functional residual capacity in the repetitive group (P = 0.05, power 80%).

Intention-to-treat analyses: yes. Losses to follow up: none stated.

Funding: American Lung Association.

Participants

Location: single centre in USA (Sacred Heart Hospital, University of Florida, Pensacola, Florida).

Timeframe: 3-year period ending in December 1999.

Eligibility criteria: women at 25-33 weeks' gestation who remained undelivered 1 week after a single course of antenatal corticosteroids (defined as 2 doses of 12 mg/dose intramuscular betamethasone), given because of increased risk of preterm delivery.

Gestational age range: 25-33 weeks.

Exclusion criteria: women were excluded if they were insulin-dependent diabetics, had a drug-addiction, or fetus had a known lethal congenital anomaly.

Total recruited: 37 women. 18 women in the repetitive courses of antenatal corticosteroid group and 19 women in the single course remote group.

Interventions

In the repetitive courses of antenatal corticosteroid group: a weekly course of betamethasone (2 doses of 12 mg/dose betamethasone (Celestone Soluspan; Schering Corporation, Kenilworth, New Jersey), intramuscularly, until delivery or 34 weeks' gestation.

In the single-course remote group: weekly courses of placebo intramuscularly, until 34 weeks or delivery.

Outcomes

Primary outcomes: functional residual capacity, respiratory compliance.

Secondary outcomes: admission head circumference, surfactant administration, days on oxygen, and mechanical ventilation.

Notes

Allocation concealment

A – Adequate

Study

Wapner 2006

Methods

Type of study: randomised controlled trial.

Method of treatment allocation: numbered kits were prepared using randomisation sequences created by an independent data co-ordinating centre. Sequences were generated using the urn design and were stratified by clinical centre, type of qualifying course, and inpatient/outpatient.

Woman was assigned to the next sequentially numbered kit - betamethasone or identical looking placebo prepared by a centralised research pharmacy.

Placebo: yes. Type of placebo not stated.

Sample-size calculation: yes.

Intention-to-treat analyses: yes.

Losses to follow up: 3 women. Funding: National Institute of Child Health and Human Development.

Participants

Location: 18 US hospitals (NICHD MFMU network centres).

Timeframe: March 2000 to April 2003.

Eligibility criteria: pregnant women with intact membranes between 23 weeks 0 days and 31 weeks and 6 days if they had received a single full course of betamethasone or dexamethasone between 7 and 10 days earlier and were at high risk for spontaneous preterm birth, or had the diagnosis of placenta praevia or chronic abruption Exclusions: preterm premature rupture of the membranes prior to randomisation, confirmed fetal lung maturity, chorioamnionitis, a major fetal anomaly, non-reassuring fetal status, systemic corticosteroid use during the current pregnancy, or insulin-dependent diabetes. Gestational age was determined from the last menstrual period provided that ultrasonography confirmed the estimate. When there was discordance, the duration of gestation at randomisation was determined from the first sonogram performed. Gestational age range: 23 weeks 0 days to 31 weeks 6 days gestation.

	Total recruited: 495 women (planned for 2400) = 591 fetuses/infants. 252 to the repeat steroid arm and 243 to the placebo.
Interventions	Repeat steroid group: each course consisted of 2 injections of betamethasone 12 mg (as 6 mg betamethasone sodium phosphate and 6 mg betamethasone acetate) repeated once in 24 hours. Placebo group: 'matching placebo' - no other details of preparation given. Initially women received courses until birth or 33 weeks 6 days' gestation, whichever was sooner. After 67 women had been enrolled, the number of courses (not including the qualifying course) was limited to 4 because of difficulty in recruitment and published literature suggesting possible harmful effects of multiple courses. 63.4% of women received 4 or more study courses.
Outcomes	Primary outcome: one of the following: severe respiratory distress syndrome (defined as clinical features of respiratory distress syndrome with the need for oxygen and respiratory support from 6 to 24 hours or more of age, an abnormal chest x-ray, and either administration of a full course of surfactant or a fraction of inspired oxygen (FiO2 of at least 60%); grade 3 or 3 intraventricular hemorrhage; periventricular leukomalacia; chronic lung disease (defined as the need for supplemental oxygen at 36 weeks' corrected age in infants born before 34 weeks' gestation); or stillbirth or neonatal death.
Notes	Planned sample size was 2400 women. Recruitment was stopped early based on safety concerns (because of a tendency towards decreased birthweight in the repeat steroid group without any reduction in the primary morbidity outcome and also because of difficulties in recruitment.
Allocation concealment	A – Adequate
ACTH: adrenocorticotropic MFMU: NICHD:	c hormone

Characteristics of excluded studies

Reason for exclusion

Study

Mercer 2001	Women recruited to the trial did not have corticosteroids before entry.
	The objective of the trial was to evaluate the need for and benefits of weekly antenatal corticosteroids in women at risk of preterm birth.
	189 women between 23 and 32 weeks at risk of preterm birth were randomised to weekly antenatal corticosteroids or to a control group where corticosteroids were given if indicated before 35 weeks, if the pregnancy was expected to last more than 1 week.

The primary outcome was antenatal corticosteroids given within 7 days of preterm birth (< 35 weeks) (optimal exposure). In the control group only one third of infants < 35 weeks' gestation received optimal antenatal corticosteroid exposure. Weekly corticosteroids doubled optimal exposure although the vast majority gave birth > 34 weeks.

Thorp 2000 Women recruited to the trial were not randomised to receive repeat corticosteroids but antenatal phenobarbital. The abstract is a secondary multivariate analysis of this trial assessing if duration of antenatal betamethasone is associated with perinatal outcome.

Characteristics of ongoing studies

Study	MACS 2001
Trial name or title	Multiple Courses of Antenatal Corticosteroids for Preterm Birth Study.
Participants	NA
Interventions	Betamethasone versus placebo (after a single course of antenatal steroids).
Outcomes	NA

Characteristics of ongoing studies (Continued)

Starting date	April 2001.
Contact information	Dr Kellie Murphy: kellie.murphy@utoronto.ca
Notes	ISRCTN 72654148

Study	Obstetrix 2003
Trial name or title	A randomised trial comparing the impact of 1 versus 2 courses of antenatal corticosteroids on neonatal outcome.
Participants	434.
Interventions	Second course of antenatal steroids versus placebo.
Outcomes	Composite neonatal morbidity.
Starting date	November 2003. Expected completion: November 2008.
Contact information	Kimberley Maurel, Obstetrix Medical Group, Inc
Notes	NCT00201643

Study	Sobhrabvand 2001
Trial name or title	Effects of single versus multiple courses of corticosteroid therapy on pregnancy results in women with PPROM.
Participants	NA
Interventions	NA
Outcomes	NA NA
Starting date	NA
Contact information	NA
Notes	NA

Study	TEAMS 1999
Trial name or title	Trial of the effects of antenatal multiple courses of steroids versus a single course (TEAMS).
Participants	4000 women.
Interventions	2 intramuscular injections of betamethasone versus placebo.
Outcomes	Death within first year after birth; developmental quotient less than 85 at 2 years.
Starting date	1/10/1999. End date (recruitment): 1/05/2001.
Contact information	Ms Helen Adams, TEAMS administrator
Notes	ISRCTN 46614711

i.m.: intramuscular NA: not available

PPROM: preterm prelabour rupture of the membranes

ANALYSES

Comparison 01. Repeat doses of corticosteroids versus single course

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Respiratory distress syndrome			Relative Risk (Fixed) 95% CI	Subtotals only
02 Severe lung disease			Relative Risk (Fixed) 95% CI	Subtotals only
03 Composite serious morbidity (variously defined)			Relative Risk (Fixed) 95% CI	Subtotals only
04 Mean birthweight (g)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
05 Birthweight Z scores			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
06 Birthweight multiples of the median			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
07 Small-for-gestational age at birth			Relative Risk (Fixed) 95% CI	Subtotals only
08 Fetal and neonatal mortality			Relative Risk (Fixed) 95% CI	Subtotals only
09 Fetal death			Relative Risk (Fixed) 95% CI	Subtotals only
10 Neonatal death			Relative Risk (Fixed) 95% CI	Subtotals only
11 Chronic lung disease			Relative Risk (Fixed) 95% CI	Subtotals only
13 Periventricular haemorrhage			Relative Risk (Fixed) 95% CI	Subtotals only
14 Periventricular haemorrhage grade 3/4			Relative Risk (Random) 95% CI	Subtotals only
15 Periventricular leucomalacia			Relative Risk (Fixed) 95% CI	Subtotals only
17 Chorioamnionitis			Relative Risk (Fixed) 95% CI	Subtotals only
18 Puerperal sepsis			Relative Risk (Fixed) 95% CI	Subtotals only
19 Use of mechanical ventilation			Relative Risk (Random) 95% CI	Subtotals only
20 Duration of respiratory support in days			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
21 Use of oxygen supplementation			Relative Risk (Fixed) 95% CI	Subtotals only
22 Duration of oxygen supplementation in days			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
23 Use of surfactant			Relative Risk (Fixed) 95% CI	Subtotals only
24 Patent ductus arteriosus requiring treatment			Relative Risk (Fixed) 95% CI	Subtotals only
25 Use of inotropic support			Relative Risk (Fixed) 95% CI	Subtotals only
26 Use of nitric oxide for respiratory support			Relative Risk (Fixed) 95% CI	Subtotals only
27 Mean gestational age at birth (weeks)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
28 Preterm birth before 37 weeks			Relative Risk (Fixed) 95% CI	Subtotals only
29 Very preterm birth before 34 weeks			Relative Risk (Fixed) 95% CI	Subtotals only
30 Extremely preterm birth before 28 weeks			Relative Risk (Fixed) 95% CI	Subtotals only
31 Mean head circumference at birth (cm)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
32 Head circumference Z scores at birth			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
33 Mean length at birth (cm)			Weighted Mean Difference (Fixed) 95% CI	Subtotals only
34 Length Z scores at birth			Weighted Mean Difference (Fixed) 95% CI	Subtotals only

35 Length multiples of the median at birth	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
36 Apgar score less than 7 at 5 minutes	Relative Risk (Fixed) 95% CI	Subtotals only
37 Systemic infection in the first 48 hours of life (suspected or confirmed)	Relative Risk (Fixed) 95% CI	Subtotals only
38 Proven infection while in the neonatal intensive care unit	Relative Risk (Fixed) 95% CI	Subtotals only
39 Admission to the neonatal intensive care unit	Relative Risk (Fixed) 95% CI	Subtotals only
40 Air leak syndrome	Relative Risk (Random) 95% CI	Subtotals only
41 Necrotising enterocolitis	Relative Risk (Fixed) 95% CI	Subtotals only
42 Retinopathy of prematurity	Relative Risk (Fixed) 95% CI	Subtotals only
43 Use of postnatal steroids	Relative Risk (Fixed) 95% CI	Subtotals only
44 Mean neonatal blood pressure on first day after birth	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
45 Mean neonatal blood pressure 6 weeks after birth	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
46 Neonatal cardiac hypertrophy as measured by interventricular septal thickness (IVSd)	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
47 Neonatal cardiac hypertrophy as measured by left ventricular wall thickness in diastole	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
48 Mean basal cortisol concentrations (nmol/L) at birth	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
49 Mean weight (g) at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
50 Weight Z scores at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
51 Mean head circumference (cm) at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
52 Head circumference Z scores at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
53 Mean length (cm) at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
54 Length Z score at primary hospital discharge	Weighted Mean Difference (Fixed) 95% CI	Subtotals only
55 Prelabour rupture of membranes after trial entry	Relative Risk (Fixed) 95% CI	Subtotals only
56 Hypertension (variously defined by the authors)	Relative Risk (Fixed) 95% CI	Subtotals only
57 Vaginal birth	Relative Risk (Random) 95% CI	Subtotals only
58 Caesarean section	Relative Risk (Fixed) 95% CI	Subtotals only
59 Postpartum haemorrhage	Relative Risk (Fixed) 95% CI	Subtotals only
60 Postnatal pyrexia (variously defined by authors)	Odds Ratio (Fixed) 95% CI	Subtotals only
61 Length of postnatal hospitalisation (days)	Weighted Mean Difference (Fixed) 95% CI	Subtotals only

62 Any maternal side-effects of	Relative Risk (Random) 95% CI	Subtotals only
therapy		
63 Maternal hyperglycaemia	Relative Risk (Fixed) 95% CI	Subtotals only
(variously defined by authors)		
64 Insomnia	Relative Risk (Fixed) 95% CI	Subtotals only
65 Pain at injection site	Relative Risk (Random) 95% CI	Subtotals only
66 Bruising at injection site	Relative Risk (Fixed) 95% CI	Subtotals only

INDEX TERMS

Medical Subject Headings (MeSH)

Adrenal Cortex Hormones [*administration & dosage]; Infant, Newborn; Infant, Premature; *Obstetric Labor, Premature; Randomized Controlled Trials; Respiratory Distress Syndrome, Newborn [*prevention & control]

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

TitleRepeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing

neonatal respiratory disease

Authors Crowther CA, Harding JE

Contribution of author(s)Both review authors helped prepare the protocol. Caroline Crowther wrote the draft of the

original review and both review authors have commented on subsequent drafts and prepared

the updates.

Issue protocol first published 2002/4

Review first published 2003/3

Date of most recent amendment 15 May 2007

Date of most recent 11 May 2007

SUBSTANTIVE amendment

What's New February 2007

Search updated in November 2006 and data from two trials now published added (Crowther 2006; Wapner 2006). We updated the search just before submission for publication and identified the published report for the previously listed Peltoniemi ongoing study. We have added it to the 'Studies awaiting assessment' section and will consider it for inclusion in

the next update (Peltoniemi 2007).

The review conclusions have not changed.

Date new studies sought but

none found

Information not supplied by author

Date new studies found but not

yet included/excluded

28 February 2007

Date new studies found and

included/excluded

30 November 2006

Date authors' conclusions

section amended

24 August 2006

Contact address Prof Caroline Crowther

Professor

Discipline of Obstetrics and Gynaecology

The University of Adelaide Women's and Children's Hospital

72 King William Road

Adelaide

South Australia

5006

AUSTRALIA

E-mail: caroline.crowther@adelaide.edu.au

Tel: +61 8 81617647 Fax: +61 8 81617652

DOI 10.1002/14651858.CD003935.pub2

Cochrane Library number CD003935

Editorial group Cochrane Pregnancy and Childbirth Group

Editorial group code HM-PREG

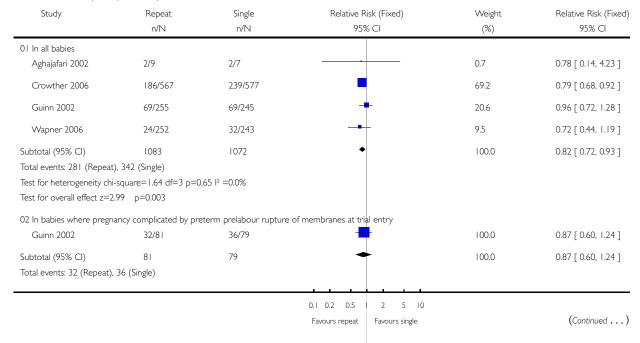
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 01 Respiratory distress syndrome

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 01 Respiratory distress syndrome



(... Continued)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl
Test for heterogeneity: no	t applicable				
Test for overall effect z=0.	77 p=0.4				
03 In babies exposed to n	epeat corticosteroids a	s betamethasone			
Aghajafari 2002	2/9	2/7		0.7	0.78 [0.14, 4.23]
Crowther 2006	186/567	239/577	•	69.2	0.79 [0.68, 0.92]
Guinn 2002	69/255	69/245	+	20.6	0.96 [0.72, 1.28]
Wapner 2006	24/252	32/243	-	9.5	0.72 [0.44, 1.19]
Subtotal (95% CI) Total events: 281 (Repeat) Test for heterogeneity chi- Test for overall effect z=2.	square=1.64 df=3 p=0	1072 0.65 I ² =0.0%	•	100.0	0.82 [0.72, 0.93]
04 In babies exposed to n		t a minimum interval of 7	days or less		
Aghajafari 2002	2/9	2/7		0.7	0.78 [0.14, 4.23]
Crowther 2006	186/567	239/577	=	69.2	0.79 [0.68, 0.92]
Guinn 2002	69/255	69/245	+	20.6	0.96 [0.72, 1.28]
Wapner 2006	24/252	32/243	-	9.5	0.72 [0.44, 1.19]
Subtotal (95% CI)	1083	1072	•	100.0	0.82 [0.72, 0.93]
Total events: 281 (Repeat) Test for heterogeneity chi- Test for overall effect z=2.	square=1.64 df=3 p=0	0.65 2 =0.0%			
05 In babies exposed to n	•		veen 8 and 14 days		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	t applicable	0		0.0	Not estimable
06 In babies exposed to n	epeat corticosteroids a	t a minimum interval of >	14 days		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	t applicable	0		0.0	Not estimable
07 In babies exposed to o	ne repeat course of pr	renatal corticosteroids			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	t applicable	0		0.0	Not estimable
08 In babies exposed to to	wo repeat courses of p	renatal corticosteroids			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no		0		0.0	Not estimable
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		(Continued)

(... Continued)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl
Test for overall effect: not a	applicable				
09 In babies exposed to th Subtotal (95% CI)	ree repeat courses of	prenatal corticosteroids		0.0	Not estimable
Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	(Single) applicable	Ü		0.0	rvot estimable
10 In babies exposed to fo	ur or more repeat cou	urses of prenatal corticoste	eroids		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not		0		0.0	Not estimable
Test for overall effect: not a	applicable				
II In babies where planned Crowther 2006	d dose per treatment	course 12 mg or less of be 239/577	stamethasone or equivalent	100.0	0.79 [0.68, 0.92]
Subtotal (95% CI)	567	577	•	100.0	0.79 [0.68, 0.92]
Total events: 186 (Repeat), Test for heterogeneity: not Test for overall effect z=3.0	applicable				
12 In babies where planned	d dose per treatment	course > 12 mg to 24 mg	or less of betamethasone or equivaler	nt	
Aghajafari 2002	2/9	2/7		2.1	0.78 [0.14, 4.23]
Guinn 2002	69/255	69/245	+	66.9	0.96 [0.72, 1.28]
Wapner 2006	24/252	32/243	-	31.0	0.72 [0.44, 1.19]
Subtotal (95% CI) Total events: 95 (Repeat), I	516	495	+	100.0	0.88 [0.69, 1.13]
Test for overall effect z=0.9	square=0.98 df=2 p=0	0.61 2 =0.0%			
13 In babies where planned	d dose per treatment	course > 24 mg of betame	ethasone or equivalent		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable	0		0.0	Not estimable
		-	of betamethasone or equivalent		
	186/567			100.0	0.79 [0.68, 0.92]
Subtotal (95% CI) Total events: 186 (Repeat), Test for heterogeneity: not Test for overall effect z=3.0	applicable	577	•	100.0	0.79 [0.68, 0.92]
15 In babies where planned	d repeat drug exposur	re was > 12 mg/week to 24	4 mg/week of betamethasone or equi	valent	
Aghajafari 2002	2/9	2/7		2.1	0.78 [0.14, 4.23]
Guinn 2002	69/255	69/245	+	66.9	0.96 [0.72, 1.28]
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		(Continued)



Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
n/N	n/N	n/N	95% CI	(%)	95% CI
Wapner 2006	24/252	32/243	-	31.0	0.72 [0.44, 1.19]
Subtotal (95% CI)	516	495	•	100.0	0.88 [0.69, 1.13]
Total events: 95 (Repeat),	, 103 (Single)				
Test for heterogeneity chi	i-square=0.98 df=2 p=	0.61 2 =0.0%			
Test for overall effect z=0).99 p=0.3				
16 In babies where plann	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.02. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 02 Severe lung disease

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

 ${\hbox{\it Comparison:}} \quad \hbox{\it O1 Repeat doses of corticosteroids versus single course}$

Outcome: 02 Severe lung disease

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all babies					
Crowther 2006	65/567	114/577	-	62.3	0.58 [0.44, 0.77]
Guinn 2002	38/255	57/245	-	32.1	0.64 [0.44, 0.93]
Wapner 2006	6/252	10/243		5.6	0.58 [0.21, 1.57]
Subtotal (95% CI)	1074	1065	•	100.0	0.60 [0.48, 0.75]
Total events: 109 (Repeat), 181 (Single)				
Test for heterogeneity chi	-square=0.18 df=2 p=	0.91 2 =0.0%			
Test for overall effect z=4	.58 p<0.00001				
02 In babies where pregn	ancy complicated by p	reterm prelabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids	as betamethasone			
Crowther 2006	65/567	114/577	-	62.3	0.58 [0.44, 0.77]
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued)

(... Continued)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl
Guinn 2002	38/255	57/245	-	32.1	0.64 [0.44, 0.93]
Wapner 2006	6/252	10/243		5.6	0.58 [0.21, 1.57]
Subtotal (95% CI) Total events: 109 (Repeat Test for heterogeneity chi Test for overall effect z=4	-square=0.18 df=2 p=	1065 0.91 ² =0.0%	•	100.0	0.60 [0.48, 0.75]
04 In babies exposed to r Crowther 2006	repeat corticosteroids a	at a minimum interval of 7 o	days or less	62.3	0.58 [0.44, 0.77]
Guinn 2002	38/255	57/245	-	32.1	0.64 [0.44, 0.93]
Wapner 2006	6/252	10/243		5.6	0.58 [0.21, 1.57]
Subtotal (95% CI) Total events: 109 (Repeat Test for heterogeneity chi Test for overall effect z=4	-square=0.18 df=2 p=	0.91 2 =0.0%	•	100.0	0.60 [0.48, 0.75]
05 In babies exposed to r Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	0 0 (Single) ot applicable	it a minimum interval betw 0	een 8 and 14 days	0.0	Not estimable
06 In babies exposed to r Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	0 O (Single) ot applicable	at a minimum interval of > 0	14 days	0.0	Not estimable
07 In babies exposed to a Subtotal (95% CI) Total events: 0 (Repeat), (Test for heterogeneity: no Test for overall effect: not	one repeat course of p 0 0 (Single) of applicable	renatal corticosteroids 0		0.0	Not estimable
08 In babies exposed to t Subtotal (95% CI) Total events: 0 (Repeat), (Test for heterogeneity: no Test for overall effect: not	owo repeat courses of p 0 0 (Single) ot applicable	orenatal corticosteroids 0		0.0	Not estimable
09 In babies exposed to t Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	three repeat courses of 0 0 (Single) of applicable	prenatal corticosteroids 0		0.0	Not estimable
10 In babies exposed to f	our or more repeat co	urses of prenatal corticoste	eroids		
			0.1 0.2 0.5 2 5 10		,
			Favours repeat Favours single		(Continued)

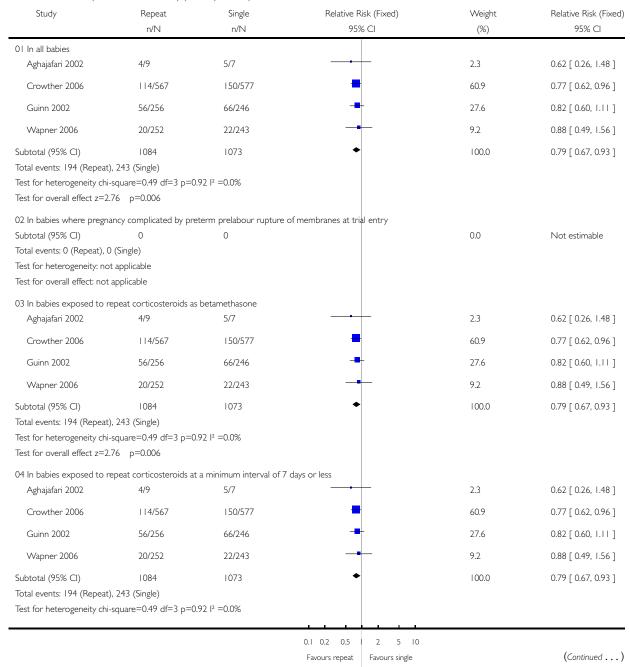
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% CI
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)	-			
Test for heterogeneity: no	, , ,				
Test for overall effect: not	• •				
II la babias ubasa alama		sauma 12 mag an lasa af h	antamathanan an an ini islant		
Crowther 2006	65/567	114/577	petamethasone or equivalent	100.0	0.58 [0.44, 0.77]
	03/30/			100.0	0.50 [0.11, 0.77]
Subtotal (95% CI)	567	577	•	100.0	0.58 [0.44, 0.77]
Total events: 65 (Repeat),	, -,				
Test for heterogeneity: no					
Test for overall effect z=3.	./9 p=0.0002				
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 mg	g or less of betamethasone or equivale	ent	
Guinn 2002	38/255	57/245		85.1	0.64 [0.44, 0.93]
Wapner 2006	6/252	10/243		14.9	0.58 [0.21, 1.57]
Subtotal (95% CI)	507	488	•	100.0	0.63 [0.45, 0.89]
Total events: 44 (Repeat),	67 (Single)				
Test for heterogeneity chi-	-square=0.04 df=1 p=	0.85 I ² =0.0%			
Test for overall effect z=2.					
13 In babies where planne	ed dose per treatment	course > 24 mg of hetan	nethasone or equivalent		
Subtotal (95% CI)	0	0	netriasorie or equivalent	0.0	Not estimable
Total events: 0 (Repeat), 0		· ·		0.0	1 40t estimasie
Test for heterogeneity: no					
Test for overall effect: not					
		12			
•		-	k of betamethasone or equivalent	100.0	0.50.50.44.077.7
Crowther 2006	65/567	114/577	-	100.0	0.58 [0.44, 0.77]
Subtotal (95% CI)	567	577	•	100.0	0.58 [0.44, 0.77]
Total events: 65 (Repeat),	114 (Single)				
Test for heterogeneity: no	• •				
Test for overall effect z=3.	79 p=0.0002				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equ	ivalent	
Guinn 2002	38/255	57/245	-	85.1	0.64 [0.44, 0.93]
Wapner 2006	6/252	10/243		14.9	0.58 [0.21, 1.57]
Subtotal (95% CI)	507	488	•	100.0	0.63 [0.45, 0.89]
Total events: 44 (Repeat),		100		100.0	0.03 [0.13, 0.07]
Test for heterogeneity chi-		0.85 12 =0.0%			
Test for overall effect z=2.		0.05 1 0.070			
		on was > 24	betamethasone or equivalent		
·	ed repeat drug exposu 0	re was > 24 mg/week or i	detamethasone or equivalent	0.0	Not estimable
Subtotal (95% CI) Total events: 0 (Repeat), 0		U		0.0	i not estimable
Test for heterogeneity: no					
Test for overall effect: not					
rest for overall effect. Hot	аррисаотс				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.03. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 03 Composite serious morbidity (variously defined)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 03 Composite serious morbidity (variously defined)



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

(... Continued)

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for overall effect z=2.76		11/11	7570 CI	(70)	75/0 CI
	•				
05 In babies exposed to rep			ween 8 and 14 days	0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (- /				
Test for heterogeneity: not a					
Test for overall effect: not ap	pplicable				
06 In babies exposed to rep	eat corticosteroids a	t a minimum interval of >	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	plicable				
07 In babies exposed to one	e repeat course of pr	enatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a					
Test for overall effect: not ap					
·					
08 In babies exposed to two				0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not a	• •				
Test for overall effect: not ap	pplicable				
09 In babies exposed to the	ee repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	pplicable				
10 In babies exposed to fou	r or more repeat cou	urses of prenatal corticos	teroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (-			
Test for heterogeneity: not a	- /				
Test for overall effect: not ap					
•		-	etamethasone or equivalent	100.0	077.50/2.00/3
Crowther 2006	114/567	150/577	•	100.0	0.77 [0.62, 0.96]
Subtotal (95% CI)	567	577	•	100.0	0.77 [0.62, 0.96]
Total events: 114 (Repeat),	I 50 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect z=2.35	p=0.02				
12 In babies where planned	dose per treatment	course > 12 mg to 24 mg	g or less of betamethasone or equivale	nt	
Aghajafari 2002	4/9	5/7		5.9	0.62 [0.26, 1.48]
Guinn 2002	56/256	66/246	_	70.6	0.82 [0.60, 1.11]
Guiiii 2002	30,230	00/210		, 0.0	0.02 [0.00, 1.11]
<u> </u>			0.1 0.2 0.5 2 5 10		
					(Continued)

					(**************************************
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Wapner 2006	20/252	22/243	_	23.5	0.88 [0.49, 1.56]
Subtotal (95% CI)	517	496	•	100.0	0.82 [0.63, 1.07]
Total events: 80 (Repeat)	, 93 (Single)				
Test for heterogeneity ch	i-square=0.44 df=2 p=	0.80 I ² =0.0%			
Test for overall effect z=1	1.49 p=0.1				
13 In babies where plann	ed dose per treatment	course > 24 mg of betar	methasone or equivalent		
Subtotal (95% CI)	0	0	·	0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
14 In babies where plann	ed repeat drug exposu	re was 12 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	114/567	150/577	<u>=</u>	100.0	0.77 [0.62, 0.96]
Subtotal (95% CI)	567	577	•	100.0	0.77 [0.62, 0.96]
Total events: 114 (Repeat	t), 150 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=2	2.35 p=0.02				
15 In babies where plann	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent	
Aghajafari 2002	4/9	5/7		5.9	0.62 [0.26, 1.48]
Guinn 2002	56/256	66/246	-	70.6	0.82 [0.60, .]
Wapner 2006	20/252	22/243	-	23.5	0.88 [0.49, 1.56]
Subtotal (95% CI)	517	496	•	100.0	0.82 [0.63, 1.07]
Total events: 80 (Repeat)	, 93 (Single)				
Test for heterogeneity chi	i-square=0.44 df=2 p=	0.80 I ² =0.0%			
Test for overall effect z=1	I.49 p=0.1				
16 In babies where plann	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
					_
			0.1 0.2 0.5 2 5 10		

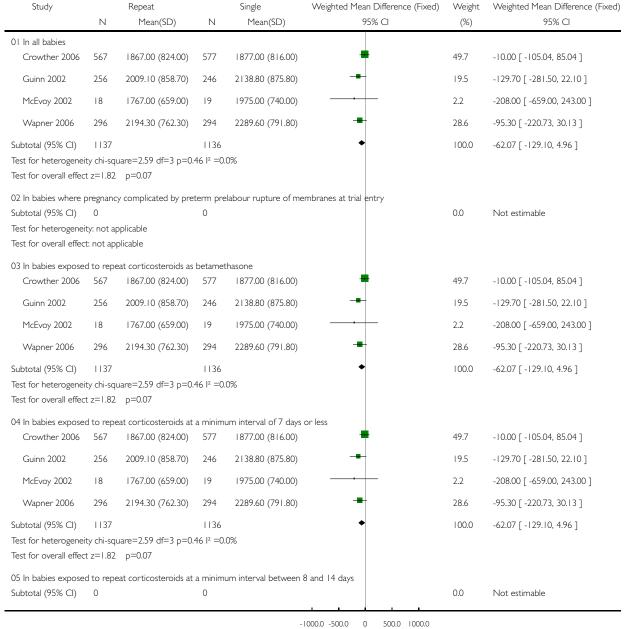
Favours repeat Favours single

Analysis 01.04. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 04 Mean birthweight (g)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 04 Mean birthweight (g)



Favours single Favours repeat (Continued . . .)

							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed 95% CI) Weight (%)	Weighted Mean Difference (Fixed 95% CI
Test for heterogenei Test for overall effect	,						
06 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 ty: not a		a minim	um interval of > 14	days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogenei Test for overall effect	0 ty: not a		natal cor 0	rticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI) Test for heterogeneid Test for overall effect	0 ty: not a		enatal co O	orticosteroids		0.0	Not estimable
09 In babies exposed Subtotal (95% CI) Test for heterogenei Test for overall effect	0 ty: not a		orenatal o	corticosteroids		0.0	Not estimable
10 In babies exposed Wapner 2006	d to foui	r or more repeat cour 2399.60 (650.60)	ses of p	renatal corticosteroi 2560.60 (617.00)	ds -	100.0	-161.00 [-290.52, -31.48]
Subtotal (95% CI) Test for heterogeneit Test for overall effect	,		177		•	100.0	-161.00 [-290.52, -31.48]
II In babies where p	olanned 567	dose per treatment co	ourse 12 577	mg or less of betam 1877.00 (816.00)	ethasone or equivalent	100.0	-10.00 [-105.04, 85.04]
Subtotal (95% CI) Test for heterogeneit Test for overall effect	567 ty: not a	pplicable	577	1077100 (0.000)	•	100.0	-10.00 [-105.04, 85.04]
12 In babies where p	olanned 256	dose per treatment co 2009.10 (858.70)	ourse >	12 mg to 24 mg or I 2138.80 (875.80)	ess of betamethasone or equivalent	38.8	12070 [20150 22101
McEvoy 2002	18	1767.00 (659.00)	19	1975.00 (740.00)		4.4	-129.70 [-281.50, 22.10] -208.00 [-659.00, 243.00]
Wapner 2006	296	2194.30 (762.30)	294	2289.60 (791.80)	-	56.8	-95.30 [-220.73, 30.13]
Subtotal (95% CI)	570 ty chi-sq	uare=0.29 df=2 p=0.	559	, ,	•	100.0	-113.60 [-208.14, -19.05]
13 In babies where p Subtotal (95% CI) Test for heterogenei Test for overall effect	0 ty: not a		ourse >	24 mg of betametha	sone or equivalent	0.0	Not estimable
					-1000.0 -500.0 0 500.0 1000.0 Favours single Favours repeat		(Continued

Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
14 In babies where	planned r	repeat drug exposure	was 12	mg or less/week of b	etamethasone or equivalent		
Crowther 2006	567	1867.00 (824.00)	577	1877.00 (816.00)	•	100.0	-10.00 [-105.04, 85.04]
Subtotal (95% CI)	567		577		•	100.0	-10.00 [-105.04, 85.04]
Test for heterogene	ity: not ap	pplicable					
Test for overall effect	t z=0.21	p=0.8					
15 In babies where	planned r	repeat drug exposure	was >	2 mg/week to 24 mg	/week of betamethasone or equivalent	:	
Guinn 2002	256	2009.10 (858.70)	246	2138.80 (875.80)	-	38.8	-129.70 [-281.50, 22.10]
McEvoy 2002	18	1767.00 (659.00)	19	1975.00 (740.00)		4.4	-208.00 [-659.00, 243.00]
Wapner 2006	296	2194.30 (762.30)	294	2289.60 (791.80)	-	56.8	-95.30 [-220.73, 30.13]
Subtotal (95% CI)	570		559		•	100.0	-113.60 [-208.14, -19.05]
Test for heterogene	ity chi-squ	uare=0.29 df=2 p=0.	86 I ² =0.	0%			
Test for overall effect	t z=2.35	p=0.02					
16 In babies where	planned r	repeat drug exposure	was > 2	24 mg/week of betam	ethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogene	ity: not ap	pplicable					
Test for overall effect	t: not app	olicable					
				-	1000.0 -500.0 0 500.0 1000.0		

Favours repeat

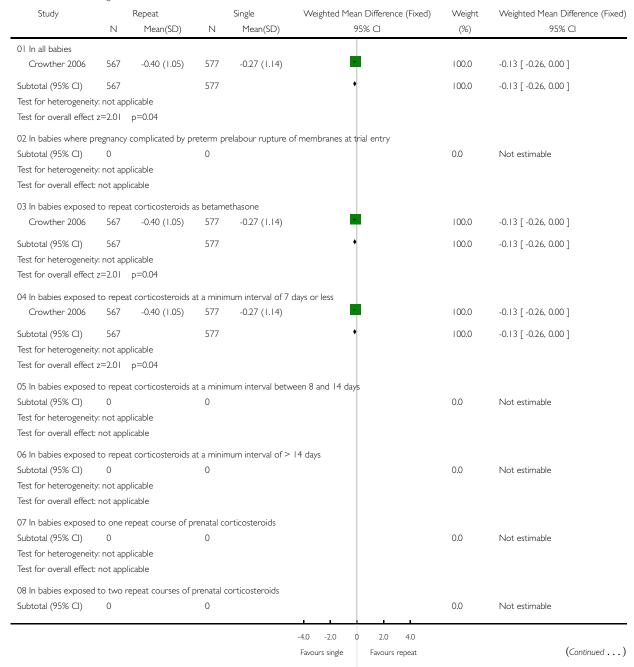
Favours single

Analysis 01.05. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 05 Birthweight Z scores

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 05 Birthweight Z scores



							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Test for heterogeneity Test for overall effect:							
09 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	prenatal 0	corticosteroids		0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	urses of p	orenatal corticost	eroids	0.0	Not estimable
II In babies where pl Crowther 2006	anned do 567	se per treatment -0.40 (1.05)	course 1	2 mg or less of be -0.27 (1.14)	etamethasone or equivalent	100.0	-0.13 [-0.26, 0.00]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			577		•	100.0	-0.13 [-0.26, 0.00]
12 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	course >	12 mg to 24 mg	or less of betamethasone or equivalent	0.0	Not estimable
13 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	course >	24 mg of betam	ethasone or equivalent	0.0	Not estimable
14 In babies where pl Crowther 2006	anned rep 567	peat drug exposul -0.40 (1.05)	re was 12 577	. mg or less/week -0.27 (1.14)	of betamethasone or equivalent	100.0	-0.13 [-0.26, 0.00]
Subtotal (95% CI) Test for heterogeneity Test for overall effect		licable	577	` ,	•	100.0	-0.13 [-0.26, 0.00]
15 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	licable	re was > 0	12 mg/week to 2	4 mg/week of betamethasone or equiva	lent 0.0	Not estimable
16 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	licable	re was > 0	24 mg/week of b	etamethasone or equivalent	0.0	Not estimable
					-4.0 -2.0 0 2.0 4.0 Favours single Favours repeat		

Analysis 01.06. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 06 Birthweight multiples of the median

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 06 Birthweight multiples of the median

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies							_
Wapner 2006	296	0.88 (0.16)	294	0.88 (0.15)	•	100.0	0.00 [-0.03, 0.03]
Subtotal (95% CI)	296		294			100.0	0.00 [-0.03, 0.03]
Test for heterogeneit Test for overall effect	,						
02 In babies where p	regnancy	complicated by p	reterm pi	relabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effect							
03 In babies exposed	d to repea	t corticosteroids	as betame	ethasone			
Wapner 2006	296	0.88 (0.16)	294	0.88 (0.15)		100.0	0.00 [-0.03, 0.03]
Subtotal (95% CI)	296		294			100.0	0.00 [-0.03, 0.03]
Test for heterogeneit Test for overall effect	,						
04 In babies exposed	d to repea	t corticosteroids	at a minir	num interval of 7	days or less		
Wapner 2006	296	0.88 (0.16)	294	0.88 (0.15)		100.0	0.00 [-0.03, 0.03]
Subtotal (95% CI)	296		294			100.0	0.00 [-0.03, 0.03]
Test for heterogeneit Test for overall effect							
05 In babies exposed	d to repea	t corticosteroids	at a minir	num interval bet	ween 8 and 14 days		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect							
06 In babies exposed	d to repea 0	t corticosteroids	at a minir 0	num interval of >	14 days	0.0	Not estimable
Subtotal (95% CI) Test for heterogeneit		olicable	U			0.0	Not estimable
Test for overall effect							
07 In babies exposed	d to one r	epeat course of p	orenatal co	orticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect							
08 In babies exposed Subtotal (95% CI)	d to two r 0	epeat courses of	prenatal o	corticosteroids		0.0	Not estimable
3UULULAI (73/6 CI)	U		U			0.0	ואטנ פגנוווומטופ
					-4.0 -2.0 0 2.0 4.0		(5)
					Favours repeat Favours single		(Continued)

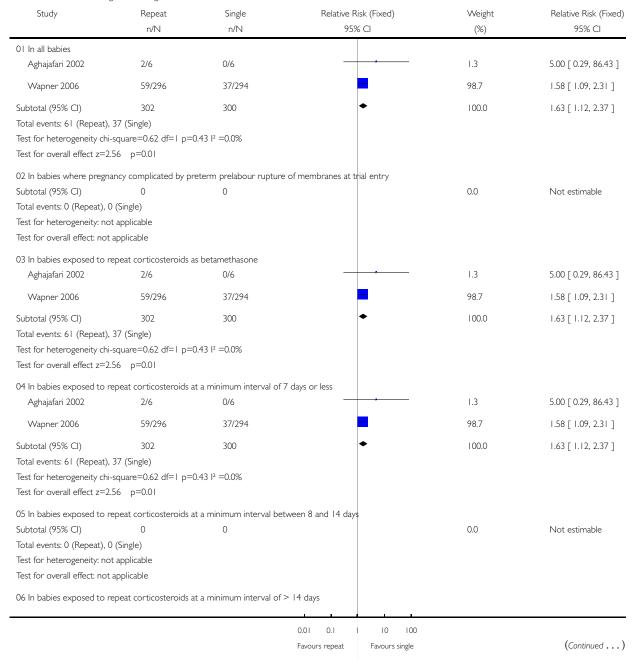
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneit Test for overall effect							
09 In babies exposed Subtotal (95% CI)	I to three 0	repeat courses c	of prenatal 0	corticosteroids		0.0	Not estimable
Test for heterogeneit		plicable	O			0.0	Not estimable
Test for overall effect	: not app	licable					
10 In babies exposed	I to four	or more repeat co	ourses of	prenatal corticos	teroids		
Wapner 2006	191	0.86 (0.15)	177	0.90 (0.14)		100.0	-0.04 [-0.07, -0.01]
Subtotal (95% CI)	191		177			100.0	-0.04 [-0.07, -0.01]
Test for heterogeneit	y: not app	plicable					
Test for overall effect	z=2.65	p=0.008					
		ose per treatmen		2 mg or less of b	petamethasone or equivalent		
Subtotal (95% CI) Test for heterogeneit	0	alicable	0			0.0	Not estimable
Test for overall effect							
			t course >	12 mg to 24 mg	g or less of betamethasone or equivalent		
Wapner 2006	296	0.88 (0.16)	294	0.88 (0.15)	g of less of betainethasone of equivalent	100.0	0.00 [-0.03, 0.03]
Subtotal (95% CI)	296	` ′	294	, ,		100.0	0.00 [-0.03, 0.03]
Test for heterogeneit		plicable	271			100.0	0.00 [-0.05, 0.05]
Test for overall effect	z=0.00	p=I					
13 In babies where p	lanned do	ose per treatmen	t course >	> 24 mg of betan	nethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect							
14 In babies where p Subtotal (95% CI)	lanned re 0	epeat drug exposi	ure was 1: 0	2 mg or less/wee	k of betamethasone or equivalent	0.0	Not estimable
Test for heterogeneit		plicable	O			0.0	NOT ESTIMABLE
Test for overall effect	: not app	licable					
15 In babies where p	lanned re	epeat drug exposi	ure was >	12 mg/week to	24 mg/week of betamethasone or equiva	alent	
Wapner 2006	296	0.88 (0.16)	294	0.88 (0.15)		100.0	0.00 [-0.03, 0.03]
Subtotal (95% CI)	296		294			100.0	0.00 [-0.03, 0.03]
Test for heterogeneit							
Test for overall effect	z=0.00	p=I					
•		epeat drug exposi		24 mg/week of I	petamethasone or equivalent		
Subtotal (95% CI) Test for heterogeneit	0	alicable	0			0.0	Not estimable
Test for overall effect							
	- Ir F						
					-4.0 -2.0 0 2.0 4.0		
					Favours repeat Favours single		

Analysis 01.07. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 07 Small-forgestational age at birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 07 Small-for-gestational age at birth



Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	t applicable	0		0.0	Not estimable
07 In babies exposed to of Subtotal (95% CI) Total events: 0 (Repeat), Of Test for heterogeneity: no Test for overall effect: not	0 O (Single) ot applicable	renatal corticosteroids 0		0.0	Not estimable
08 In babies exposed to t		aranatal continectoroids			
Subtotal (95% CI) Total events: 0 (Repeat), (Test for heterogeneity: no Test for overall effect: not	0 O (Single) ot applicable	0		0.0	Not estimable
09 In babies exposed to t Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	0 O (Single) ot applicable	prenatal corticosteroids 0		0.0	Not estimable
10 In babies exposed to f	our or more repeat co	urses of prenatal cortico	steroids		
Wapner 2006	50/191	27/177	=	100.0	1.72 [1.13, 2.61]
Subtotal (95% CI) Total events: 50 (Repeat), Test for heterogeneity: no Test for overall effect z=2	t applicable	177	•	100.0	1.72 [1.13, 2.61]
II In babies where planne	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	0 O (Single) ot applicable	0		0.0	Not estimable
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 r	ng or less of betamethasone or equivale	nt	
Aghajafari 2002	2/6	0/6	-	1.3	5.00 [0.29, 86.43]
Wapner 2006	59/296	37/294	<u>-</u>	98.7	1.58 [1.09, 2.31]
Subtotal (95% CI) Total events: 61 (Repeat), Test for heterogeneity chi Test for overall effect z=2	-square=0.62 df=1 p=	300 0.43 ² =0.0%	•	100.0	1.63 [1.12, 2.37]
13 In babies where planno Subtotal (95% CI) Total events: 0 (Repeat), (Test for heterogeneity: no	0 O (Single)	course > 24 mg of beta 0	methasone or equivalent	0.0	Not estimable
			001 01 10 100		
			0.01 0.1 1 10 100 Favours repeat Favours single		(Continued

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/we	ek of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent	
Aghajafari 2002	2/6	0/6	-	1.3	5.00 [0.29, 86.43]
Wapner 2006	59/296	37/294		98.7	1.58 [1.09, 2.31]
Subtotal (95% CI)	302	300	•	100.0	1.63 [1.12, 2.37]
Total events: 61 (Repeat),	37 (Single)				
Test for heterogeneity chi-	-square=0.62 df=1 p=0	0.43 I ² =0.0%			
Test for overall effect z=2.	56 p=0.01				
16 In babies where planne	ed repeat drug exposu	re was >24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.01 0.1 1 10 100		

Favours repeat

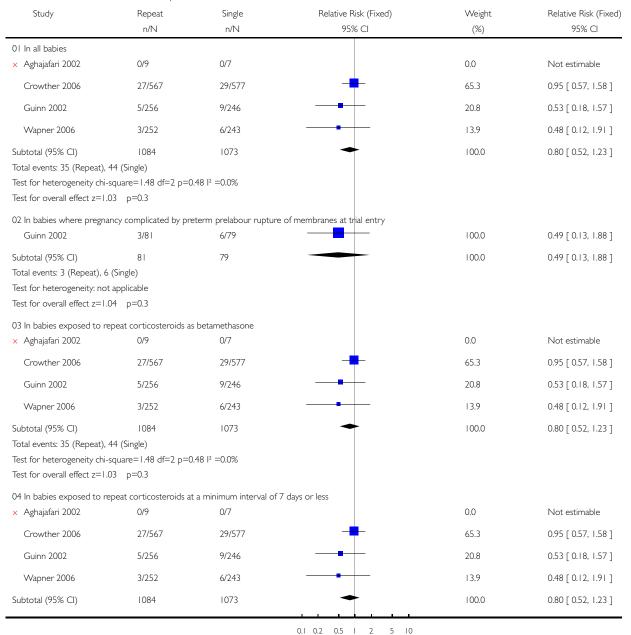
Favours single

Analysis 01.08. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 08 Fetal and neonatal mortality

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 08 Fetal and neonatal mortality



Favours single

Favours repeat

(Continued ...)

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl	
Total events: 35 (Repeat), 4 Test for heterogeneity chi-s Test for overall effect z=1.0	square=1.48 df=2 p=	0.48 ² =0.0%				
05 In babies exposed to re Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	0 (Single) applicable	it a minimum interval bet 0	tween 8 and 14 days	0.0	Not estimable	
06 In babies exposed to re Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	0 (Single) applicable	t a minimum interval of 3	> 14 days	0.0	Not estimable	
07 In babies exposed to or Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	ne repeat course of p 0 (Single) applicable	renatal corticosteroids 0		0.0	Not estimable	
08 In babies exposed to tw Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not	vo repeat courses of p 0 (Single) applicable	orenatal corticosteroids 0		0.0	Not estimable	
Test for overall effect: not a 09 In babies exposed to th Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	ree repeat courses of 0 (Single) applicable	prenatal corticosteroids 0		0.0	Not estimable	
10 In babies exposed to fo Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	ur or more repeat co 0 (Single) applicable	urses of prenatal cortico: 0	steroids	0.0	Not estimable	
		course 12 mg or less of 1 29/577	betamethasone or equivalent	100.0	0.95 [0.57, 1.58]	
Subtotal (95% CI) Total events: 27 (Repeat), 2 Test for heterogeneity: not Test for overall effect z=0.2	applicable	577	+	100.0	0.95 [0.57, 1.58]	
12 In babies where planned × Aghajafari 2002	d dose per treatment 0/9	course > 12 mg to 24 m 0/7	ng or less of betamethasone or equivalen	t 0.0	Not estimable	
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		(Continued)	

					(Continued
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Guinn 2002	5/256	9/246		60.0	0.53 [0.18, 1.57]
Wapner 2006	3/252	6/243		40.0	0.48 [0.12, 1.91]
Subtotal (95% CI)	517	496	-	100.0	0.51 [0.22, 1.20]
Total events: 8 (Repeat),	15 (Single)				
Test for heterogeneity chi	-square=0.01 df=1 p=	0.9 l l ² =0.0%			
Test for overall effect z=1	.54 p=0.1				
13 In babies where planne	ed dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/we	eek of betamethasone or equivalent		
Crowther 2006	27/567	29/577	-	100.0	0.95 [0.57, 1.58]
Subtotal (95% CI)	567	577	•	100.0	0.95 [0.57, 1.58]
Total events: 27 (Repeat),	29 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	.21 p=0.8				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equi	valent	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Guinn 2002	5/256	9/246		60.0	0.53 [0.18, 1.57]
Wapner 2006	3/252	6/243		40.0	0.48 [0.12, 1.91]
Subtotal (95% CI)	517	496	-	100.0	0.51 [0.22, 1.20]
Total events: 8 (Repeat),	I5 (Single)				
Test for heterogeneity chi	-square=0.01 df=1 p=	0.9 l l² =0.0%			
Test for overall effect $z=1$.54 p=0.1				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week o	f betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 1 2 5 10		

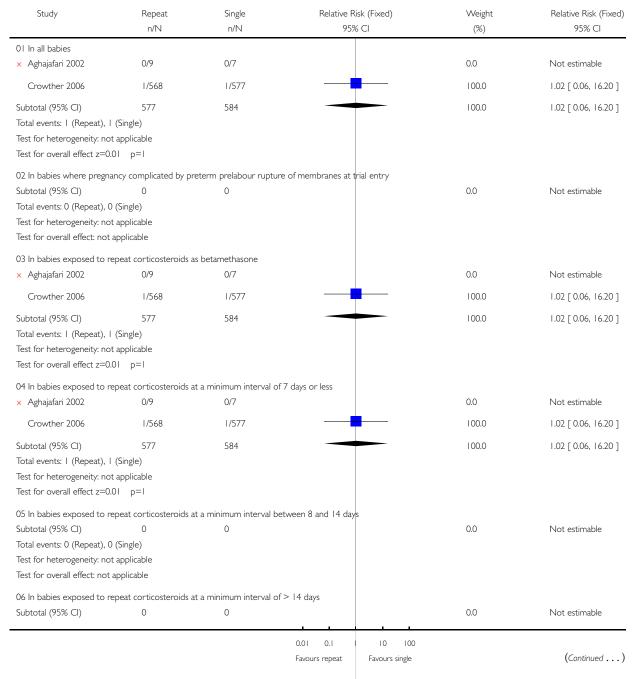
0.1 0.2 0.5 | 2 5 10 Favours repeat Favours single

Analysis 01.09. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 09 Fetal death

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 09 Fetal death



					(Condinued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Total events: 0 (Repeat), 0	, - ,				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
07 In babies exposed to o	one repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
08 In babies exposed to t	wo repeat courses of p	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
00 la babies avenued to t	buss uspect services of	Connected continues to unide			
09 In babies exposed to t Subtotal (95% CI)	nree repeat courses of: 0	prenatal corticosteroids 0		0.0	Not estimable
Total events: 0 (Repeat), (U		0.0	NOT estimable
Test for heterogeneity: no					
Test for overall effect: not					
lest for overall effect. Hot	. аррпсавіе				
10 In babies exposed to f	our or more repeat co	•	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
I I In babies where planne	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Crowther 2006	1/568	1/577		100.0	1.02 [0.06, 16.20]
Subtotal (95% CI)	568	577		100.0	1.02 [0.06, 16.20]
Total events: I (Repeat),		377		100.0	1.02 [0.00, 10.20]
Test for heterogeneity: no	, - ,				
Test for overall effect z=0					
	•				
			ng or less of betamethasone or equivaler		
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Subtotal (95% CI)	9	7		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
13 In habies where plans	ed dose per treatment	course > 24 mg of hoto	methasone or equivalent		
13 In babies where plann Subtotal (95% CI)	ed dose per treatment 0	Course > 24 mg of Detai	поставоне от ециманент	0.0	Not estimable
Total events: 0 (Repeat), (Ŭ		5.5	1 voc estimable
Test for heterogeneity: no					
Test for overall effect: not					
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/wee	ek of betamethasone or equivalent		
			0.01 0.1 10 100		(6 : 1
			Favours repeat Favours single		(Continued)



Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Crowther 2006	1/568	1/577		100.0	1.02 [0.06, 16.20]
Subtotal (95% CI)	568	577		100.0	1.02 [0.06, 16.20]
Total events: I (Repeat), I	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0.	01 p=1				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week t	o 24 mg/week of betamethasone or	equivalent	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Subtotal (95% CI)	9	7		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week c	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.01 0.1 10 10	0	
			Favours repeat Favours single	:	

Analysis 01.10. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 10 Neonatal death

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 10 Neonatal death

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all babies					
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Crowther 2006	26/567	28/577	+	100.0	0.94 [0.56, 1.59]
Subtotal (95% CI)	576	584	-	100.0	0.94 [0.56, 1.59]
Total events: 26 (Repeat),	28 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0.	21 p=0.8				
02 In babies where pregna	ancy complicated by pr	eterm prelabour ruptur	re of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued)

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl	
Test for heterogeneity: not	applicable					
Test for overall effect: not a	pplicable					
03 In babies exposed to re	oeat corticosteroids a	s betamethasone				
× Aghajafari 2002	0/9	0/7		0.0	Not estimable	
Crowther 2006	26/567	28/577	-	100.0	0.94 [0.56, 1.59]	
Subtotal (95% CI) Total events: 26 (Repeat), 2 Test for heterogeneity: not Test for overall effect z=0.2	applicable	584		100.0	0.94 [0.56, 1.59]	
04 In babies exposed to rep	peat corticosteroids a	t a minimum interval of	7 days or less			
× Aghajafari 2002	0/9	0/7		0.0	Not estimable	
Crowther 2006	26/567	28/577	-	100.0	0.94 [0.56, 1.59]	
Subtotal (95% CI) Total events: 26 (Repeat), 2 Test for heterogeneity: not Test for overall effect z=0.2	applicable	584		100.0	0.94 [0.56, 1.59]	
05 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	0 (Single) applicable	t a minimum interval bet 0	ween 8 and 14 days	0.0	Not estimable	
06 In babies exposed to rep	peat corticosteroids a	t a minimum interval of	> 14 days			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable	0		0.0	Not estimable	
07 In babies exposed to on Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not	0 (Single) applicable	renatal corticosteroids 0		0.0	Not estimable	
Test for overall effect: not a	pplicable					
08 In babies exposed to tw Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not	0 (Single) applicable	orenatal corticosteroids 0		0.0	Not estimable	
Test for overall effect: not a	pplicable					
09 In babies exposed to the Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not	0 (Single)	prenatal corticosteroids 0		0.0	Not estimable	
			0.1 0.2 0.5 1 2 5 10			
			Favours repeat Favours single		(Continued)	

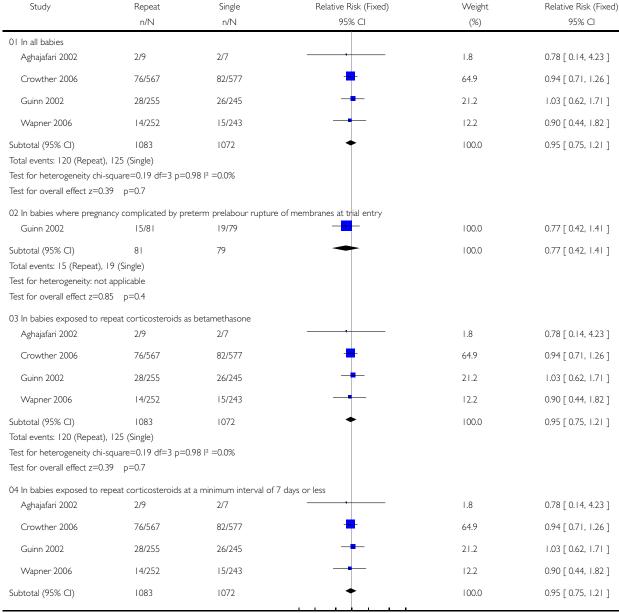
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for overall effect: not a	applicable			. , ,	
10 In babies exposed to fo	our or more repeat co	urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0	ster ords	0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
I I In babies where planne	d dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Crowther 2006	26/567	28/577	-	100.0	0.94 [0.56, 1.59]
Subtotal (95% CI)	567	577	•	100.0	0.94 [0.56, 1.59]
Total events: 26 (Repeat),	28 (Single)				
Test for heterogeneity: not	/				
Test for overall effect z=0.3					
I 2 In babies where planne	d dose per treatment	course > 12 mg to 24 m	ng or less of betamethasone or equivaler	nt	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Subtotal (95% CI)	9	7		0.0	Not estimable
Total events: 0 (Repeat), 0		,		0.0	1 VOE CSUITIADIC
Test for heterogeneity: not	, ,				
Test for overall effect: not					
13 In babies where planne	d dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
14 In babies where planne	d repeat drug exposu	re was 12 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	26/567	28/577	-	100.0	0.94 [0.56, 1.59]
Subtotal (95% CI)	567	577	•	100.0	0.94 [0.56, 1.59]
Total events: 26 (Repeat),	28 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.2	21 p=0.8				
15 In babies where planne	d repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Subtotal (95% CI)	9	7		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
l 6 In babies where planne	d repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		

Analysis 01.11. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 11 Chronic lung disease

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: II Chronic lung disease



0.1 0.2 0.5 | 2 5 10

Favours repeat Favours single (Continued . . .)

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% CI
Total events: 120 (Repeat), 12		101 4	7370 GI	(70)	7970 CI
Test for heterogeneity chi-squ		0.98 12 =0.0%			
Test for overall effect $z=0.39$		0.701 -0.070			
	•				
05 In babies exposed to repe			ween 8 and 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si	0 ,				
Test for heterogeneity: not ap	•				
Test for overall effect: not app	olicable				
06 In babies exposed to repe	at corticosteroids	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si	ngle)				
Test for heterogeneity: not ap	plicable				
Test for overall effect: not app	olicable				
071.1.1.					
07 In babies exposed to one i				2.2	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si					
Test for heterogeneity: not ap					
Test for overall effect: not app	olicable				
08 In babies exposed to two	repeat courses of	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si	ngle)				
Test for heterogeneity: not ap	plicable				
Test for overall effect: not app	olicable				
09 In babies exposed to three	e reneat courses o	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si		· ·		0.0	1 VOE CSUITIABLE
Test for heterogeneity: not ap					
Test for overall effect: not app					
10 In babies exposed to four		•	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Si					
Test for heterogeneity: not ap					
Test for overall effect: not app	olicable				
I I In babies where planned d	lose per treatment	course 12 mg or less of I	petamethasone or equivalent		
Crowther 2006	76/567	82/577	-	100.0	0.94 [0.71, 1.26]
Subtatal (95% CI)	567	577	•	100.0	0945071 1277
Subtotal (95% CI)		311		100.0	0.94 [0.71, 1.26]
Total events: 76 (Repeat), 82	/				
Test for heterogeneity: not ap Test for overall effect z=0.40	•				
rest for overall effect 2—0.40	p=0.7				
12 In babies where planned d			g or less of betamethasone or equivaler		
Aghajafari 2002	2/9	2/7	•	5.1	0.78 [0.14, 4.23]
			0.1 0.2 0.5 2 5 10		,
			Favours repeat Favours single		(Continued

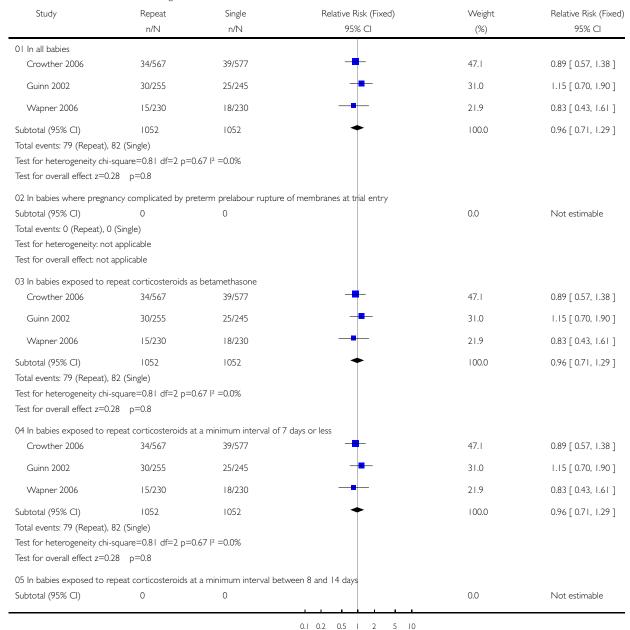
					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Guinn 2002	28/255	26/245	-	60.2	1.03 [0.62, 1.71]
Wapner 2006	14/252	15/243	_	34.7	0.90 [0.44, 1.82]
Subtotal (95% CI)	516	495	•	100.0	0.97 [0.65, 1.45]
Total events: 44 (Repeat),					
Test for heterogeneity chi-	` 0 /	0.92 2 =0.0%			
Test for overall effect z=0.					
13 In babies where planne	d dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
14 In babies where planne	d repeat drug exposul	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	76/567	82/577	-	100.0	0.94 [0.71, 1.26]
Subtotal (95% CI)	567	577	+	100.0	0.94 [0.71, 1.26]
Total events: 76 (Repeat),	82 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.4	40 p=0.7				
15 In babies where planne	d repeat drug exposui	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent	
Aghajafari 2002	2/9	2/7		5.1	0.78 [0.14, 4.23]
Guinn 2002	28/255	26/245	+	60.2	1.03 [0.62, 1.71]
Wapner 2006	14/252	15/243	-	34.7	0.90 [0.44, 1.82]
Subtotal (95% CI)	516	495	+	100.0	0.97 [0.65, 1.45]
Total events: 44 (Repeat),	43 (Single)				
Test for heterogeneity chi-	square=0.17 df=2 p=0	0.92 2 =0.0%			
Test for overall effect z=0.	13 p=0.9				
16 In babies where planne	d repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 1 2 5 10		

Analysis 01.13. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 13 Periventricular haemorrhage

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 13 Periventricular haemorrhage



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours repeat

Favours single

(Continued ...)

					(Continued
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% Cl
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a					
Test for overall effect: not ap	pplicable				
06 In babies exposed to rep	eat corticosteroids a	t a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	oplicable				
07 In babies exposed to one	e repeat course of pr	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	oplicable				
08 In babies exposed to two	o repeat courses of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	oplicable				
09 In babies exposed to thr	ee repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	oplicable				
10 In babies exposed to fou	ır or more repeat co	urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	oplicable				
II In babies where planned	dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Crowther 2006	34/567	39/577	+	100.0	0.89 [0.57, 1.38]
Subtotal (95% CI)	567	577	-	100.0	0.89 [0.57, 1.38]
Total events: 34 (Repeat), 39	9 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect z=0.53	3 p=0.6				
12 In babies where planned	dose per treatment	course > 12 mg to 24 m	ng or less of betamethasone or equivaler	nt	
Guinn 2002	30/255	25/245	-	58.6	1.15 [0.70, 1.90]
Wapner 2006	15/230	18/230	-	41.4	0.83 [0.43, 1.61]
Subtotal (95% CI)	485	475	+	100.0	1.02 [0.69, 1.52]
Total events: 45 (Repeat), 43	3 (Single)				-
Test for heterogeneity chi-sc	quare=0.59 df=1 p=0	0.44 l² =0.0%			
Test for overall effect z=0.10) p=0.9				
			0.1 0.2 0.5 1 2 5 10		,
			Favours repeat Favours single		(Continued

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
13 In babies where plann	ed dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
14 In babies where plann	ed repeat drug exposur	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	34/567	39/577	-	100.0	0.89 [0.57, 1.38]
Subtotal (95% CI)	567	577	•	100.0	0.89 [0.57, 1.38]
Total events: 34 (Repeat)	, 39 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0).53 p=0.6				
		re was > 12 mg/week to	o 24 mg/week of betamethasone or equiv	valent	
		re was > 12 mg/week to 25/245	24 mg/week of betamethasone or equiv	valent 58.6	1.15 [0.70, 1.90]
15 In babies where plann	ed repeat drug exposur	-	24 mg/week of betamethasone or equiv		1.15 [0.70, 1.90] 0.83 [0.43, 1.61]
15 In babies where plann Guinn 2002	ed repeat drug exposur 30/255	25/245	24 mg/week of betamethasone or equiv	58.6	
15 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI)	ed repeat drug exposur 30/255 15/230 485	25/245 18/230	24 mg/week of betamethasone or equiv	58.6 41.4	0.83 [0.43, 1.61]
15 In babies where plann Guinn 2002 Wapner 2006	ed repeat drug exposur 30/255 15/230 485 , 43 (Single)	25/245 18/230 475	24 mg/week of betamethasone or equiv	58.6 41.4	0.83 [0.43, 1.61]
I5 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI) Total events: 45 (Repeat)	ed repeat drug exposur 30/255 15/230 485 , 43 (Single) i-square=0.59 df=1 p=0	25/245 18/230 475	24 mg/week of betamethasone or equiv	58.6 41.4	0.83 [0.43, 1.61]
15 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI) Total events: 45 (Repeat) Test for heterogeneity ch Test for overall effect z=0	ed repeat drug exposur 30/255 15/230 485 , 43 (Single) i-square=0.59 df=1 p=0	25/245 18/230 475 0.44 I ² =0.0%	24 mg/week of betamethasone or equiv	58.6 41.4	0.83 [0.43, 1.61]
I5 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI) Total events: 45 (Repeat) Test for heterogeneity ch Test for overall effect z=0	ed repeat drug exposur 30/255 15/230 485 , 43 (Single) i-square=0.59 df=1 p=0	25/245 18/230 475 0.44 I ² =0.0%	• • • • • • • • • • • • • • • • • • •	58.6 41.4	0.83 [0.43, 1.61]
I5 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI) Total events: 45 (Repeat) Test for heterogeneity ch Test for overall effect z=0 I6 In babies where plann Subtotal (95% CI)	ed repeat drug exposur 30/255 15/230 485 , 43 (Single) i-square=0.59 df=1 p=0 0.10 p=0.9 ed repeat drug exposur 0	25/245 18/230 475 0.44 I ² =0.0% The was > 24 mg/week of	• • • • • • • • • • • • • • • • • • •	58.6 41.4 100.0	0.83 [0.43, 1.61] 1.02 [0.69, 1.52]
15 In babies where plann Guinn 2002 Wapner 2006 Subtotal (95% CI) Total events: 45 (Repeat) Test for heterogeneity ch Test for overall effect z=0	ed repeat drug exposur 30/255 15/230 485 , 43 (Single) i-square=0.59 df=1 p=0 0.10 p=0.9 ed repeat drug exposur 0 0 (Single)	25/245 18/230 475 0.44 I ² =0.0% The was > 24 mg/week of	• • • • • • • • • • • • • • • • • • •	58.6 41.4 100.0	0.83 [0.43, 1.61] 1.02 [0.69, 1.52]

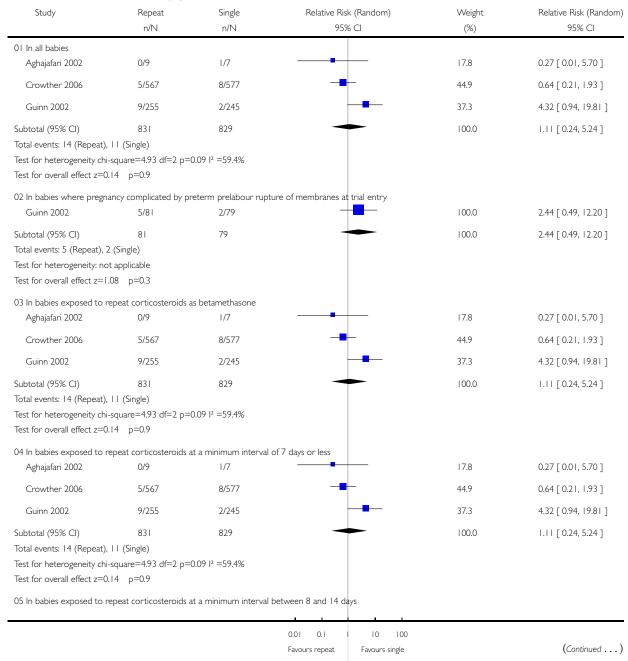
0.1 0.2 0.5 | 2 5 10 Favours repeat Favours single

Analysis 01.14. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 14 Periventricular haemorrhage grade 3/4

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 14 Periventricular haemorrhage grade 3/4



Not estimable Not estimable						(Continued	
Total events: 0 (Repeat), 0 (Single) Test for heterrogeneity: not applicable Test for heterrogeneity and applicable Test for heterrogeneity on applicable Test for heterrogeneity and applicable Test for heterrogeneity a	Study		-	· · · ·	-	Relative Risk (Random 95% CI	
Test for heterogeneity, not applicable Test for overall effect not applicable Subtoal (95% CI) 0 0 0 0 0 Not estimable Test for coverall effect not applicable Test for overall effect not applicable Test for excernage of Repeat), 0 (Single) Test for extraction (Repeat), 0 (Single) Test for overall effect not applicable Test for overall effect not applicabl	Subtotal (95% CI)	0	0		0.0	Not estimable	
Test for overall effect: not applicable 06 In bables exposed to repeat corticosteroids at a minimum interval of > 14 days Subtotal (95% C)	Total events: 0 (Repeat),	0 (Single)					
06 In babbes exposed to repeat corriscosteroids at a minimum interval of > 14 days Subtroat (95% C) 0 0 0. Not estimable Total events 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity not the process of prenatal corticosteroids Subtroat (95% C) 0 0 0. Not estimable Total events 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Tes	Test for heterogeneity: no	ot applicable					
Subtoral (95% CI) 0 0 0 0 0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for overall effect: not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not	Test for overall effect: not	t applicable					
Total events: 0 (Repeat), 0 (Single) lists for heterogeneity, not applicable 07 In babies exposed to one repeat course of prenatal corticosteroids Substraid (95% C) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) lists for heterogeneity, not applicable 1805 (1) 0 0 0 0.0 Not estimable 1805 (1) 0 0 0.0 Not estimable 1805 (1) 0 0 0.0 Not estimable 1805 (1) 0 0 0.0 Not estimable 1806 (1) 0 0 0.0 Not estimable 1806 (1) 0 0 0.0 Not estimable 1807 (1) 0 0 0.0 Not estimable 1808 (1) 0 0 0.0 Not estimable 1809 (1) babies exposed to two repeat courses of prenatal corticosteroids 1806 (1) 0 0 0.0 Not estimable 1809 (1) babies exposed to three repeat courses of prenatal corticosteroids 1806 (1) 0 0 0 0.0 Not estimable 1809 (1) babies exposed to three repeat courses of prenatal corticosteroids 1806 (1) 0 0 0 0.0 Not estimable 1807 (1) 0 0 0 0.0 Not estimable 1808 (1) 0 0 0 0.0 Not estimable 1808 (1) 0 0 0 0.0 Not estimable 1809 (1) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	06 In babies exposed to r	repeat corticosteroids	at a minimum interval	of > 14 days			
Test for heterogeneity, not applicable Test for overall effect not applicable Subtotal (5% C) 0 0 0.00 Not estimable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect	Subtotal (95% CI)	0	0		0.0	Not estimable	
Test for overall effect not applicable 07 In babies exposed to one repeat course of prenatal corticosteroids Subtotal (95% C)	Total events: 0 (Repeat),	0 (Single)					
07 In bables exposed to one repeat course of prenatal corticosteroids Subtotal (95% C)	Test for heterogeneity: no	ot applicable					
Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for neterrogeneity, not applicable Test for neterrogeneity in the subject of the subj	Test for overall effect: not	t applicable					
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect possed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0, Not estimable Test for heterogeneity not applicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for heterogeneity not applicable Test for overall effect. not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect. 2000 p=0.4 I lin bables where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93.] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity not applicable Test for overall effect z=0.80 p=0.4 I lin bables where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafan 2002 0/9 1/7 382 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 4 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity not applicable Test for heterogeneity not a	07 In babies exposed to	one repeat course of p	orenatal corticosteroids	5			
Test for heterogeneity, not applicable Test for overall effect not applicable Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betanethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 I ² =60.8%	Subtotal (95% CI)	0	0		0.0	Not estimable	
Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect in the polylicable of the properties of the pro	Total events: 0 (Repeat), (0 (Single)					
08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% C) 0 0 0 0.0 Not estimable Tistal events: 0 (Repeat), 0 (Single) Test for Note of the property, not applicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for not applicable Test for not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for not applicable Test for heterogeneity not applicable Test for hetero	Test for heterogeneity: no	ot applicable					
Subtotal (95% CI) 0 0 0 0 0 0 0 Not estimable Test for Neterogeneity, not applicable Test for overall effect not applicable Total events: 0 (Repeat), 0 (Single) Test for overall effect not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0 0 Not estimable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity chi-square=2.55 df=1 p=0.11 P=60.8%	Test for overall effect: not	t applicable					
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% C1) 0 0 0.0 Not estimable Test for overall effect not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% C1) 0 0 0.0 Not estimable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity not applic	08 In babies exposed to t	two repeat courses of	prenatal corticosteroio	ds			
Test for heterogeneity not applicable Test for overall effect: not applicable O9 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for noverall effect not	Subtotal (95% CI)	0	0		0.0	Not estimable	
Test for overall effect; not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0. Not estimable Test for heterogeneity; not applicable Test for heterogeneity; not applicable Test for overall effect; not applicable Test for overall effect; not applicable Total events: 0 (Repeat), 0 (Single) Total events: 0 (Repeat), 0 (Single) Total events: 0 (Repeat), 0 (Single) Test for overall effect; not applicable Test for not app	Total events: 0 (Repeat), (0 (Single)					
09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect not applicable Total events: 0 (Repeat), 0 (Single) Total events: 0 (Repeat), 0 (Single) Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect not applicable Test for heterogeneity; not applicable Test for overall effect not applicable Test for overall effect zeo.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajarian 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 4.32 0.27 [0.01, 5.70] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity; not applicable Test for overall effect zeo.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajarian 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 100.0 1.49 [0.11, 21.19 Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 P =60.8%	Test for heterogeneity: no	ot applicable					
Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Test for heterogeneity; not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Total events: 0 (Repeat), 0 (Single) Test for overall effect: not applicable Test for overall effect and applicable Test for overall effect and applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 P =60.8%	Test for overall effect: not	t applicable					
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0. Not estimable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect: applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 2.1.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 I? =60.8%	09 In babies exposed to t	three repeat courses c	of prenatal corticostero	ids			
Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0. 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 P =60.8%	Subtotal (95% CI)	0	0		0.0	Not estimable	
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10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect not applicable Total events: 0 (Repeat), 0 (Single) Test for overall effect not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect ze-0.80 p=0.4 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for overall effect ze-0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 P =60.8%	Test for heterogeneity: no	ot applicable					
Subtotal (95% CI) 0 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 38.2 0.27 [0.01, 5.70] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Test for overall effect: not	t applicable					
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 I/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 38.2 0.27 [0.01, 5.70] Subtotal (95% CI) 264 252 61.8 4.32 [0.94, 19.81] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	10 In babies exposed to f	four or more repeat co	ourses of prenatal cort	icosteroids			
Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 38.2 0.27 [0.01, 5.70] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	, ,		0		0.0	Not estimable	
Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 P =60.8%	Total events: 0 (Repeat), (0 (Single)					
1 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent 100.0 0.64 [0.21, 1.93] 100.0	Test for heterogeneity: no	ot applicable					
Crowther 2006 5/567 8/577 100.0 0.64 [0.21, 1.93] Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Test for overall effect: not	t applicable					
Subtotal (95% CI) 567 577 100.0 0.64 [0.21, 1.93] Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	I I In babies where plann	ed dose per treatment	t course 12 mg or less	of betamethasone or equivalent			
Total events: 5 (Repeat), 8 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 I ² =60.8%	Crowther 2006	5/567	8/577	-	100.0	0.64 [0.21, 1.93]	
Test for heterogeneity: not applicable Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Subtotal (95% CI)	567	577	-	100.0	0.64 [0.21, 1.93]	
Test for overall effect z=0.80 p=0.4 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Total events: 5 (Repeat),	8 (Single)					
12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Test for heterogeneity: no	ot applicable					
Aghajafari 2002 0/9 1/7 38.2 0.27 [0.01, 5.70] Guinn 2002 9/255 2/245 61.8 4.32 [0.94, 19.81] Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19] Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Test for overall effect z=0).80 p=0.4					
Guinn 2002 9/255 2/245 Subtotal (95% CI) 264 252 Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	12 In babies where plann	ed dose per treatment	t course > 12 mg to 2	4 mg or less of betamethasone or equiva	alent		
Subtotal (95% CI) 264 252 100.0 1.49 [0.11, 21.19 Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8%	Aghajafari 2002	0/9	1/7		38.2	0.27 [0.01, 5.70]	
Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 l² =60.8% 0.01 0.1 10 100	Guinn 2002	9/255	2/245	-	61.8	4.32 [0.94, 19.81]	
Total events: 9 (Repeat), 3 (Single) Test for heterogeneity chi-square=2.55 df=1 p=0.11 2 =60.8% 0.01 0.1 10 100	Subtotal (95% CI)	264	252		100.0	1.49 [0.11, 21.19]	
0.01 0.1 10 100	Total events: 9 (Repeat),	3 (Single)				-	
	Test for heterogeneity chi	i-square=2.55 df=1 p=	=0.11 I ² =60.8%				
ravours repeat ravours single (Continued						(Cantinuad	
				ravours repeat Favours single		(Continued ,	

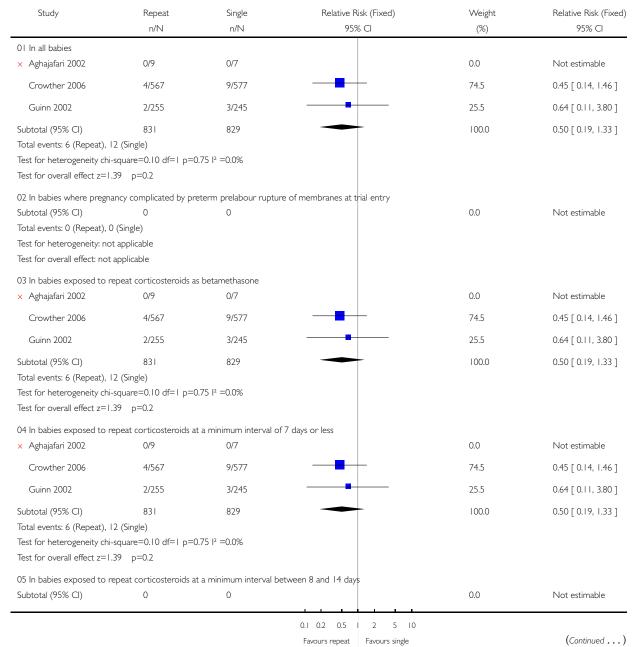
					(Continued
Study	Repeat	Single	Relative Risk (Random)	Weight	Relative Risk (Random
	n/N	n/N	95% CI	(%)	95% CI
Test for overall effect z=0	0.30 p=0.8				
13 In babies where plann	ed dose per treatment	course > 24 mg of be	etamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
14 In babies where plann	ed repeat drug exposi	re was 12 mg or less/\	week of betamethasone or equivalent		
Crowther 2006	5/567	8/577	-	100.0	0.64 [0.21, 1.93]
Subtotal (95% CI)	567	577	-	100.0	0.64 [0.21, 1.93]
Total events: 5 (Repeat),	8 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	0.80 p=0.4				
15 In babies where plann	ed repeat drug exposi	ıre was > 12 mg/week	to 24 mg/week of betamethasone or eq	uivalent	
Aghajafari 2002	0/9	1/7	-	38.2	0.27 [0.01, 5.70]
Guinn 2002	9/255	2/245	-	61.8	4.32 [0.94, 19.81]
Subtotal (95% CI)	264	252		100.0	1.49 [0.11, 21.19]
Total events: 9 (Repeat),	3 (Single)				
Test for heterogeneity chi	i-square=2.55 df=1 p=	:0.1112 =60.8%			
Test for overall effect z=0	0.30 p=0.8				
16 In babies where plann	ed repeat drug exposi	ıre was > 24 mg/week	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.01 0.1 10 100		
			Favours repeat Favours single		

Analysis 01.15. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 15 Periventricular leucomalacia

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 15 Periventricular leucomalacia



					(Continued,
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% CI
Total events: 0 (Repeat), 0 ((Single)			. ,	
Test for heterogeneity: not					
Test for overall effect: not a					
06 In babies exposed to rep	pest corticosteroids	t a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0	> 14 Udys	0.0	Not estimable
Total events: 0 (Repeat), 0 (Ü		0.0	1 vot estimable
Test for heterogeneity: not					
Test for overall effect: not a					
07 In babies exposed to on	e repeat course of pr	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not	/				
Test for overall effect: not a					
08 In babies exposed to tw	o repeat courses of r	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
09 In babies exposed to thr	ree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
10 In babies exposed to fou	ur or more repeat co	urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
II In babies where planned	I dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Crowther 2006	4/567	9/577	-	100.0	0.45 [0.14, 1.46]
Subtotal (95% CI)	567	577		100.0	0.45 [0.14, 1.46]
Total events: 4 (Repeat), 9 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=1.3	3 p=0.2				
12 In babies where planned	I dose per treatment	course > 12 mg to 24 n	ng or less of betamethasone or equivaler	nt	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Guinn 2002	2/255	3/245		100.0	0.64 [0.11, 3.80]
Subtotal (95% CI)	264	252		100.0	0.64 [0.11, 3.80]
Total events: 2 (Repeat), 3 (- •			[,]
Test for heterogeneity: not	/				
Test for overall effect z=0.4					
			0.1 0.2 0.5 2 5 10		,
			Favours repeat Favours single		(Continued

13 In babies where planned dose Subtotal (95% CI)	n/N e per treatment	n/N	95% CI	(%)	000/ 01
	e per treatment		95% CI	(%)	95% CI
Subtotal (95% CI)		course > 24 mg of beta	methasone or equivalent		
	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single	e)				
Test for heterogeneity: not applic	cable				
Test for overall effect: not applica	able				
14 In babies where planned repe	eat drug exposur	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	4/567	9/577		100.0	0.45 [0.14, 1.46]
Subtotal (95% CI)	567	577		100.0	0.45 [0.14, 1.46]
Total events: 4 (Repeat), 9 (Single	e)				
Test for heterogeneity: not applic	cable				
Test for overall effect z=1.33 p	=0.2				
15 In babies where planned repe	eat drug exposur	re was > 12 mg/week to	24 mg/week of betamethasone or equi	valent	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Guinn 2002	2/255	3/245		100.0	0.64 [0.11, 3.80]
Subtotal (95% CI)	264	252		100.0	0.64 [0.11, 3.80]
Total events: 2 (Repeat), 3 (Single	e)				
Test for heterogeneity: not applic	cable				
Test for overall effect z=0.49 p	=0.6				
16 In babies where planned repe	eat drug exposur	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single	e)				
Test for heterogeneity: not applic	cable				
Test for overall effect: not applica	able				

0.1 0.2 0.5 1 2 5 10

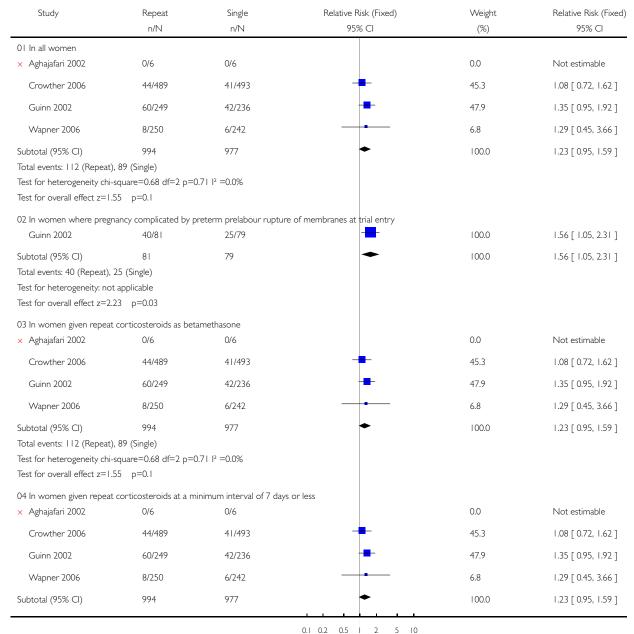
Favours repeat Favours single

Analysis 01.17. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 17 Chorioamnionitis

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 17 Chorioamnionitis



Favours repeat Favours single

(Continued . . .)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Total events: 112 (Repeat), 8	, ,				
Test for heterogeneity chi-sc		$0.711^2 = 0.0\%$			
Test for overall effect z=1.55	5 p=0.1				
05 In women given repeat o	orticosteroids at a m	ninimum interval between 8 an	d 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	pplicable				
06 In women given repeat c	orticosteroids at a m	ninimum interval of > 14 days			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	- /				
Test for overall effect: not ap					
07 In women given one rep		al aportina atamai da			
	eat course of prenat	ai corticosteroids 0		0.0	Not estimable
Subtotal (95% CI) Total events: 0 (Repeat), 0 (U		0.0	NOL estimable
Test for heterogeneity: not a	- /				
- /					
Test for overall effect: not ap	pplicable				
08 In women given two rep	'				
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not a					
Test for overall effect: not ap	pplicable				
09 In women given three re	peat courses of prer	atal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect: not ap	pplicable				
10 In women given four or r	more repeat courses	of prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not a					
Test for overall effect: not ap					
·	•				
·	•	t course 12 mg or less of beta	methasone or equivalent	1000	1001072 1/27
Crowther 2006	44/489	41/493	T .	100.0	1.08 [0.72, 1.62]
Subtotal (95% CI)	489	493	+	100.0	1.08 [0.72, 1.62]
Total events: 44 (Repeat), 4	l (Single)				
Test for heterogeneity: not a	applicable				
Test for overall effect z=0.38	3 p=0.7				
12 In women where planne	d dose per treatmen	t course > 12 mg to 24 mg or	less of betamethasone or equivale	ent	
× Aghajafari 2002	0/6	0/6	,	0.0	Not estimable
		0	.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
C : 2002	n/N	n/N	95% CI	(%)	95% CI
Guinn 2002	60/249	42/236		87.6	1.35 [0.95, 1.92]
Wapner 2006	8/250	6/242		12.4	1.29 [0.45, 3.66]
Subtotal (95% CI)	505	484	•	100.0	1.35 [0.96, 1.88]
otal events: 68 (Repeat),	48 (Single)				
est for heterogeneity chi-	square=0.01 df=1 p=0	0.93 I ² =0.0%			
est for overall effect z=1.7	74 p=0.08				
3 In women where plann	ed dose per treatmen	t course > 24 mg of bet	amethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
otal events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
4 In women where plann	ed repeat drug expos	ure was 12 mg or less/w	eek of betamethasone or equivalent		
Crowther 2006	44/489	41/493	+	100.0	1.08 [0.72, 1.62]
ubtotal (95% CI)	489	493	•	100.0	1.08 [0.72, 1.62]
otal events: 44 (Repeat),	41 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.3	38 p=0.7				
5 In women where plann	ed repeat drug expos	ure was > 12 mg/week t	o 24 mg/week of betamethasone or equ	ivale	
× Aghajafari 2002	0/6	0/6		0.0	Not estimable
Guinn 2002	60/249	42/236	-	87.6	1.35 [0.95, 1.92]
Wapner 2006	8/250	6/242		12.4	1.29 [0.45, 3.66]
Subtotal (95% CI)	505	484	•	100.0	1.35 [0.96, 1.88]
Total events: 68 (Repeat),	48 (Single)				
Test for heterogeneity chi-	square=0.01 df=1 p=0	0.93 l² =0.0%			
Test for overall effect z=1.7	74 p=0.08				
6 In women where plann	ed repeat drug expos	ure was > 24 mg/week o	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
			0.1 0.2 0.5 1 2 5 10		

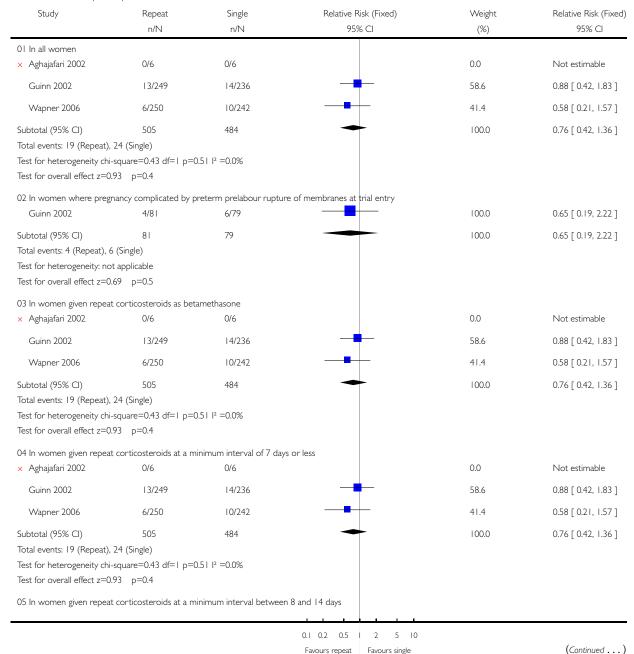
Favours repeat Favours single

Analysis 01.18. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 18 Puerperal sepsis

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 18 Puerperal sepsis



Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
06 In women given repeat	corticosteroids at a m	ninimum interval of > 14	days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	/				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
07 In women given one rep	•				
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: not					
Test for overall effect: not a					
08 In women given two rep	•			0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: not Test for overall effect: not a	• •				
09 In women given three re	epeat courses of pren 0	atal corticosteroids 0		0.0	Not estimable
Subtotal (95% CI) Total events: 0 (Repeat), 0		O		0.0	TAOL ESUITIADIE
Test for heterogeneity: not					
Test for overall effect: not a					
10 In women given four or	more repeat courses	of prenatal corticosteroi	ids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
I I In women where planne	ed dose per treatmen	t course 12 mg or less of	f betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
12 In women where planne	ed dose per treatmen	t course > 12 mg to 24 r	mg or less of betamethasone or equivale	en	
× Aghajafari 2002	0/6	0/6		0.0	Not estimable
Guinn 2002	13/249	14/236	_	58.6	0.88 [0.42, 1.83]
Wapner 2006	6/250	10/242		41.4	0.58 [0.21, 1.57]
Subtotal (95% CI)	505	484	•	100.0	0.76 [0.42, 1.36]
Total events: 19 (Repeat), 2	4 (Single)				
Test for heterogeneity chi-s	, ,	0.51 2 =0.0%			
	0.1 0.2 0.5 1 2 5 10				
			Favours repeat Favours single		(Continued

					(****	
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)	
	n/N	n/N	95% CI	(%)	95% CI	
Test for overall effect z=0	.93 p=0.4					
13 In women where plans	ned dose per treatmen	t course > 24 mg of bet	amethasone or equivalent			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0) (Single)					
Test for heterogeneity: no	t applicable					
Test for overall effect: not	applicable					
14 In women where plans	ned repeat drug expos	ure was 12 mg or less/w	eek of betamethasone or equivalent			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0) (Single)					
Test for heterogeneity: no	t applicable					
Test for overall effect: not	applicable					
15 In women where plans	ned repeat drug expos	ure was > 12 mg/week t	o 24 mg/week of betamethasone or equ	ivale		
× Aghajafari 2002	0/6	0/6		0.0	Not estimable	
Guinn 2002	13/249	14/236	-	58.6	0.88 [0.42, 1.83]	
Wapner 2006	6/250	10/242		41.4	0.58 [0.21, 1.57]	
Subtotal (95% CI)	505	484	-	100.0	0.76 [0.42, 1.36]	
Total events: 19 (Repeat),	24 (Single)					
Test for heterogeneity chi	-square=0.43 df=1 p=0	0.5 2 =0.0%				
Test for overall effect z=0	.93 p=0.4					
16 In women where plans	ned repeat drug expos	ure was > 24 mg/week o	of betamethasone or equivalent			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0) (Single)					
Test for heterogeneity: no	t applicable					
Test for overall effect: not	applicable					

0.1 0.2 0.5 1 2 5 10

Favours repeat Favours single

Analysis 01.19. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 19 Use of mechanical ventilation

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 19 Use of mechanical ventilation

Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% Cl
01 In all babies					
Crowther 2006	167/567	204/577	<u></u>	61.0	0.83 [0.70, 0.99]
Wapner 2006	36/250	60/242	-	39.0	0.58 [0.40, 0.84]
Subtotal (95% CI)	817	819	•	100.0	0.72 [0.51, 1.02]
Total events: 203 (Repeat), 264 (Single)				
Test for heterogeneity chi	-square=3.00 df=1 p=	:0.08 I ² =66.7%			
Test for overall effect z=1	.83 p=0.07				
02 In babies where pregn	ancy complicated by p	reterm prelabour ruptur	e of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids	as betamethasone			
Crowther 2006	167/567	204/577	<u>→</u>	61.0	0.83 [0.70, 0.99]
Wapner 2006	36/250	60/242	-	39.0	0.58 [0.40, 0.84]
Subtotal (95% CI)	817	819	•	100.0	0.72 [0.51, 1.02]
Total events: 203 (Repeat), 264 (Single)				
Test for heterogeneity chi	-square=3.00 df=1 p=	:0.08 I ² =66.7%			
Test for overall effect z=1	.83 p=0.07				
04 In babies exposed to r	repeat corticosteroids	at a minimum interval of	7 days or less		
Crowther 2006	167/567	204/577	•	61.0	0.83 [0.70, 0.99]
Wapner 2006	36/250	60/242	-	39.0	0.58 [0.40, 0.84]
Subtotal (95% CI)	817	819	•	100.0	0.72 [0.51, 1.02]
Total events: 203 (Repeat), 264 (Single)				
Test for heterogeneity chi	-square=3.00 df=1 p=	:0.08 I ² =66.7%			
Test for overall effect z=1	.83 p=0.07				
05 In babies exposed to r	repeat corticosteroids	at a minimum interval be	etween 8 and 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
06 In babies exposed to r	repeat corticosteroids	at a minimum interval of	> 14 days		
			0.1 0.2 0.5 2 5 10		/-
			Favours repeat Favours single		(Continued

					(Continued)		
Study	Repeat	Single	Relative Risk (Random)	Weight	Relative Risk (Random)		
	n/N	n/N	95% CI	(%)	95% CI		
Subtotal (95% CI)	0	0		0.0	Not estimable		
Total events: 0 (Repeat), 0	O (Single)						
Test for heterogeneity: no	t applicable						
Test for overall effect: not	applicable						
07 In babies exposed to o	one repeat course of p	renatal corticosteroids					
Subtotal (95% CI)	0	0		0.0	Not estimable		
Total events: 0 (Repeat), 0) (Single)						
Test for heterogeneity: no	t applicable						
Test for overall effect: not	applicable						
08 In babies exposed to t	wo repeat courses of	prenatal corticosteroids					
Subtotal (95% CI)	0	0		0.0	Not estimable		
Total events: 0 (Repeat), (O (Single)						
Test for heterogeneity: no							
Test for overall effect: not	applicable						
09 In babies exposed to t	hree repeat courses o	f prenatal corticosteroic	ds				
Subtotal (95% CI)	0	0		0.0	Not estimable		
Total events: 0 (Repeat), () (Single)						
Test for heterogeneity: no							
Test for overall effect: not							
		6					
10 In babies exposed to f Subtotal (95% CI)	our or more repeat co	ourses of prenatal cortic	osteroias	0.0	Not estimable		
Total events: 0 (Repeat), (U		0.0	Not estimable		
Test for heterogeneity: no	/						
Test for overall effect: not							
•	•		f betamethasone or equivalent				
Crowther 2006	167/567	204/577		100.0	0.83 [0.70, 0.99]		
Subtotal (95% CI)	567	577	•	100.0	0.83 [0.70, 0.99]		
Total events: 167 (Repeat), 204 (Single)						
Test for heterogeneity: no	t applicable						
Test for overall effect z=2	.12 p=0.03						
12 In babies where planne	ed dose per treatment	course > 12 mg to 24	mg or less of betamethasone or equival	lent			
Wapner 2006	36/250	60/242	-	100.0	0.58 [0.40, 0.84]		
Subtotal (95% CI)	250	242	•	100.0	0.58 [0.40, 0.84]		
Total events: 36 (Repeat),		212		100.0	0.50 [0.10, 0.01]		
Test for heterogeneity: no	/						
Test for overall effect z=2							
		e	amethasone or equivalent				
Subtotal (95% CI)	0	0		0.0	Not estimable		
Total events: 0 (Repeat), (, - ,						
Test for heterogeneity: no							
Test for overall effect: not	аррисавіе						
			0.1 0.2 0.5 2 5 10				
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		(Continued)		
			ravours repeat Tavours single		(Contanued)		

Study	Repeat	Single	Relative Risk (Random)	Weight	Relative Risk (Random)
	n/N	n/N	95% CI	(%)	95% CI
14 In babies where plann	ed repeat drug exposu	re was 12 mg or less/w	eek of betamethasone or equivalent		
Crowther 2006	167/567	204/577	-	100.0	0.83 [0.70, 0.99]
Subtotal (95% CI)	567	577	•	100.0	0.83 [0.70, 0.99]
Total events: 167 (Repeat	t), 204 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=2	2.12 p=0.03				
15 In babies where plann	ed repeat drug exposu	re was > 12 mg/week t	to 24 mg/week o <u>f b</u> etamethasone or equ	ivalent	
Wapner 2006	36/250	60/242		100.0	0.58 [0.40, 0.84]
Subtotal (95% CI)	250	242	•	100.0	0.58 [0.40, 0.84]
Total events: 36 (Repeat)	, 60 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=2	2.85 p=0.004				
16 In babies where plann	ed repeat drug exposu	re was > 24 mg/week o	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
			0.1 0.2 0.5 2 5 10		

Favours repeat Favours single

Analysis 01.20. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 20 Duration of respiratory support in days

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 20 Duration of respiratory support in days

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies	18	0.90 (2.40)	19	0.50 (1.00)		100.0	0.20 [0.00 E0.3
McEvoy 2002		0.80 (2.40)		0.50 (1.00)			0.30 [-0.90, 1.50]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			19		Ť	100.0	0.30 [-0.90, 1.50]
02 In babies where p	regnancy	complicated by p	oreterm p	relabour rupture	of membranes at trial entry		
Subtotal (95% CI) Test for heterogeneit Test for overall effects			0			0.0	Not estimable
03 In babies exposed	to repea	at corticosteroids	as betam	ethasone			
McEvoy 2002	18	0.80 (2.40)	19	0.50 (1.00)	-	100.0	0.30 [-0.90, 1.50]
Subtotal (95% CI) Test for heterogeneit Test for overall effect			19		†	100.0	0.30 [-0.90, 1.50]
04 In babies exposed	to repea	at corticosteroids	at a mini	mum interval of 7	days or less		
McEvoy 2002	18	0.80 (2.40)	19	0.50 (1.00)	-	100.0	0.30 [-0.90, 1.50]
Subtotal (95% CI) Test for heterogeneit Test for overall effect			19		+	100.0	0.30 [-0.90, 1.50]
05 In babies exposed	to repea	at corticosteroids	at a mini	mum interval bet	ween 8 and 14 days		
Subtotal (95% CI) Test for heterogeneit Test for overall effect:			0			0.0	Not estimable
06 In babies exposed	to repea	at corticosteroids	at a mini	mum interval of >	· 14 days		
Subtotal (95% CI) Test for heterogeneit Test for overall effect:			0			0.0	Not estimable
07 In babies exposed	to one r	repeat course of p	orenatal c	orticosteroids			
Subtotal (95% CI) Test for heterogeneit Test for overall effect:			0			0.0	Not estimable
08 In babies exposed	to two r	repeat courses of	prenatal	corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		(Continued)

							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Test for heterogeneit	y: not ap _l	plicable					
Test for overall effects	not app	licable					
09 In babies exposed		repeat courses of		l corticosteroids		0.0	AL
Subtotal (95% CI) Test for heterogeneit	0 v: not adi	plicable	0			0.0	Not estimable
Test for overall effect:							
10 In babies exposed	to four	or more repeat c	ourses of	prenatal corticos	steroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit: Test for overall effect:							
			t course	12 mg or less of h	petamethasone or equivalent		
Subtotal (95% CI)	0	ose per d'ederien	0	12 mg or less or t	Setamethasone of Equivalent	0.0	Not estimable
Test for heterogeneit							
Test for overall effect:	not app	licable					
·				-	g or less of betamethasone or equivalent	100.0	0.20 [0.00 [0.1
McEvoy 2002	18	0.80 (2.40)	19	0.50 (1.00)		100.0	0.30 [-0.90, 1.50]
Subtotal (95% CI) Test for heterogeneit	18 v: not adi	plicable	19			100.0	0.30 [-0.90, 1.50]
Test for overall effect							
13 In babies where p	lanned de	ose per treatmen	t course :	> 24 mg of betan	nethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effects							
			ure was I	2 mg or less/wee	ek of betamethasone or equivalent		
× Crowther 2006	56	0.00 (0.00)	577	0.00 (0.00)	ix of betametrasone of equivalent	0.0	Not estimable
Subtotal (95% CI)	56		577			0.0	Not estimable
Test for heterogeneit							
Test for overall effect:	not app	licable					
			ure was > 19		24 mg/week of betamethasone or equiva		0.20 [0.00 E0.1
McEvoy 2002	18	0.80 (2.40)		0.50 (1.00)	I	100.0	0.30 [-0.90, 1.50]
Subtotal (95% CI) Test for heterogeneit	18 y: not api	plicable	19			100.0	0.30 [-0.90, 1.50]
Test for overall effect							
16 In babies where p	lanned re	epeat drug expos	ure was >	· 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effects							
	-11						
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.21. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 21 Use of oxygen supplementation

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 21 Use of oxygen supplementation

Repeat n/N	Single n/N	Relative Risk (Fixed) 95% Cl	Weight (%)	Relative Risk (Fixed) 95% CI
317/567	361/577	-	100.0	0.89 [0.81, 0.98]
567 361 (Single) applicable	577	•	100.0	0.89 [0.81, 0.98]
18 p=0.02				
ncy complicated by pre	eterm prelabour rupture o	f membranes at trial entry		
0	0		0.0	Not estimable
(Single) applicable applicable				
peat corticosteroids a	s betamethasone			
317/567	361/577	<u> </u>	100.0	0.89 [0.81, 0.98]
567 361 (Single) applicable 18 p=0.02	577	•	100.0	0.89 [0.81, 0.98]
neat corticosteroids a	t a minimum interval of 7 o	lavs or less		
317/567	361/577	+	100.0	0.89 [0.81, 0.98]
567 361 (Single) applicable 8 p=0.02	577	•	100.0	0.89 [0.81, 0.98]
peat corticosteroids a	t a minimum interval betwe	een 8 and 14 days		
0 (Single) applicable applicable	0		0.0	Not estimable
peat corticosteroids a 0 (Single) applicable pplicable	t a minimum interval of > 0	14 days	0.0	Not estimable
	n/N 317/567 567 361 (Single) applicable 8 p=0.02 ncy complicated by pn 0 (Single) applicable peat corticosteroids a 317/567 567 361 (Single) applicable 8 p=0.02 peat corticosteroids a 317/567 567 361 (Single) applicable 8 p=0.02 peat corticosteroids a 0 (Single) applicable 9 peat corticosteroids a 0 (Single) applicable	n/N n/N 317/567 361/577 567 577 361 (Single) applicable 8 p=0.02 ncy complicated by preterm prelabour rupture or 0 0 (Single) applicable ppalicable ppalicable peat corticosteroids as betamethasone 317/567 361/577 567 577 361 (Single) applicable 8 p=0.02 peat corticosteroids at a minimum interval of 7 or 317/567 361/577 567 577 361 (Single) applicable 8 p=0.02 peat corticosteroids at a minimum interval between 0 0 (Single) applicable 9 peat corticosteroids at a minimum interval between 0 0 (Single) applicable ppat corticosteroids at a minimum interval of > 0 (Single) applicable ppat corticosteroids at a minimum interval of > 0 (Single) applicable ppat corticosteroids at a minimum interval of > 0 (Single) applicable	n/N n/N 95% CI 317/567 361/577 567 577 361 (Single) applicable 88 p=0.02 ncy complicated by preterm prelabour rupture of membranes at trial entry 0 0 (Single) applicable pplicable peat corticosteroids as betamethasone 317/567 361/577 567 577 361 (Single) applicable 88 p=0.02 peat corticosteroids at a minimum interval of 7 days or less 317/567 361/577 567 577 361 (Single) applicable 88 p=0.02 peat corticosteroids at a minimum interval between 8 and 14 days 0 (Single) applicable pplicable pplicable pplicable pplicable pplicable pplicable pplicable pplicable pplicable ppart corticosteroids at a minimum interval of > 14 days 0 (Single) applicable ppart corticosteroids at a minimum interval of > 14 days 0 (Single) applicable ppart corticosteroids at a minimum interval of > 14 days 0 (Single) applicable	n/N n/N 95% CI (%) 317/567 361/577 100.0 567 577 100.0 361 (Single) applicable 8. p=0.02 ncy complicated by preterm prelabour rupture of membranes at trial entry 0 0 0.0 (Single) applicable pipicable pipicable pipicable peat corticosteroids as betamethasone 317/567 361/577 100.0 361 (Single) applicable 8. p=0.02 peat corticosteroids at a minimum interval of 7 days or less 317/567 361/577 100.0 361 (Single) applicable 8. p=0.02 peat corticosteroids at a minimum interval of 7 days or less 317/567 361/577 100.0 361 (Single) applicable 8. p=0.02 peat corticosteroids at a minimum interval between 8 and 14 days 0 0 0.0 (Single) applicable pipicable pipicable peat corticosteroids at a minimum interval of > 14 days 0 0 0.0 (Single) applicable pipicable pipicable peat corticosteroids at a minimum interval of > 14 days 0 0 0.0 (Single) applicable

Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours single

(Continued . . .)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
07 In babies exposed to o	ne repeat course of pr	enatal corticosteroids		. , ,	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
08 In babies exposed to tw	vo repeat courses of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
09 In babies exposed to th	nree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
10 In babies exposed to fo	our or more repeat cou	urses of prenatal corticost	eroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not	applicable				
I I In babies where planne	d dose per treatment	course 12 mg or less of b	etamethasone or equivalent		
Crowther 2006	317/567	361/577	-	100.0	0.89 [0.81, 0.98]
C. l-+-+-1 (0F0/ CI)	F/7	577		100.0	
Subtotal (95% CI) Total events: 317 (Repeat)	567	3//		100.0	0.89 [0.81, 0.98]
Test for heterogeneity: not					
Test for overall effect z=2.2					
		\ 12+- 24			
Subtotal (95% CI)	d dose per treatment (course > 12 mg to 24 mg	or less of betamethasone or equivaler	0.0	Not estimable
Total events: 0 (Repeat), 0	-	O		0.0	NOT ESTIMABLE
Test for heterogeneity: not					
Test for overall effect: not					
			athanana an an ii alant		
13 In babies where planne Subtotal (95% CI)	0	O Detam	ethasone or equivalent	0.0	Not estimable
Total events: 0 (Repeat), 0		O		0.0	TAOL ESTITIABLE
Test for heterogeneity: not	/				
Test for overall effect: not	• •				
		12 1 / 1			
			of betamethasone or equivalent	100.0	00010010001
Crowther 2006	317/567	361/577	T	100.0	0.89 [0.81, 0.98]
Subtotal (95% CI)	567	577	•	100.0	0.89 [0.81, 0.98]
Total events: 317 (Repeat)	(0)				
Test for heterogeneity: not	applicable				
			01 02 05 12		
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		(Continued)
			i avour s repeat i avour s single		(Continued)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Test for overall effect z=2	2.28 p=0.02				
15 In babies where plann	ed repeat drug exposui	re was > 12 mg/week to	24 mg/week of betamethasone or equ	uivalent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
16 In babies where plann	ed repeat drug exposui	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.22. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 22 Duration of oxygen supplementation in days

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease Comparison: 01 Repeat doses of corticosteroids versus single course Outcome: 22 Duration of oxygen supplementation in days Study Weighted Mean Difference (Fixed) Weight Weighted Mean Difference (Fixed) Repeat Single Ν Mean(SD) Ν Mean(SD) 95% CI (%) 95% CI 01 In all babies McEvoy 2002 4.00 (12.00) 0.70 (1.90) 100.0 3.30 [-2.31, 8.91] 18 19 3.30 [-2.31, 8.91] Subtotal (95% CI) 19 100.0 Test for heterogeneity: not applicable Test for overall effect z=1.15 p=0.202 In babies where pregnancy complicated by preterm prelabour rupture of membranes at trial entry Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 03 In babies exposed to repeat corticosteroids as betamethasone Subtotal (95% CI) 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 04 In babies exposed to repeat corticosteroids at a minimum interval of 7 days or less Subtotal (95% CI) 0.0 Not estimable -10.0 -5.0 10.0 5.0 (Continued ...) Favours repeat Favours single

								(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean	Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95	5% CI
Test for heterogeneity	: not ap	plicable						
Test for overall effect:	not app	olicable						
05 In babies exposed	to rene	at corticosteroids	at a mini	mum interval het	tween 8 and 14 days			
Subtotal (95% CI)	0	at cor ticosteroids	0	man interval bet	tween o and 11 days	0.0	Not estimable	
Test for heterogeneity		policable	U			0.0	140t estillable	
Test for overall effect:								
06 In babies exposed		at corticosteroids		mum interval of	> 14 days			
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity	: not ap	plicable						
Test for overall effect:	not app	olicable						
07 In babies exposed	to one	repeat course of	prenatal c	orticosteroids				
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity	r. not ap	plicable						
Test for overall effect:								
08 In babies exposed		repeat courses of		corticosteroids				
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity								
Test for overall effect:	not app	olicable						
09 In babies exposed	to three	e repeat courses	of prenata	l corticosteroids				
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity	: not ap	plicable						
Test for overall effect:	not app	olicable						
10 In babies exposed	to four	or more report o	ources of	propostal contico	ctoroids			
·	0	or more repeat c	0	prenatal conticos	steroids	0.0	Not estimable	
Subtotal (95% CI)		-0	U			0.0	Not estimable	
Test for heterogeneity								
Test for overall effect:	not app	olicable						
II In babies where pla	anned d	lose per treatmer	nt course	12 mg or less of I	betamethasone or equivalent			
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity	: not ap	plicable						
Test for overall effect:	not app	olicable						
12 In hahies where n	anned d	lose per treatmer	nt course '	> 12 mg to 24 m	ng or less of betamethasone or equivalent			
Subtotal (95% CI)	0	iose per treatmer	0	121118 to 21111	ig of less of betaffettiasone of equivalent	0.0	Not estimable	
Test for heterogeneity		plicable	U			0.0	NOT ESTIMABLE	
Test for overall effect:	пот арр	DIICADIE						
13 In babies where pla	anned d	lose per treatmer	nt course :	> 24 mg of betar	methasone or equivalent			
Subtotal (95% CI)	0		0			0.0	Not estimable	
Test for heterogeneity	: not ap	plicable						
Test for overall effect:	not app	olicable						
14 In babies where nl:	anned n	epeat drug expos	sure was I	2 mg or less/wee	ek of betamethasone or equivalent			
Subtotal (95% CI)	0	, ag a po	0		Separation	0.0	Not estimable	
Test for heterogeneity		pplicable	3			0.0	. tot communic	
	эс ар							
					-10.0 -5.0 0 5.0 10.0			
					Favours repeat Favours single			(Continued)
					. 2.2.5. opeac			(00.10.1000)

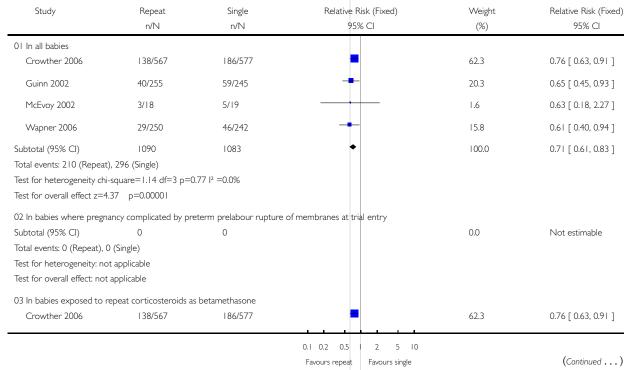
Study	Repeat		itudy Repeat		Repeat Single Weigh		Weighted Me	an Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)		95% CI	(%)	95% CI		
Test for overall effect	: not app	licable								
15 In babies where p	lanned re	epeat drug exposi	ure was :	> 12 mg/week to	24 mg/week of b	etamethasone or equiv	alent			
Subtotal (95% CI)	0		0				0.0	Not estimable		
Test for heterogeneit	y: not ap	plicable								
Test for overall effect	: not app	licable								
16 In babies where p	lanned re	epeat drug exposi	ure was :	> 24 mg/week of	betamethasone o	or equivalent				
Subtotal (95% CI)	0		0				0.0	Not estimable		
Test for heterogeneit	y: not ap	plicable								
Test for overall effect	: not app	licable								
					1 1					
		·			-10.0 -5.0	0 5.0 10.0				
					Favours repeat	Favours single				

Analysis 01.23. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 23 Use of surfactant

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 23 Use of surfactant



					(Continued)	
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed	
	n/N	n/N	95% CI	(%)	95% CI	
Guinn 2002	40/255	59/245	-	20.3	0.65 [0.45, 0.93]	
McEvoy 2002	3/18	5/19		1.6	0.63 [0.18, 2.27]	
Wapner 2006	29/250	46/242	-	15.8	0.61 [0.40, 0.94]	
Subtotal (95% CI) Total events: 210 (Repeat), Test for heterogeneity chi-so Test for overall effect z=4.3	quare=1.14 df=3 p=0	1083	•	100.0	0.71 [0.61, 0.83]	
04 In babies exposed to rep Crowther 2006	oeat corticosteroids a 138/567	t a minimum interval of 7	days or less	62.3	0.76 [0.63, 0.91]	
Guinn 2002	40/255	59/245	_	20.3	0.65 [0.45, 0.93]	
					-	
McEvoy 2002	3/18	5/19		1.6	0.63 [0.18, 2.27]	
Wapner 2006	29/250	46/242		15.8	0.61 [0.40, 0.94]	
Subtotal (95% CI) Total events: 210 (Repeat), Test for heterogeneity chi-so Test for overall effect z=4.3	quare=1.14 df=3 p=0	1083 0.77 ² =0.0%	•	100.0	0.71 [0.61, 0.83]	
05 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	0 (Single) applicable	t a minimum interval betv 0	veen 8 and 14 days	0.0	Not estimable	
06 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	0 (Single) applicable	t a minimum interval of > 0	14 days	0.0	Not estimable	
07 In babies exposed to on Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	0 (Single) applicable	enatal corticosteroids O		0.0	Not estimable	
08 In babies exposed to two Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	o repeat courses of p 0 (Single) applicable	renatal corticosteroids 0		0.0	Not estimable	
09 In babies exposed to thr Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not	0 (Single)	prenatal corticosteroids 0		0.0	Not estimable	
			01 02 05 12 5 12			
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		(Continued)	

				(Con		
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed	
Test for overall effect: not	applicable					
10 In babies exposed to fo	our or more repeat co	urses of prenatal corticos	teroids			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0) (Single)					
Test for heterogeneity: no	t applicable					
Test for overall effect: not	applicable					
II In babies where planne	ed dose per treatment	course 12 mg or less of b	petamethasone or equivalent			
Crowther 2006	138/567	186/577	-	100.0	0.76 [0.63, 0.91]	
Subtotal (95% CI)	567	577	•	100.0	0.76 [0.63, 0.91]	
Total events: 138 (Repeat)), 186 (Single)					
Test for heterogeneity: no	t applicable					
Test for overall effect z=2.	.94 p=0.003					
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 m	g or less of betamethasone or equivaler	nt		
Guinn 2002	40/255	59/245	-	53.8	0.65 [0.45, 0.93]	
McEvoy 2002	3/18	5/19		4.4	0.63 [0.18, 2.27]	
Wapner 2006	29/250	46/242	-	41.8	0.61 [0.40, 0.94]	
'						
Subtotal (95% CI)	523	506		100.0	0.63 [0.48, 0.83]	
Total events: 72 (Repeat),	, , ,	0.07 120.00/				
Test for heterogeneity chi- Test for overall effect z=3.		J.77 I ⁻ -0.0%				
	·	> 24 (1)				
13 In babies where planne Subtotal (95% CI)	o dose per treatment	Course > 24 mg of betan	netnasone or equivalent	0.0	Not estimable	
Total events: 0 (Repeat), 0		O .		0.0	Not estimable	
Test for heterogeneity: no						
Test for overall effect: not						
14 In habies where planne	ed reneat drug exposui	re was 12 mg or less/wee	k of betamethasone or equivalent			
Crowther 2006	138/567	186/577		100.0	0.76 [0.63, 0.91]	
Culturated (0F9/ CI)	F/7	F 77	•	100.0	-	
Subtotal (95% CI) Total events: 138 (Repeat)	567	577		100.0	0.76 [0.63, 0.91]	
Test for heterogeneity: no						
Test for overall effect z=2.						
15 In habies whom planns	d report drug eveneru	m uns > 12 malusoli to	24 mg/week of betamethasone or equi	alont		
Guinn 2002	40/255	59/245	24 filg/week of betained asone of equi	53.8	0.65 [0.45, 0.93]	
McEvoy 2002	3/18	5/19	_	4.4	0.63 [0.18, 2.27]	
Wapner 2006	29/250	46/242	-	41.8	0.61 [0.40, 0.94]	
Subtotal (95% CI)	523	506	•	100.0	0.63 [0.48, 0.83]	
Total events: 72 (Repeat),	, , ,					
Test for heterogeneity chi-		0.97 I ² =0.0%				
Test for overall effect z=3.	.31 p=0.0009					
			0.1 0.2 0.5 2 5 10		(
			Favours repeat Favours single		(Continued)	

Study	Repeat	Single	Relative Ri	sk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95%	S CI	(%)	95% CI
16 In babies where plann	ned repeat drug exposur	e was > 24 mg/week of	betamethasone or eq	uivalent		_
Subtotal (95% CI)	0	0			0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect: no	t applicable					
			0.1 0.2 0.5	2 5 10		
			Favours repeat	Favours single		

Analysis 01.24. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 24 Patent ductus arteriosus requiring treatment

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 24 Patent ductus arteriosus requiring treatment

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all babies					
Aghajafari 2002	2/9	1/7	- - 	1.4	1.56 [0.17, 13.87]
Crowther 2006	40/567	67/577	=	81.2	0.61 [0.42, 0.88]
Wapner 2006	7/250	14/242		17.4	0.48 [0.20, 1.18]
Subtotal (95% CI)	826	826	•	100.0	0.60 [0.43, 0.84]
Total events: 49 (Repeat),	82 (Single)				
Test for heterogeneity chi	-square=0.96 df=2 p=	0.62 l ² =0.0%			
Test for overall effect z=2	.96 p=0.003				
02 In babies where pregn	ancy complicated by p	reterm prelabour ruptu	ıre of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids a	as betamethasone			
Aghajafari 2002	2/9	1/7		1.4	1.56 [0.17, 13.87]
Crowther 2006	40/567	67/577	=	81.2	0.61 [0.42, 0.88]
Wapner 2006	7/250	14/242		17.4	0.48 [0.20, 1.18]
Subtotal (95% CI)	826	826	•	100.0	0.60 [0.43, 0.84]
Total events: 49 (Repeat),	82 (Single)				
Test for heterogeneity chi	-square=0.96 df=2 p=	0.62 2 =0.0%			
_			<u> </u>		
			0.01 0.1 1 10 100		(5)
			Favours repeat Favours single		(Continued)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for overall effect z=2.9	96 p=0.003				
04 In babies exposed to re	peat corticosteroids	at a minimum interval of	7 days or less		
Aghajafari 2002	2/9	1/7		1.4	1.56 [0.17, 13.87]
Crowther 2006	40/567	67/577	<u>.</u>	81.2	0.61 [0.42, 0.88]
Wapner 2006	7/250	14/242	-	17.4	0.48 [0.20, 1.18]
Subtotal (95% CI)	826	826	•	100.0	0.60 [0.43, 0.84]
Total events: 49 (Repeat), 8 Test for heterogeneity chi-s Test for overall effect z=2.9	32 (Single) square=0.96 df=2 p=				
05 In babies exposed to re	peat corticosteroids	at a minimum interval be	tween 8 and 14 days		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable	0		0.0	Not estimable
06 In babies exposed to re	peat corticosteroids	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable				
07 In babies exposed to or	ne repeat course of p	renatal corticosteroids			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable	0		0.0	Not estimable
08 In babies exposed to tw	vo repeat courses of i	prenatal corticosteroids			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	0 (Single) applicable	0		0.0	Not estimable
09 In babies exposed to th	ree repeat courses o	f prenatal corticosteroids	;		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable	0		0.0	Not estimable
10 In babies exposed to fo		urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not a	applicable				
II In babies where planned	d dose per treatment	course 12 mg or less of	betamethasone or equivalent		
			0.01 0.1 1 10 100 Favours repeat Favours single		(Continued)
			. 2.00.3 repeat		(continued)

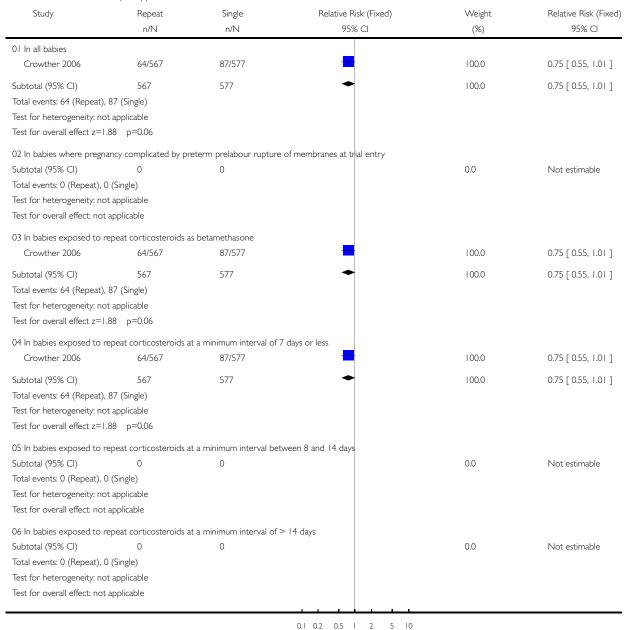
					(Continued
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Crowther 2006	40/567	67/577		100.0	0.61 [0.42, 0.88]
Subtotal (95% CI) Total events: 40 (Repeat), Test for heterogeneity: no Test for overall effect z=2.	t applicable	577	•	100.0	0.61 [0.42, 0.88]
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 n	ng or less of betamethasone or equivale	nt	
Aghajafari 2002	2/9	1/7		7.3	1.56 [0.17, 13.87]
Wapner 2006	7/250	14/242	-	92.7	0.48 [0.20, 1.18]
Subtotal (95% CI) Total events: 9 (Repeat), I Test for heterogeneity chi- Test for overall effect z=1.	-square=0.94 df=1 p=0	249 0.33 l² =0.0%		100.0	0.56 [0.25, 1.26]
13 In babies where planne Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: no Test for overall effect: not	0 (Single) t applicable	course > 24 mg of beta 0	methasone or equivalent	0.0	Not estimable
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	40/567	67/577	<mark></mark>	100.0	0.61 [0.42, 0.88]
Subtotal (95% CI) Total events: 40 (Repeat), Test for heterogeneity: no Test for overall effect z=2.	t applicable	577	•	100.0	0.61 [0.42, 0.88]
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equ	ivalent	
Aghajafari 2002	2/9	1/7		7.3	1.56 [0.17, 13.87]
Wapner 2006	7/250	14/242	-	92.7	0.48 [0.20, 1.18]
Subtotal (95% CI) Total events: 9 (Repeat), I Test for heterogeneity chi- Test for overall effect z=1.	-square=0.94 df=1 p=0	249 0.33 I ² =0.0%	-	100.0	0.56 [0.25, 1.26]
16 In babies where planne Subtotal (95% CI) Total events: 0 (Repeat), C Test for heterogeneity: no Test for overall effect: not	0) (Single) t applicable	re was > 24 mg/week of 0	betamethasone or equivalent	0.0	Not estimable
			0.01 0.1 10 100		
			Favours repeat Favours single		
			ravours repeat ravours single		

Analysis 01.25. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 25 Use of inotropic support

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 25 Use of inotropic support



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Favours repeat

Favours single

(Continued ...)

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
07111:	n/N	n/N	95% CI	(%)	95% CI
07 In babies exposed to on				0.0	Not estimable
Subtotal (95% CI)	0 (Single)	0		0.0	inot estimable
Total events: 0 (Repeat), 0 (Test for heterogeneity: not	/				
Test for overall effect: not a					
lest for overall effect. Hot a	ррпсавіе				
08 In babies exposed to tw					
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (/				
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
09 In babies exposed to the	ree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
10 In babies exposed to fou	ir or more repeat coi	urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0	5.6.6.6.6	0.0	Not estimable
Total events: 0 (Repeat), 0 (· ·		0.0	r voc osamasie
Test for heterogeneity: not					
Test for overall effect: not a					
•	·	-	betamethasone or equivalent	1000	0755055 1013
Crowther 2006	64/567	87/577	_	100.0	0.75 [0.55, 1.01]
Subtotal (95% CI)	567	577	•	100.0	0.75 [0.55, 1.01]
Total events: 64 (Repeat), 8	7 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=1.8	8 p=0.06				
12 In babies where planned	dose per treatment	course > 12 mg to 24	mg or less of betamethasone or equival	ent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not					
Test for overall effect: not a					
		. 24			
13 In babies where planned	·	_	methasone or equivalent	0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
14 In babies where planned	l repeat drug exposui	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	64/567	87/577	=	100.0	0.75 [0.55, 1.01]
Subtotal (95% CI)	567	577	•	100.0	0.75 [0.55, 1.01]
Total events: 64 (Repeat), 8					[,]
Test for heterogeneity: not					
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued)
					(

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)	
	n/N	n/N	95% CI	(%)	95% CI	
Test for overall effect z=	1.88 p=0.06					
15 In babies where plann	ned repeat drug exposur	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent		
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat),	0 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect: no	t applicable					
16 In babies where plann	ned repeat drug exposui	re was > 24 mg/week of	betamethasone or equivalent			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat),	0 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect: no	t applicable					
			0.1 0.2 0.5 1 2 5 10			

Analysis 01.26. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 26 Use of nitric oxide for respiratory support

Favours repeat Favours single

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 26 Use of nitric oxide for respiratory support

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all babies					
Crowther 2006	12/567	21/577	-	100.0	0.58 [0.29, 1.17]
Subtotal (95% CI)	567	577	-	100.0	0.58 [0.29, 1.17]
Total events: 12 (Repeat),	21 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.52 p=0.1				
02 In babies where pregn	ancy complicated by pr	reterm prelabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids a	as betamethasone			
Crowther 2006	12/567	21/577	-	100.0	0.58 [0.29, 1.17]
Subtotal (95% CI)	567	577	-	100.0	0.58 [0.29, 1.17]
Total events: 12 (Repeat),	21 (Single)				
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued)

					(continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl
Test for heterogeneity: not	t applicable				
Test for overall effect z=1.5	52 p=0.1				
04 In babies exposed to re	eneat corticosteroids	at a minimum interval of	7 days or less		
Crowther 2006	12/567	21/577	- days on less	100.0	0.58 [0.29, 1.17]
Subtotal (95% CI)	567	577		100.0	0.58 [0.29, 1.17]
Total events: 12 (Repeat), Test for heterogeneity: not	. 0 /				
Test for overall effect z=1					
	•				
05 In babies exposed to re	•		ween 8 and 14 days	0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: not Test for overall effect: not :					
est for overall effect. Hot i	аррисаріе				
06 In babies exposed to re	•		> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	, -,				
Test for heterogeneity: not					
Test for overall effect: not	applicable				
07 In babies exposed to o	ne repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
08 In babies exposed to tv	wo repeat courses of p	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
09 In babies exposed to th	nree repeat courses of	f prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not					
10 In babies exposed to fo	our or more repeat co	urses of prenatal corticos	teroids		
Subtotal (95% CI)	0 0	0	steroids	0.0	Not estimable
Total events: 0 (Repeat), 0		o .		0.0	1 VOC CSUITIABLE
Test for heterogeneity: not					
Test for overall effect: not					
			and the same of th		
I I In babies where planne Crowther 2006	ed dose per treatment 12/567	course 12 mg or less of 1 21/577	petamethasone or equivalent	100.0	058[020 171
Crowtrier 2006	12/30/	21/3//	_	100.0	0.58 [0.29, 1.17]
Subtotal (95% CI)	567	577		100.0	0.58 [0.29, 1.17]
			0.1 0.2 0.5 2 5 10		(= : : : : : : : : : : : : : : : : : : :
			Favours repeat Favours single		(Continued)

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Total events: 12 (Repeat),	21 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.52 p=0.1				
12 In babies where plann	ed dose per treatment o	course > 12 mg to 24 m	ng or less of betamethasone or equivalen	t	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
13 In babies where plann	ed dose per treatment o	course > 24 mg of betai	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
14 In babies where plann	ed repeat drug exposur	e was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	12/567	21/577		100.0	0.58 [0.29, 1.17]
Subtotal (95% CI)	567	577	-	100.0	0.58 [0.29, 1.17]
Total events: 12 (Repeat),	21 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.52 p=0.1				
15 In babies where plann	ed repeat drug exposur	e was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
16 In babies where plann	ed repeat drug exposur	e was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	: applicable				

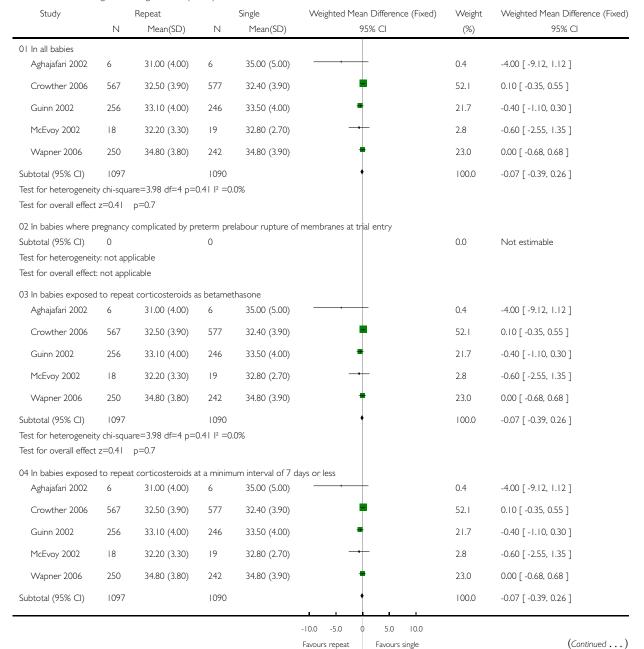
0.1 0.2 0.5 | 2 5 10 Favours repeat Favours single

Analysis 01.27. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 27 Mean gestational age at birth (weeks)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 27 Mean gestational age at birth (weeks)



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review)
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Study	N	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	(Continued Weighted Mean Difference (Fixed
Test for heterogeneit	y chi-squa	re=3.98 df=4 p=0		. ,	7576 CI	(70)	7570 Ci
05 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	to repea 0 y: not app	t corticosteroids a	t a minim 0	num interval betw	een 8 and 14 days	0.0	Not estimable
06 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	olicable	t a minim 0	num interval of >	l 4 days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	licable	enatal co 0	orticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	licable	renatal c	orticosteroids		0.0	Not estimable
09 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	licable	prenatal 0	corticosteroids		0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	licable	urses of p O	orenatal corticoste	proids	0.0	Not estimable
		·		_	tamethasone or equivalent	1000	0101 025 055 1
Crowther 2006 Subtotal (95% CI) Test for heterogeneit Test for overall effect	,		577 577	32.40 (3.90)	Ī	100.0	0.10 [-0.35, 0.55]
		·			or less of betamethasone or equivalent		
Aghajafari 2002 Guinn 2002	6 256	31.00 (4.00)	6	35.00 (5.00) 33.50 (4.00)		0.8 45.3	-4.00 [-9.12, 1.12] -0.40 [-1.10, 0.30]
McEvoy 2002	18	33.10 (4.00) 32.20 (3.30)	246 19	33.50 (4.00)		5.9	-0.40 [-1.10, 0.30]
Wapner 2006	250	34.80 (3.80)	242	34.80 (3.90)	.	48.0	0.00 [-0.68, 0.68]
iubtotal (95% CI) Test for heterogeneit Test for overall effect	530 y chi-squa	re=2.88 df=3 p=(513	, ,	•	100.0	-0.25 [-0.72, 0.22]
					-10.0 -5.0 0 5.0 10.0 Favours repeat Favours single		(Continued

Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
13 In babies where p	lanned do	se per treatment	course >	24 mg of betame	thasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect:	not appl	icable					
14 In babies where p	lanned re	peat drug exposur	e was 12	mg or less/week	of betamethasone or equivalent		
Crowther 2006	567	32.50 (3.90)	577	32.40 (3.90)	-	100.0	0.10 [-0.35, 0.55]
Subtotal (95% CI)	567		577		†	100.0	0.10 [-0.35, 0.55]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.43	p=0.7					
15 In babies where p	lanned re	peat drug exposur	e was >	12 mg/week to 24	mg/week of betamethasone or equivale	ent	
Aghajafari 2002	6	31.00 (4.00)	6	35.00 (5.00)		0.8	-4.00 [-9.12, 1.12]
Guinn 2002	256	33.10 (4.00)	246	33.50 (4.00)	•	45.3	-0.40 [-1.10, 0.30]
McEvoy 2002	18	32.20 (3.30)	19	32.80 (2.70)	-	5.9	-0.60 [-2.55, 1.35]
Wapner 2006	250	34.80 (3.80)	242	34.80 (3.90)	•	48.0	0.00 [-0.68, 0.68]
Subtotal (95% CI)	530		513		•	100.0	-0.25 [-0.72, 0.22]
Test for heterogeneit	y chi-squa	re=2.88 df=3 p=0).41 I ² =0.	.0%			
Test for overall effect	z=1.04	p=0.3					
16 In babies where p	lanned re	peat drug exposur	re was > 2	24 mg/week of be	tamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effects	not appl	icable					
					-10.0 -5.0 0 5.0 10.0		

Favours repeat

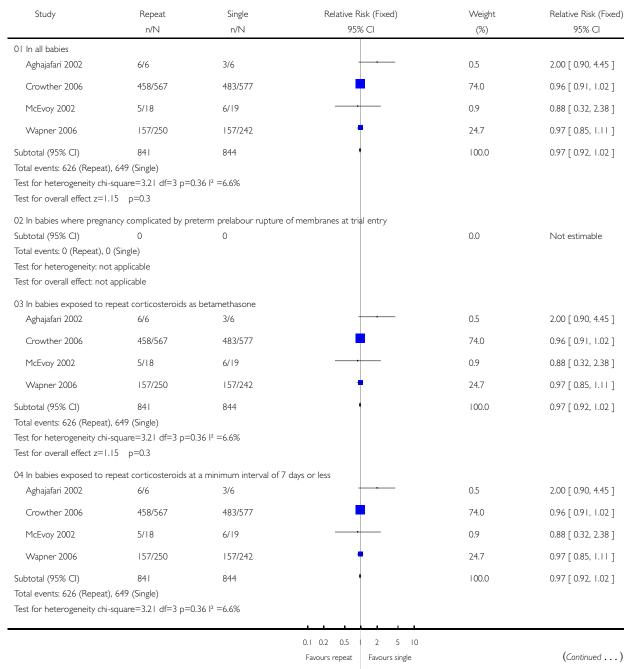
Favours single

Analysis 01.28. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 28 Preterm birth before 37 weeks

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 28 Preterm birth before 37 weeks



					(Containaed,
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Test for overall effect z=1.	15 p=0.3				
05 In babies exposed to re	epeat corticosteroids a	at a minimum interval bet	ween 8 and 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
06 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
07 In babies exposed to or	ne repeat course of pr	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
08 In babies exposed to tv	vo repeat courses of p	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not					
Test for overall effect: not a	• •				
09 In babies exposed to th	aree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0		Ü		0.0	r toe osamasie
Test for heterogeneity: not					
Test for overall effect: not a					
10 In babies exposed to fo	ur or man mant co	urror of propostal corticos	toroids		
Subtotal (95% CI)	0	urses or prenatar corticos	teroids	0.0	Not estimable
Total events: 0 (Repeat), 0		Ü		0.0	r toe osamasie
Test for heterogeneity: not					
Test for overall effect: not a					
II In habies where planne	d dose per treatment	course 12 mg or less of h	petamethasone or equivalent		
Crowther 2006	458/567	483/577	etamethasone or equivalent	100.0	0.96 [0.91, 1.02]
			Ţ		
Subtotal (95% CI)	567	577		100.0	0.96 [0.91, 1.02]
Total events: 458 (Repeat)					
Test for heterogeneity: not					
Test for overall effect z=1.3	30 p=0.2				
·		_	g or less of betamethasone or equivale		
Aghajafari 2002	6/6	3/6		1.8	2.00 [0.90, 4.45]
McEvoy 2002	5/18	6/19		3.5	0.88 [0.32, 2.38]
_					
			0.1 0.2 0.5 2 5 10		(5 :
			Favours repeat Favours single		(Continued \dots)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed
Wapner 2006	157/250	157/242	-	94.8	0.97 [0.85, 1.11]
Subtotal (95% CI)	274	267	•	100.0	0.98 [0.86, 1.12]
Total events: 168 (Repeat), 166 (Single)				
Test for heterogeneity chi-	-square=3.13 df=2 p=0	0.21 I ² =36.0%			
Test for overall effect z=0	0.25 p=0.8				
13 In babies where planne	ed dose per treatment	course > 24 mg of betam	nethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/weel	of betamethasone or equivalent		
Crowther 2006	458/567	483/577	•	100.0	0.96 [0.91, 1.02]
Subtotal (95% CI)	567	577	•	100.0	0.96 [0.91, 1.02]
Total events: 458 (Repeat)), 483 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect $z=1$.30 p=0.2				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to 3	24 mg/week of betamethasone or equiv	alent	
Aghajafari 2002	6/6	3/6		1.8	2.00 [0.90, 4.45]
McEvoy 2002	5/18	6/19		3.5	0.88 [0.32, 2.38]
Wapner 2006	157/250	157/242	=	94.8	0.97 [0.85, 1.11]
Subtotal (95% CI)	274	267	•	100.0	0.98 [0.86, 1.12]
Total events: 168 (Repeat)), 166 (Single)				
Test for heterogeneity chi-	-square=3.13 df=2 p=0	0.21 12 =36.0%			
Test for overall effect z=0	0.25 p=0.8				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week of l	petamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		

0.1 0.2 0.5 2 5 10

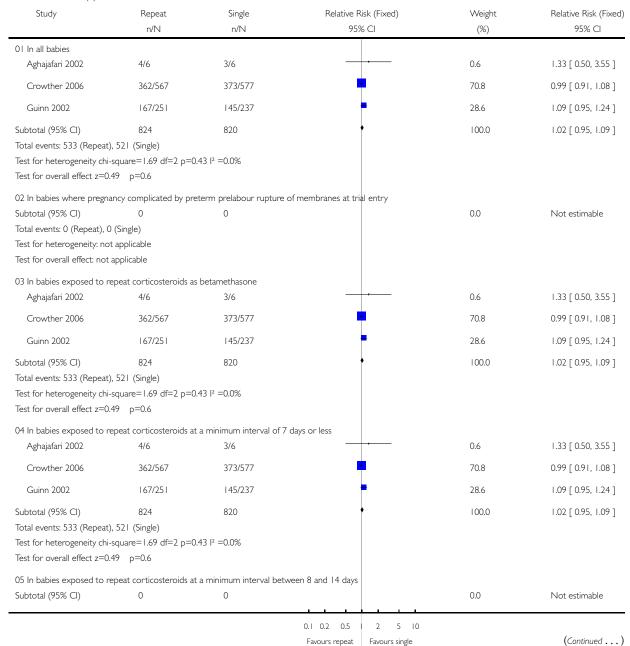
Favours repeat Favours single

Analysis 01.29. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 29 Very preterm birth before 34 weeks

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 29 Very preterm birth before 34 weeks



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Table events: 0 (Repeat), 0 (Single) Tast for heterogeneity, not applicable 06 in bables exposed to repost corticosteroids at a minimum interval of > 14 days Subtoal (PSK C) 0 0 0 0 0 0 0 0 0 0 0 0 Not estimable 10 fotal events: 0 (Repeat), 0 (Single) 10 fest for heterogeneity, not applicable 12 fest for overall effect: not applicable 12 fest for provent effect: not applicable 12 fest for revents: 0 (Repeat), 0 (Single) 12 fest for heterogeneity, not applicable 12 fest for provent effect: not applicable 12 fest for heterogeneity, not applicable 13 fest for heterogeneity, not applicable 14 fest for heterogeneity, not applicable 15 fest for event effect: not applicable 16 fest for heterogeneity, not applicable 17 fest events: 0 (Repeat), 0 (Single) 18 fest for heterogeneity, not applicable 19 in bables exposed to three repeat courses of prenatal corticosteroids 15 Subtoal (PSK C) 0 0 0 0 Not estimable 16 fest for event effect: not applicable 17 in bables exposed to three repeat courses of prenatal corticosteroids 18 subtrait (PSK C) 0 0 0 0 Not estimable 19 in bables exposed to four or more repeat courses of prenatal corticosteroids 19 subtrait (PSK C) 0 0 0 0 Not estimable 10 in bables exposed to four or more repeat courses of prenatal corticosteroids 10 in bables exposed to four or more repeat courses of prenatal corticosteroids 10 in bables exposed to four or more repeat courses of prenatal corticosteroids 10 in bables exposed to four or more repeat courses of prenatal corticosteroids 11 in bables where planned dose per treatment course 12 mg or less of betamethasone or equivalent 12 in bables where planned dose per treatment course 12 mg or less of betamethasone or equivalent 12 in bables where planned dose per treatment course 12 mg or less of betamethasone or equivalent 12 in bables where planned dose per treatment course 12 mg or less of betamethaso	Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
Test for heterogeneity, not applicable Test for overall effect not applicable Test for overall effect not applicable Substants (PRSS C) D D D Not estimabili Total events (0 Repeat), 0 (Single) Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effec		n/N	n/N	95% CI	(%)	95% CI
Test for overall effect: not applicable 86 In bables exposed to repeat corticosteroids at a minimum interval of > 14 days 50 total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect not opplicable Test for overall effect not opplicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for heterogeneity of heterogeneity	Total events: 0 (Repeat), 0	(Single)				
06 in habbes exposed to repeat corrisosteroids at a minimum interval of > 14 days Subtrotal (95% C) 0 0 0 0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogenety: not applicable Test for heterogenety: not applicable Test for heterogenety: not applicable Test for overall effect not applicable Test for preventil effect not applicable Test for overall effect not applicable Test for heterogenety: not applicable Test for overall effect not applicable Test for heterogeneity: not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect not applicable Test for heterogeneity: not applicable Test for heteroge	Test for heterogeneity: not	applicable				
Subtotal (95% CI) 0 0 0. Not estimable Total events (9 (Repeat), 0 Clingle) Total events (9 (Repeat), 0 Clingle) Test for heterogeneity, not applicable Test for overall effect not applicable Test for overall effect not applicable Total events (9 (Repeat), 0 Clingle) Test for heterogeneity, not applicable Test for overall effect	Test for overall effect: not a	applicable				
Total events: 0 (Repeat), 0 (Single) Test for heterrogeneity, not applicable 107 In babies exposed to one repeat course of prenatal corticosteroids Subtroal (95% C) 0 0 0.0 Not estimabil Total events: 0 (Repeat), 0 (Single) Test for heterrogeneity, not applicable 108 In babies exposed to two repeat courses of prenatal corticosteroids Subtroal (95% C) 0 0 0.0 Not estimabil Test for overall effect: not applicable 108 In babies exposed to two repeat courses of prenatal corticosteroids Subtroal (95% C) 0 0 0.0 Not estimabil Test for overall effect: not applicable 106 In babies exposed to two repeat courses of prenatal corticosteroids Subtroal (95% C) 0 0 0.0 Not estimabil Test for overall effect: not applicable 107 In babies exposed to three repeat courses of prenatal corticosteroids Subtroal (95% C) 0 0 0.0 Not estimabil Test for overall effect: not applicable 108 Total events: 0 (Repeat), 0 (Single) 109 Total events: 0 (Repeat), 0 (Single) 100 Total events: 0 (Repeat)	·	epeat corticosteroids a	t a minimum interval of >	14 days		
Test for heterogeneity; not applicable lest for overall effect: not applicable lest for overall effect: not applicable Substotal (95% C) 0 0 0. Total events: 0 (Repeat), 0 (Single) lest for heterogeneity; not applicable lest for overall effect: not applicable lost for overall effect: not applicable lost for overall effect: not applicable lost for overall effect: not applicable lest for overall effect:	` '		0		0.0	Not estimable
Test for overall effect not applicable 70 in babies exposed to one repeat course of prenatal corticosteroids 5. Subtonal (95% CI) 0 0 0. Not estimability of the test for overall effect not applicable 18st for overall effect not applicable 19st for heterogeneity not applicable 19st for heterogeneity not applicable 19st for overall effect not applicable 10st for overal	, , ,	, - ,				
07 In bables exposed to one repeat course of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0,0 Not estimable Total events 0 (Repeat), 0 (Single) Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect y=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg or less of betamethasone or equivalent Aghajafara 2002 446 3/6 Guina 2002 1677251 145/237 98.0 1.09 [0.95, 1.500] Total events: 71 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 P=0.0% Test for overall effect z=1.30 p=0.2	- ,					
Subtotal (95% CI) 0 0 0.0 Not estimable (Total events: 0 (Repeat), 0 (Single) (First for heterogeneity, not applicable (First for overall effect not applicable (First for heterogeneity, not applicable (First for heterogeneity, not applicable (First for overall effect not applicable (First for heterogeneity, not applicable (First for overall effect not applicable (First for heterogeneity, not applicable	lest for overall effect: not a	applicable				
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect not applicable Test for overall effect and applicable Test for overall effect and applicable Test for overall effect and applicable Test for heterogeneity: not applicable Test for overall effect not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heterogeneity: not applicable Test for overall effect not applicable Test for heterogeneity: Not applicable Test for heterogenei	07 In babies exposed to or	ne repeat course of pr	enatal corticosteroids			
Test for heterogeneity, not applicable Test for overall effect z=0.28 p=0.8 Total events: 362 (Repeat), 373 (Single) Test for overall effect z=0.28 p=0.8 Total events: 362 (Repeat), 373 (Single) Test for overall effect z=0.28 p=0.8 Total events: 362 (Repeat), 373 (Single) Test for overall effect z=0.28 p=0.8 Total events: 362 (Repeat), 446 3/6 Zo 1.33 (5.50, 3 Total events: 171 (Repeat), 148 (Single) Test for overall effect z=1.30 p=0.2	Subtotal (95% CI)	0	0		0.0	Not estimable
Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% C) 0 0 0 0 0 Not estimabil Test for heterogeneity; not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for heterogeneity; not applicable Test for overall effect not applicable Test for heterogeneity; not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for ov	, , ,	/				
88 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% C) 0 0 0 0. Not estimabilization (Single) Test for Note (Repeat), 0 (Single) Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect z=1.30 p=0.2 0.0 Not estimabilized Test for overall effect z=1.30 p=0.2 0.0 Not estimabilized Test for overall effect z=1.30 p=0.2 0.0 Not estimabilized Test for overall effect z=1.30 p=0.2 0.0 Not estimabilized Test for overall effect z=1.30 p=0.2						
Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for neterose ((Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect not applicable Test for neterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect z=1.30 p=0.8 Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect z=1.30 p=0.2 Output Ou	Test for overall effect: not a	applicable				
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity; not applicable Test for overall effect: 2=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3.6] Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1.5] Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1.5] Total events: 71 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 P=0.0% Test for overall effect z=1.30 p=0.2	08 In babies exposed to tv	vo repeat courses of p	renatal corticosteroids			
Test for heterogeneity not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for overall effect not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 IP=0.0% Test for overall effect z=1.30 p=0.2	Subtotal (95% CI)	0	0		0.0	Not estimable
Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for not effect not app						
99 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% C) 0 0 0. Not estimable Test for heterogeneity: not applicable Test for overall effect not applicable Test for overall effect on applicable Test for overall effect point of the property of the proper	9 ,					
Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect not applicable Total events: 362 (Repeat), 373 (Single) Test for heterogeneity, not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajariar 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity, not applicable Test for heterogeneity chi-square=0.16 df=1 p=0.69 P =0.0% Test for overall effect z=1.30 p=0.2	Test for overall effect: not a	applicable				
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, 1. Subtotal (95% CI) 567 577 100.0 0.99 [0.91, 1. Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 112 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafan 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.30 p=0.2	09 In babies exposed to th	ree repeat courses of	prenatal corticosteroids			
Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, I. Subtotal (95% CI) 567 577 100.0 0.99 [0.91, I. Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafan 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, I. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 P =0.0% Test for overall effect z=1.30 p=0.2	Subtotal (95% CI)	0	0		0.0	Not estimable
Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI)	Total events: 0 (Repeat), 0	(Single)				
10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, I. Subtotal (95% CI) 567 577 100.0 0.99 [0.91, I. Total events: 362 (Repeat), 373 (Single) Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, I. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, I. Total events: 171 (Repeat), 148 (Single) Test for overall effect z=1.30 p=0.2						
Subtotal (95% CI) 0 0 0 0 0. Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 I00.0 0.99 [0.91, I. o.	Test for overall effect: not a	applicable				
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, 1. 0.00 0.99 [0.91, 1. 0. 0.99 [0.91, 1. 0.00 0.99 [0.91, 1	10 In babies exposed to fo	our or more repeat cou	irses of prenatal corticoste	eroids		
Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, 1. Subtotal (95% CI) 567 577 100.0 0.99 [0.91, 1. Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 P =0.0% Test for overall effect z=1.30 p=0.2	Subtotal (95% CI)	0	0		0.0	Not estimable
Test for overall effect: not applicable II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Crowther 2006 362/567 373/577 100.0 0.99 [0.91, 1. 100.0		/				
11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent						
Crowther 2006 362/567 373/577 100.0 0.99 [0.91, 1. Subtotal (95% CI) 567 577 100.0 0.99 [0.91, 1. Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 98.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Test for overall effect: not a	applicable				
Subtotal (95% CI) 567 577 100.0 0.99 [0.91, 1. Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/25 1 145/237 98.0 1.09 [0.95, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	II In babies where planne	d dose per treatment (course 12 mg or less of be	tamethasone or equivalent		
Total events: 362 (Repeat), 373 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betameth asone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Crowther 2006	362/567	373/577	-	100.0	0.99 [0.91, 1.08]
Test for heterogeneity: not applicable Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 ² =0.0% Test for overall effect z=1.30 p=0.2	Subtotal (95% CI)	567	577	+	100.0	0.99 [0.91, 1.08]
Test for overall effect z=0.28 p=0.8 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Aghajafari 2002 4/6 3/6 Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Total events: 362 (Repeat),	, 373 (Single)				
12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betameth asone or equivalent Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Test for heterogeneity: not	applicable				
Aghajafari 2002 4/6 3/6 2.0 1.33 [0.50, 3. Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Test for overall effect z=0.2	28 p=0.8				
Guinn 2002 167/251 145/237 98.0 1.09 [0.95, 1. Subtotal (95% CI) 257 243 100.0 1.09 [0.96, 1. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	12 In babies where planne	d dose per treatment o	course > 12 mg to 24 mg	or less of betamethasone or equivalen	t	
Subtotal (95% CI) 257 243 100.0 1.09 [0.96, I. Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 2 = 0.0% Test for overall effect z=1.30 p=0.2	Aghajafari 2002	4/6	3/6		2.0	1.33 [0.50, 3.55]
Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 ² =0.0% Test for overall effect z=1.30 p=0.2 0.1 0.2 0.5 2 5 10	Guinn 2002	167/251	145/237	-	98.0	1.09 [0.95, 1.24]
Total events: 171 (Repeat), 148 (Single) Test for heterogeneity chi-square=0.16 df=1 p=0.69 $ ^2$ =0.0% Test for overall effect z=1.30 p=0.2 0.1 0.2 0.5 2 5 10	Subtotal (95% CI)	257	243	•	100.0	1.09 [0.96, 1.25]
Test for heterogeneity chi-square=0.16 df=1 p=0.69 l^2 =0.0% Test for overall effect z=1.30 p=0.2 0.1 0.2 0.5 2 5 10	, ,		· -			[0, 1.20]
Test for overall effect z=1.30 p=0.2 0.1 0.2 0.5 2 5 10	` ' '	, - ,	0.69 l² =0.0%			
	- '					
Favours repeat Favours single (Continued				0.1 0.2 0.5 2 5 10		
				Favours repeat Favours single		(Continued)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed	
	n/N	n/N	95% CI	(%)	95% CI	
13 In babies where plann	ed dose per treatment o	course > 24 mg of betam	nethasone or equivalent			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat),	0 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect: no	t applicable					
14 In babies where plann	ned repeat drug exposur	e was 12 mg or less/weel	k of betamethasone or equivalent			
Crowther 2006	362/567	373/577	•	100.0	0.99 [0.91, 1.08]	
Subtotal (95% CI)	567	577	•	100.0	0.99 [0.91, 1.08]	
Total events: 362 (Repea	t), 373 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect z=0	0.28 p=0.8					
15 In babies where plann	ned repeat drug exposur	e was > 12 mg/week to 2	24 mg/week of betamethasone or equiv	alent		
15 In babies where plann Aghajafari 2002	ned repeat drug exposur 4/6	e was > 12 mg/week to 2 3/6	24 mg/week of betamethasone or equiv	alent 2.0	1.33 [0.50, 3.55]	
		9	24 mg/week of betamethasone or equiv		1.33 [0.50, 3.55] 1.09 [0.95, 1.24]	
Aghajafari 2002	4/6	3/6	24 mg/week of betamethasone or equiv	2.0		
Aghajafari 2002 Guinn 2002	4/6 167/251 257	3/6 145/237	24 mg/week of betamethasone or equiv	2.0 98.0	1.09 [0.95, 1.24]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI)	4/6 167/251 257 t), 148 (Single)	3/6 145/237 243	24 mg/week of betamethasone or equiv	2.0 98.0	1.09 [0.95, 1.24]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI) Total events: 171 (Repeat	4/6 167/251 257 t), 148 (Single) i-square=0.16 df=1 p=0	3/6 145/237 243	24 mg/week of betamethasone or equiv.	2.0 98.0	1.09 [0.95, 1.24]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI) Total events: 171 (Repeat Test for heterogeneity ch Test for overall effect z=	4/6 167/251 257 t), 148 (Single) i-square=0.16 df=1 p=0 1.30 p=0.2	3/6 145/237 243 0.69 ² =0.0%	24 mg/week of betamethasone or equivi-	2.0 98.0	1.09 [0.95, 1.24]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI) Total events: 171 (Repeat Test for heterogeneity ch Test for overall effect z=	4/6 167/251 257 t), 148 (Single) i-square=0.16 df=1 p=0 1.30 p=0.2	3/6 145/237 243 0.69 ² =0.0%		2.0 98.0	1.09 [0.95, 1.24]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI) Total events: 171 (Repeat Test for heterogeneity chartest for overall effect z=16 In babies where plann	4/6 167/251 257 t), 148 (Single) i-square=0.16 df=1 p=0 1.30 p=0.2 i-square exposur 0	3/6 145/237 243 0.69 ² =0.0% e was > 24 mg/week of b		2.0 98.0 100.0	1.09 [0.95, 1.24] 1.09 [0.96, 1.25]	
Aghajafari 2002 Guinn 2002 Subtotal (95% CI) Total events: 171 (Repear Test for heterogeneity ch Test for overall effect z=1 16 In babies where plann Subtotal (95% CI)	4/6 167/25 I 257 t), 148 (Single) i-square=0.16 df=1 p=0 1.30 p=0.2 ted repeat drug exposur 0 0 (Single)	3/6 145/237 243 0.69 ² =0.0% e was > 24 mg/week of b		2.0 98.0 100.0	1.09 [0.95, 1.24] 1.09 [0.96, 1.25]	

0.1 0.2 0.5 2 5 10

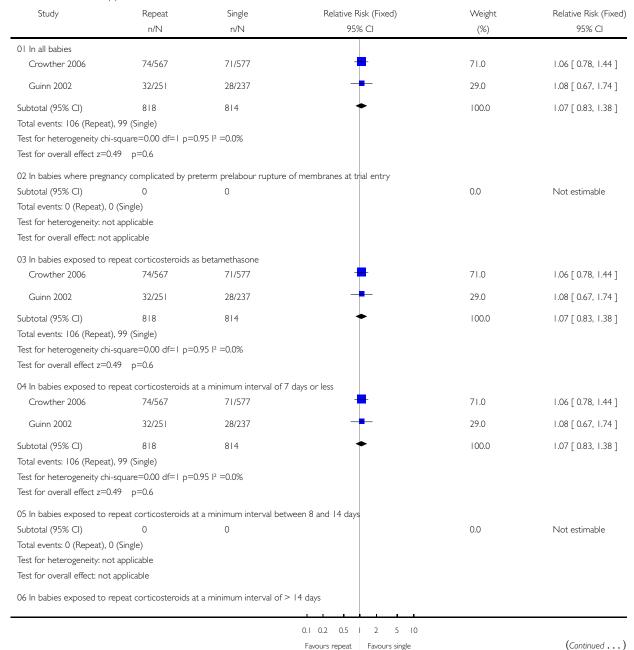
Favours repeat Favours single

Analysis 01.30. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 30 Extremely preterm birth before 28 weeks

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 30 Extremely preterm birth before 28 weeks



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours repeat Favours single

					(continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI	
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not a	applicable					
)7 In babies exposed to or	ne repeat course of p	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
otal events: 0 (Repeat), 0	(Single)					
est for heterogeneity: not	applicable					
est for overall effect: not a	applicable					
8 In babies exposed to tw	vo repeat courses of p	orenatal corticosteroids				
ubtotal (95% CI)	0	0		0.0	Not estimable	
otal events: 0 (Repeat), 0	(Single)					
est for heterogeneity: not	applicable					
est for overall effect: not a	applicable					
9 In babies exposed to th	ree repeat courses of	prenatal corticosteroids				
ubtotal (95% CI)	0	0		0.0	Not estimable	
otal events: 0 (Repeat), 0	(Single)					
est for heterogeneity: not	applicable					
est for overall effect: not a	applicable					
0 In babies exposed to fo	ur or more repeat co	urses of prenatal cortico	steroids			
ubtotal (95% CI)	0	0		0.0	Not estimable	
otal events: 0 (Repeat), 0	(Single)					
est for heterogeneity: not	applicable					
est for overall effect: not a	applicable					
I In babies where planned	d dose per treatment	course 12 mg or less of	betamethasone or equivalent			
Crowther 2006	74/567	71/577	=	100.0	1.06 [0.78, 1.44]	
ubtotal (95% CI)	567	577	•	100.0	1.06 [0.78, 1.44]	
otal events: 74 (Repeat), 7	71 (Single)					
est for heterogeneity: not	applicable					
est for overall effect z=0.3	88 p=0.7					
2 In babies where planned	d dose per treatment	course > 12 mg to 24 m	ng or less of betamethasone or equivaler	nt		
Guinn 2002	32/251	28/237	+	100.0	1.08 [0.67, 1.74]	
ubtotal (95% CI)	251	237	-	100.0	1.08 [0.67, 1.74]	
otal events: 32 (Repeat), 2	28 (Single)					
est for heterogeneity: not	applicable					
est for overall effect z=0.3	81 p=0.8					
3 In babies where planned	d dose per treatment	course > 24 mg of betai	methasone or equivalent			
ubtotal (95% CI)	0	0		0.0	Not estimable	
otal events: 0 (Repeat), 0	(Single)					
est for heterogeneity: not	applicable					
est for overall effect: not a	applicable					
			0.1 0.2 0.5 1 2 5 10		,	
			Favours repeat Favours single		(Continued)	

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
14 In babies where plann	ed repeat drug exposur	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	74/567	71/577	#	100.0	1.06 [0.78, 1.44]
Subtotal (95% CI)	567	577	*	100.0	1.06 [0.78, 1.44]
Total events: 74 (Repeat),	71 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0	.38 p=0.7				
15 In babies where plann	ed repeat drug exposur	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent valent	
Guinn 2002	32/25	28/237	+	100.0	1.08 [0.67, 1.74]
Subtotal (95% CI)	251	237	•	100.0	1.08 [0.67, 1.74]
Total events: 32 (Repeat),	28 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0	.31 p=0.8				
16 In babies where plann	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), ((Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				

0.1 0.2 0.5 1 2 5 10

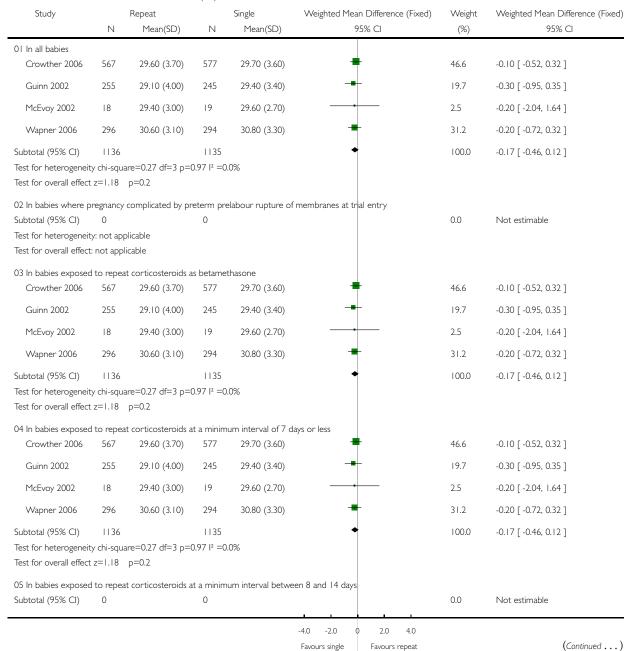
Favours repeat Favours single

Analysis 01.31. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 31 Mean head circumference at birth (cm)

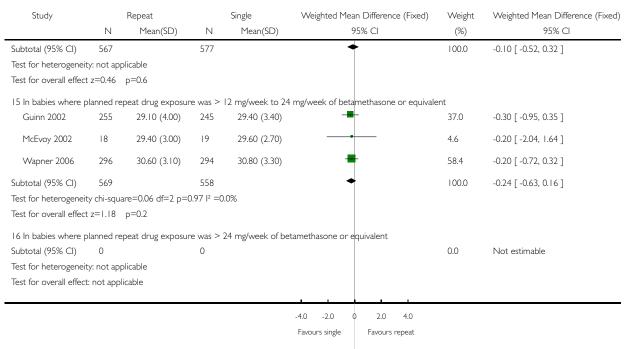
Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 31 Mean head circumference at birth (cm)



							(Continued
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed 95% CI) Weight (%)	Weighted Mean Difference (Fixed 95% CI
Test for heterogeneit	ty: not app	olicable					
Test for overall effect	t: not appl	licable					
06 In babies exposed	to renea	at corticosteroids a	t a minin	num interval of > I	14 days		
Subtotal (95% CI)	0	ar cor acostor oras a	0	indiri inter var er	1 54/3	0.0	Not estimable
Test for heterogeneit		olicable	Ü			0.0	T tot ostillasio
Test for overall effect							
07 la babina avanana		annot solves of se	anatal aa	uticactaucida			
07 In babies exposed Subtotal (95% CI)	0	epeat course or pr	0	or ticosteroids		0.0	Not estimable
Test for heterogeneit		alicable	U			0.0	NOT ESTIMABLE
Test for overall effect	,						
08 In babies exposed		repeat courses of p		orticosteroids			
Subtotal (95% CI)	0	P 11	0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect	:: пот аррі	licable					
09 In babies exposed		repeat courses of		corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	,						
Test for overall effect	t: not appl	licable					
10 In babies exposed	d to four o	or more repeat cou	urses of p	orenatal corticoste	roids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	ty: not app	olicable					
Test for overall effect	: not appl	licable					
I I In babies where p	olanned do	ose per treatment	course l	2 mg or less of bet	tamethasone or equivalent		
Crowther 2006	567	29.60 (3.70)	577	29.70 (3.60)	=	100.0	-0.10 [-0.52, 0.32]
Subtotal (95% CI)	567		577		•	100.0	-0.10 [-0.52, 0.32]
Test for heterogeneit	ty: not app	olicable					
Test for overall effect	z=0.46	p=0.6					
12 In babies where r	olanned do	ose per treatment	course >	· 12 mg to 24 mg c	or less of betamethasone or equivaler	nt	
Guinn 2002	255	29.10 (4.00)	245	29.40 (3.40)	-	37.0	-0.30 [-0.95, 0.35]
McEvoy 2002	18	29.40 (3.00)	19	29.60 (2.70)		4.6	-0.20 [-2.04, 1.64]
Wapner 2006	296	30.60 (3.10)	294	30.80 (3.30)	-	58.4	-0.20 [-0.72, 0.32]
·		30.00 (3.10)		30.00 (3.30)			-
Subtotal (95% CI)	569		558	0.00/	_	100.0	-0.24 [-0.63, 0.16]
Test for heterogeneit Test for overall effect			J.7/ l² =(J.U%			
lest for overall effect	2-1.10	p=0.2					
		ose per treatment		· 24 mg of betamet	thasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect	:: not appl	licable					
					of betamethasone or equivalent		
Crowther 2006	567	29.60 (3.70)	577	29.70 (3.60)	=	100.0	-0.10 [-0.52, 0.32]
					40 30 0 30 10		
					-4.0 -2.0 0 2.0 4.0		(Continued
					Favours single Favours repeat		(Conunded

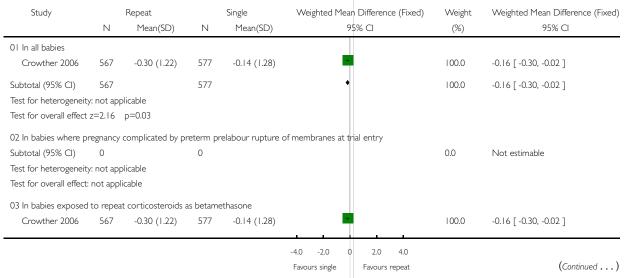


Analysis 01.32. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 32 Head circumference Z scores at birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 32 Head circumference Z scores at birth



							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Subtotal (95% CI) Test for heterogeneity Test for overall effect			577		•	100.0	-0.16 [-0.30, -0.02]
04 In babies exposed Crowther 2006	to repeat	corticosteroids a	at a minin 577	num interval of 7 -0.14 (1.28)	days or less	100.0	-0.16 [-0.30, -0.02]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			577		•	100.0	-0.16 [-0.30, -0.02]
05 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	to repeat 0 v: not app	corticosteroids a	at a minin 0	num interval betv	veen 8 and 14 days	0.0	Not estimable
06 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	at a minin 0	num interval of >	14 days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	to one re 0 v: not app	epeat course of p	renatal co	orticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	orenatal c	orticosteroids		0.0	Not estimable
09 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	to three of	repeat courses o	f prenatal 0	corticosteroids		0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	licable	urses of p	orenatal corticost	eroids	0.0	Not estimable
II In babies where place Crowther 2006	anned do	se per treatment -0.30 (1.22)	course I	2 mg or less of be	etamethasone or equivalent	100.0	-0.16 [-0.30, -0.02]
Subtotal (95% CI) Test for heterogeneity Test for overall effect	567 /: not app	licable	577	()	•	100.0	-0.16 [-0.30, -0.02]
12 In babies where pla Subtotal (95% CI) Test for heterogeneity	0	·	course >	· 12 mg to 24 mg	or less of betamethasone or equivalent	0.0	Not estimable
					-4.0 -2.0 0 2.0 4.0 Favours single Favours repeat		(Continued)

Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for overall effect	: not appli	icable					
13 In babies where p	lanned do	se per treatment	course >	24 mg of betam	ethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appl	icable					
14 In babies where p	lanned re	peat drug exposu	re was 12	! mg or less/week	of betamethasone or equivalent		
Crowther 2006	567	-0.30 (1.22)	577	-0.14 (1.28)	-	100.0	-0.16 [-0.30, -0.02]
Subtotal (95% CI)	567		577		•	100.0	-0.16 [-0.30, -0.02]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=2.16	p=0.03					
15 In babies where p	lanned re	peat drug exposu	re was >	12 mg/week to 2	24 mg/week of betamethasone or equiva	llent	
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appli	icable					
16 In babies where p	lanned re	peat drug exposu	re was >	24 mg/week of b	etamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appli	icable					
					-4.0 -2.0 0 2.0 4.0		

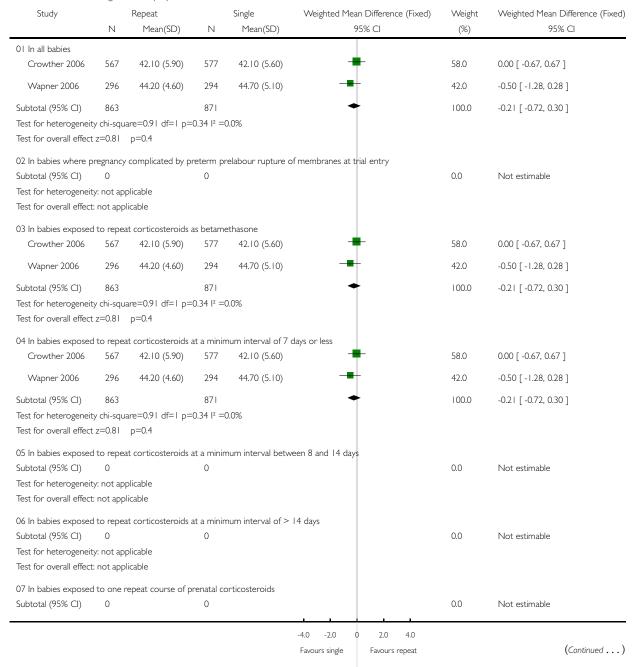
Favours single

Analysis 01.33. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 33 Mean length at birth (cm)

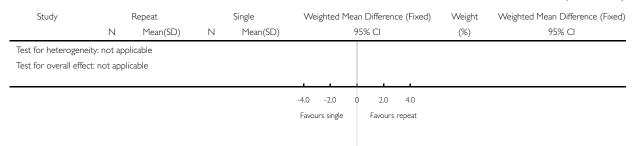
Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 33 Mean length at birth (cm)



							(Continued
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed
	Ν	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity							
Test for overall effect:	not appl	licable					
08 In babies exposed	to two r	repeat courses of p	orenatal o	corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	y: not app	plicable					
Test for overall effect:	not appl	licable					
09 In babies exposed	to three	repeat courses of	f prenatal	corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	v: not apr	olicable					
Test for overall effect:							
					.,		
10 In babies exposed	to four o	or more repeat co	urses of	prenatai corticost	eroids	0.0	Not estimable
Subtotal (95% CI)		aliaabla	U			0.0	Not estimable
Test for heterogeneit; Test for overall effect:							
•		•		-	etamethasone or equivalent		
Crowther 2006	567	42.10 (5.90)	577	42.10 (5.60)		100.0	0.00 [-0.67, 0.67]
Subtotal (95% CI)	567		577		+	100.0	0.00 [-0.67, 0.67]
Test for heterogeneity	y: not app	plicable					
Test for overall effect	z=0.00	p=I					
12 In habies where n	anned do	ose per treatment	course >	12 mg to 24 mg	or less of betamethasone or equivalent		
Wapner 2006	296	44.20 (4.60)	294	44.70 (5.10)	——————————————————————————————————————	100.0	-0.50 [-1.28, 0.28]
·		()		()			-
Subtotal (95% CI)	296	P 11	294			100.0	-0.50 [-1.28, 0.28]
Test for heterogeneity							
Test for overall effect	Z=1.25	p=0.2					
13 In babies where pl	anned do	ose per treatment	course >	24 mg of betam	ethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	y: not app	plicable					
Test for overall effect:	not appl	licable					
I 4 In babies where pl	anned re	epeat drug exposu	re was 12	2 mg or less/week	of betamethasone or equivalent		
Crowther 2006	567	42.10 (5.90)	577	42.10 (5.60)	-	100.0	0.00 [-0.67, 0.67]
C. h+-+-1 (0E9/ CI)	F/7		F 77		_	100.0	000 0 0 7 0 7 1
Subtotal (95% CI)	567	aliaabla	577		T	100.0	0.00 [-0.67, 0.67]
Test for heterogeneit; Test for overall effect							
lest for overall effect	2-0.00	p=1					
15 In babies where pl	anned re	epeat drug exposu	re was >		24 mg/week of betamethasone or equival	lent	
Wapner 2006	296	44.20 (4.60)	294	44.70 (5.10)		100.0	-0.50 [-1.28, 0.28]
Subtotal (95% CI)	296		294		-	100.0	-0.50 [-1.28, 0.28]
Test for heterogeneity	y: not app	plicable					
Test for overall effect	z=1.25	p=0.2					
16 In habies where o	anned re	neat drug evnocu	re W/2¢ >	24 mg/week of h	etamethasone or equivalent		
Subtotal (95% CI)	0	hear ai as exhosa	re was \sim	Z i mg/week of D	Cumulasonie or equivalent	0.0	Not estimable
345 (7376 CI)						0.0	1 40t Catimabic
					-4.0 -2.0 0 2.0 4.0		
					Favours single Favours repeat		(Continued
					<u> </u>		(22.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2.2



Analysis 01.34. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 34 Length Z scores at birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 34 Length Z scores at birth

Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 In all babies							
Crowther 2006	567	-0.53 (1.31)	577	-0.48 (1.22)	•	100.0	-0.05 [-0.20, 0.10]
Subtotal (95% CI)	567		577		•	100.0	-0.05 [-0.20, 0.10]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.67	p=0.5					
02 In babies where p	regnancy	complicated by p	reterm pr	relabour rupture o	of membranes at trial entry		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appl	icable					
03 In babies exposed	I to repea	t corticosteroids a	as betame	ethasone			
Crowther 2006	567	-0.53 (1.31)	577	-0.48 (1.22)	-	100.0	-0.05 [-0.20, 0.10]
Subtotal (95% CI)	567		577		†	100.0	-0.05 [-0.20, 0.10]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.67	p=0.5					
04 In babies exposed	I to repea	t corticosteroids a	at a minin	num interval of 7	days or less		
Crowther 2006	567	-0.53 (1.31)	577	-0.48 (1.22)	<u>*</u>	100.0	-0.05 [-0.20, 0.10]
Subtotal (95% CI)	567		577		†	100.0	-0.05 [-0.20, 0.10]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.67	p=0.5					
05 In babies exposed	I to repea	t corticosteroids a	at a minin	num interval betw	veen 8 and 14 days		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appl	icable					
					-4.0 -2.0 0 2.0 4.0		
					Favours single Favours repeat		(Continued)
							(

								(Continue
Study		Repeat		Single	Weighted	Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixe
	Ν	Mean(SD)	Ν	Mean(SD)		95% CI	(%)	95% CI
06 In babies exposed t	o repeat	corticosteroids	at a minim	num interval of >	> 14 days			
Subtotal (95% CI)	0		0				0.0	Not estimable
Test for heterogeneity:	not app	licable						
Test for overall effect: r	not appli	cable						
07 In babies exposed t	o one re	epeat course of p	renatal co	rticosteroids				
Subtotal (95% CI)	0		0				0.0	Not estimable
Test for heterogeneity:	not app	licable						
Test for overall effect: r	not appli	cable						
08 In babies exposed t	o two re	epeat courses of	orenatal c	orticosteroids				
Subtotal (95% CI)	0		0				0.0	Not estimable
Test for heterogeneity:		licable						
Test for overall effect: r								
09 In babies exposed t	o three	repeat courses o	forenatal	corticosteroids				
Subtotal (95% CI)	0	repeat courses o	О	corticosteroids			0.0	Not estimable
Test for heterogeneity:		licable	O				0.0	NOT CSTITIABLE
Test for overall effect: r								
			c					
10 In babies exposed t	.o 10ur o	r more repeat co	ourses of p	renatai corticos	teroias		0.0	Net estimable
Subtotal (95% CI)		Carleta	U				0.0	Not estimable
Test for heterogeneity:								
Test for overall effect: r	10т арріі	cable						
I I n babies where pla					etamethasone	or equivalent		
Crowther 2006	567	-0.53 (1.31)	577	-0.48 (1.22)		_	100.0	-0.05 [-0.20, 0.10]
Subtotal (95% CI)	567		577			•	100.0	-0.05 [-0.20, 0.10]
Test for heterogeneity:	not app	licable						
Test for overall effect z	=0.67	p=0.5						
12 In babies where pla	nned do	se per treatment	course >	12 mg to 24 mg	g or less of beta	amethasone or equivalent		
Subtotal (95% CI)	0		0				0.0	Not estimable
Test for heterogeneity:	not app	licable						
Test for overall effect: r	not appli	cable						
3 In babies where pla	nned do	se per treatment	course >	24 mg of hetan	nethasone or e	nuivalent		
Subtotal (95% CI)	0		0	6			0.0	Not estimable
Test for heterogeneity:	not ann	licable	-					
Test for overall effect: r								
14 In babies where pla	nned rer	peat drug exposu	re was 12	ma or less/wee	k of hetametha	sone or equivalent		
Crowther 2006	567	-0.53 (1.31)	577	-0.48 (1.22)	K Of Detailletild	+	100.0	-0.05 [-0.20, 0.10]
		0.05 (1.51)		0110 (1122)		Ţ		-
Subtotal (95% CI)	567	P 1.1	577				100.0	-0.05 [-0.20, 0.10]
Test for heterogeneity:								
Test for overall effect z	=0.6/	p=0.5						
5 In babies where pla	nned rep	oeat drug exposu	re was >	12 mg/week to	24 mg/week of	betamethasone or equival	lent	
Subtotal (95% CI)	0		0				0.0	Not estimable
						1 1		
					-4.0 -2.0	0 2.0 4.0		/
					Favours single	Favours repeat		(Continued

Study	Repeat Single Weighted Mean Difference (Fixed		ce (Fixed)	Weight	Weighted Mean Difference (Fixed)					
	Ν	Mean(SD)	Ν	Mean(SD)			95% CI		(%)	95% CI
Test for heterogene	eity: not app	olicable								
Test for overall effe	ct: not appl	icable								
16 In babies where	planned re	peat drug exposu	ire was >	24 mg/week of b	oetameth	nasone or	equivalent			
Subtotal (95% CI)	0		0						0.0	Not estimable
Test for heterogene	eity: not app	olicable								
Test for overall effe	ct: not appl	icable								
					-4.0	-2.0	0 2.0	4.0		
					Favou	rs single	Favours	repeat		

Analysis 01.35. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 35 Length multiples of the median at birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 35 Length multiples of the median at birth

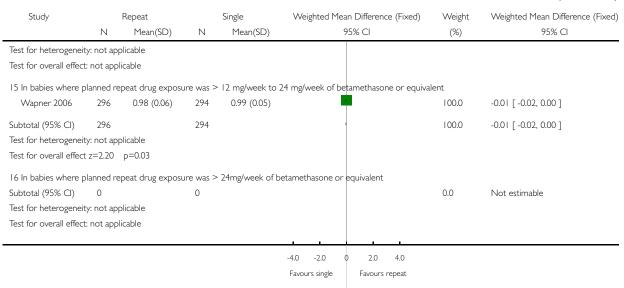
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 In all babies							
Wapner 2006	296	0.98 (0.06)	294	0.99 (0.05)		0.001	-0.01 [-0.02, 0.00]
Subtotal (95% CI)	296		294			100.0	-0.01 [-0.02, 0.00]
Test for heterogeneit	ty: not app	plicable					
Test for overall effect	z=2.20	p=0.03					
02 In babies where p	regnancy	complicated by p	reterm pi	relabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	ty: not ap _l	plicable					
Test for overall effect	t: not app	licable					
03 In babies exposed	d to repea	at corticosteroids	as betame	ethasone			
Wapner 2006	296	0.98 (0.06)	294	0.99 (0.05)	•	0.001	-0.01 [-0.02, 0.00]
Subtotal (95% CI)	296		294			100.0	-0.01 [-0.02, 0.00]
Test for heterogeneit	ty: not ap _l	plicable					
Test for overall effect	z=2.20	p=0.03					
04 In babies exposed	d to repea	at corticosteroids	at a minir	num interval of 7	days or less		
Wapner 2006	296	0.98 (0.06)	294	0.99 (0.05)	•	100.0	-0.01 [-0.02, 0.00]
Subtotal (95% CI)	296		294		-	100.0	-0.01 [-0.02, 0.00]
Test for heterogeneit	ty: not app	plicable					
Test for overall effect	z=2.20	p=0.03					
					-4.0 -2.0 0 2.0 4.0		

Favours single

Favours repeat

(Continued . . .)

10 10 10 10 10 10 10 10	Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixe
Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for heteregeneity, not applicable Test for heteregeneity not applicable Test for heteregeneity not applicable Test for overall effect not applicable Test for heteregeneity not applicable Test for heteregeneity not applicable Test for heteregeneity not applicable Test for overall effect not applicable Of in bables exposed to one repeat course of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect not applicable Bit hables exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for heteregeneity not applicable Test for overall effect not applicable Test for overall effect not applicable Test for heteregeneity not applicable Test for heteregeneity not applicable Test for heteregeneity not applicable Test for overall effect not applicable Test for heteregeneity not applicable Test for overall effect not applicable Test for heteregeneity not applicable Test for overall effect not applicable Test for heteregeneity not appli	05 In habies exposed		. ,		` ′		(/0)	7570 G
Tiest for heterogeneity, not applicable Tiest for coveral effect not applicable Of in bables exposed to repeat courses of prenatal corticosteroids Subrotal (95% C) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0			it cor ticosteroids		nam interval bet	weem o and in days	0.0	Not estimable
Test for overall effect: not applicable 0.0 Not estimable Subtotal (95% C) 0 0 0.0 Not estimable Test for heterogeneity not applicable 1 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0.0 Not estimable Test for heterogeneity not applicable 0 0 0.0 Not estimable Test for heterogeneity not applicable 0 0 0.0 Not estimable Test for heterogeneity not applicable 0 0 0.0 Not estimable Test for heterogeneity not applicable 1 1 1 1 1 1 0.0 0.0 2 0.0	, ,		alicable	O			0.0	NOT CSTITIABLE
Subtotal (95% CI) 0 0 0 0 0 0 Not estimable Text for heterogeneity, not applicable Text for yearl effect not applicable Text for yearl effect not applicable Text for yearl effect not applicable Text for heterogeneity not applicable Text for overall effect	_							
Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for overall	06 In babies exposed	I to repea	at corticosteroids	at a minir	num interval of >	> 14 days		
Test for overall effect not applicable 07 In bables exposed to one repeat course of prenatal corticosteroids Subtratal (75% C)	Subtotal (95% CI)	0		0			0.0	Not estimable
77 In bables exposed to one repeat course of prenatal corticosteroids 0.0 Not estimable	Test for heterogeneit	y: not app	plicable					
Subtotal (95% CI)	Test for overall effect	: not app	licable					
Test for heterogeneity, not applicable Test for overall effect not applicable Test for heterogeneity, not applicable Test for overall effect not applicable Test for heterogeneity not applicable Test for overall effect rest applicable Test for overall effect rest applicable Test for overall effect rest applicable Test for overall effect not applicable Test for overall effect planned dose per treatment course 12 mg or less of betamethasone or equivalent Vaponer 2006 296 098 (006) 294 099 (005) Subtotal (95% CI) 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	07 In babies exposed	I to one r	repeat course of p	orenatal co	orticosteroids			
Test for heterogeneity not applicable 10 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0 0 Not estimable Test for heterogeneity not applicable 10 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0 0 0 Not estimable Test for heterogeneity not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) 100 0 -0.02 [-0.03, -0.01] Subtotal (95% CI) 191 177 100 0 0.02 [-0.03, -0.01] Test for heterogeneity not applicable Test for overall effect a policable Test for overall effect applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect applicable Test for heterogeneity, not applicable Test for overall effect appli	Subtotal (95% CI)	0		0			0.0	Not estimable
88 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% C) 0 0 0 0.0 Not estimable Test for heterogeneity not applicable Test for overall effect possible Test for overall effect not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not appli	Test for heterogeneit	y: not app	plicable					
Subtotal (95% CI)	Test for overall effect	: not app	licable					
Test for heterogeneity, not applicable Test for overall effect: not applicable O9 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0.00 Not estimable Test for overall effect not applicable Test for overall effect z=3.46 p=0.0005 Test for heterogeneity, not applicable Test for overall effect z=3.46 p=0.0005 Test for heterogeneity not applicable Test for overall effect z=2.20 p=0.03 Test for heterogeneity, not applicable Test for overall effect z=2.20 p=0.03 Test for heterogeneity, not applicable Test for overall effect z=2.20 p=0.03 Test for overall effect not applicable Test for overall effec	08 In babies exposed	l to two r	repeat courses of		corticosteroids			
Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 0. Not estimable Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) 1000 -0.02 [-0.03, -0.01] Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for overall effect not applicable Test for overall effect; not applicable Test for overall effect; not applicable Test for overall effect not applicable Test for overall effect; not applicable Test for overall effect; not applicable Test for heterogeneity, not applicable Test for overall effect not applicable Test for neterogeneity, not applicable Test for neterogeneity, not applicable Test for heterogeneity not applicable Test for heterogeneity not applicable Test for neterogeneity not applicable Test for not a	Subtotal (95% CI)	0		0			0.0	Not estimable
Subtotal (95% CI) 0 0 0 0. Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) 1000 -0.02 [-0.03, -0.01] Subtotal (95% CI) 191 177 1000 -0.02 [-0.03, -0.01] Test for heterogeneity: not applicable Test for overall effect z=3.46 p=0.0005 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0. Not estimable Test for overall effect not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0. Not estimable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0. Not estimable Test for overall effect not applicable Test for overall effect: not applicable Test for overall effect not applicable	_							
Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) Subtotal (95% CI) 191 177 100.0 -0.02 [-0.03, -0.01] Test for heterogeneity: not applicable Test for overall effect z=3.46 p=0.0005 II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.000 Not estimable Test for heterogeneity: not applicable Test for overall effect not applicable Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.000 Not estimable Test for overall effect: not applicable	09 In babies exposed	I to three	repeat courses o	of prenatal	corticosteroids			
Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) 1000 -0.02 [-0.03, -0.01] Subtotal (95% CI) 191 177 Test for heterogeneity: not applicable Test for overall effect z=3.46 p=0.0005 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0 Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 Not estimable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 Not estimable Test for overall effect z=2.20 p=0.03 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 Not estimable	Subtotal (95% CI)	0		0			0.0	Not estimable
10 In babies exposed to four or more repeat courses of prenatal corticosteroids Wapner 2006	Test for heterogeneit	y: not app	plicable					
Wapner 2006 191 0.97 (0.05) 177 0.99 (0.06) 100.0 -0.02 [-0.03, -0.01]	Test for overall effect	: not app	licable					
Subtotal (95% CI) 191 177 100.0 -0.02 [-0.03, -0.01] Test for heterogeneity: not applicable Test for overall effect z=3.46 p=0.0005 II In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) Subtotal (95% CI) 296 294 Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect z=0.00 p=0.03 Test for heterogeneity: not applicable Test for overall effect z=0.00 p=0.03 Test for overall effect z=0.00 p=0.03 Not estimable Test for overall effect not applicable	10 In babies exposed	I to four (or more repeat co	ourses of	prenatal corticos	teroids		
Test for heterogeneity: not applicable Test for overall effect z=3.46 p=0.0005 Il In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0. Not estimable Test for overall effect not applicable Test for overall effect not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) Subtotal (95% CI) 296 294 Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0. Not estimable Test for overall effect not applicable	Wapner 2006	191	0.97 (0.05)	177	0.99 (0.06)	•	100.0	-0.02 [-0.03, -0.01]
Test for overall effect z=3.46 p=0.0005 Il I In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for heterogeneity: not applicable I2 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) Subtotal (95% CI) 296 294 I00.0 -0.01 [-0.02, 0.00] Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 I3 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect rot applicable Test for overall effect not applicable	Subtotal (95% CI)	191		177			100.0	-0.02 [-0.03, -0.01]
11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 0. Not estimable Test for heterogeneity: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) 100.0 -0.01 [-0.02, 0.00] Subtotal (95% CI) 296 294 100.0 -0.01 [-0.02, 0.00] Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0 0. Not estimable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0. Not estimable	Test for heterogeneit	y: not app	plicable					
Subtotal (95% CI) 0 0 0 0 0.0 Not estimable Test for heterogeneity: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) 100.0 -0.01 [-0.02, 0.00] Subtotal (95% CI) 296 294 100.0 -0.01 [-0.02, 0.00] Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable	Test for overall effect	z=3.46	p=0.0005					
Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006	I I In babies where p	lanned do	ose per treatmen	t course I	2 mg or less of b	petamethasone or equivalent		
Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006	, ,			0			0.0	Not estimable
12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) Subtotal (95% CI) 296 294 Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable	_							
Wapner 2006 296 0.98 (0.06) 294 0.99 (0.05) Subtotal (95% CI) 296 294 100.0 -0.01 [-0.02, 0.00] Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 I3 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for overall effect: not applicable Test for overall effect: not applicable I4 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable	Test for overall effect	: not app	licable					
Subtotal (95% CI) 296 294 100.0 -0.01 [-0.02, 0.00] Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0 0.0 Not estimable						g or less of betamethasone or equivale		0.01.1.003.000.3
Test for heterogeneity: not applicable Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable	·		0.98 (0.06)		0.99 (0.05)			-
Test for overall effect z=2.20 p=0.03 13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable	` ,			294			100.0	-0.01 [-0.02, 0.00]
13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable	_							
Subtotal (95% CI) 0 0 0.0 Not estimable Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable			•	t course >	· 24 mg of hetan	nethasone or equivalent		
Test for heterogeneity: not applicable Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable -4.0 -2.0 0 2.0 4.0	·				5. 554411		0.0	Not estimable
Test for overall effect: not applicable 14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0 0.0 Not estimable -4.0 -2.0 0 2.0 4.0	` ,	-	olicable	Ü			0.0	Trot estimate
Subtotal (95% CI) 0 0 0.0 Not estimable	· ·	,						
-4.0 -2.0 0 2.0 4.0	14 In babies where p	lanned re	epeat drug exposi	ure was 1	2 mg or less/wee	k of betamethasone or equivalent		
	Subtotal (95% CI)	0		0			0.0	Not estimable
						40 20 0 20 40		
(60)								(Continued
						1 aroar 3 repeate		(35,13,1464).



Analysis 01.36. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 36 Apgar score less than 7 at 5 minutes

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease Comparison: 01 Repeat doses of corticosteroids versus single course Outcome: 36 Apgar score less than 7 at 5 minutes Study Single Relative Risk (Fixed) Weight Relative Risk (Fixed) Repeat n/N n/N 95% CI 95% CI (%) 01 In all babies Crowther 2006 34/567 38/577 100.0 0.91 [0.58, 1.43] Subtotal (95% CI) 577 100.0 0.91 [0.58, 1.43] Total events: 34 (Repeat), 38 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.41 p=0.7 02 In babies where pregnancy complicated by preterm prelabour rupture of membranes at trial entry 0 Subtotal (95% CI) 0 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 03 In babies exposed to repeat corticosteroids as betamethasone Crowther 2006 34/567 1000 0.91 [0.58, 1.43] 38/577 Subtotal (95% CI) 567 577 1000 0.91 [0.58, 1.43] Total events: 34 (Repeat), 38 (Single) 0.1 0.2 0.5 1 2 5 10 Favours repeat Favours single (Continued ...)

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% Cl	
Test for heterogeneity: not	t applicable					
Test for overall effect z=0.	41 p=0.7					
04 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	7 days or less			
Crowther 2006	34/567	38/577	· •	100.0	0.91 [0.58, 1.43]	
Subtotal (95% CI)	567	577	•	100.0	0.91 [0.58, 1.43]	
Total events: 34 (Repeat),		377		100.0	0.71 [0.50, 1.15]	
Test for heterogeneity: not						
Test for overall effect z=0.	41 p=0.7					
05 In babies exposed to re	epeat corticosteroids a	at a minimum interval bet	tween 8 and 14 days			
Subtotal (95% CI)	0	0	'	0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
06 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	> 14 days			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
07 In babies exposed to o	ne repeat course of p	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
08 In babies exposed to tv	wo repeat courses of p	orenatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
09 In babies exposed to th	nree repeat courses of	f prenatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not	applicable					
10 In babies exposed to fo	our or more repeat co	urses of prenatal cortico	steroids			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not	applicable					
I I In babies where planne	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent			
Crowther 2006	34/567	38/577	-	100.0	0.91 [0.58, 1.43]	
Subtotal (95% CI)	567	577	•	100.0	0.91 [0.58, 1.43]	
			0.1 0.2 0.5 1 2 5 10		,	
			Favours repeat Favours single		(Continued	

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Total events: 34 (Repeat), 3	8 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.4	I p=0.7				
12 In babies where planned	dose per treatment of	course > 12 mg to 24 m	ng or less of betamethasone or equivalen	t	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
13 In babies where planned	dose per treatment o	course > 24 mg of betar	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
14 In babies where planned	l repeat drug exposur	e was 12 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	34/567	38/577	-	100.0	0.91 [0.58, 1.43]
Subtotal (95% CI)	567	577	•	100.0	0.91 [0.58, 1.43]
Total events: 34 (Repeat), 3	8 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.4	l p=0.7				
15 In babies where planned	l repeat drug exposur	e was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
16 In babies where planned	l repeat drug exposur	e was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
			01 02 05 1 2 5 10		

0.1 0.2 0.5 1 2 5 10

Favours repeat Favours single

Analysis 01.37. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 37 Systemic infection in the first 48 hours of life (suspected or confirmed)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 37 Systemic infection in the first 48 hours of life (suspected or confirmed)

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 In all babies					
Crowther 2006	173/567	188/577		100.0	0.94 [0.79, 1.11]
Subtotal (95% CI)	567	577	+	100.0	0.94 [0.79, .]
Total events: 173 (Repeat	:), 188 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	0.75 p=0.5				
02 In babies where pregn	ancy complicated by pr	eterm prelabour rupture o	of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids a	s betamethasone			
Crowther 2006	173/567	188/577	=	100.0	0.94 [0.79, 1.11]
Subtotal (95% CI)	567	577	•	100.0	0.94 [0.79, 1.11]
Total events: 173 (Repeat	t), 188 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0	0.75 p=0.5				
04 In babies exposed to r	repeat corticosteroids a	t a minimum interval of 7	days or less		
Crowther 2006	173/567	188/577	=	100.0	0.94 [0.79, 1.11]
Subtotal (95% CI)	567	577	+	100.0	0.94 [0.79, 1.11]
Total events: 173 (Repeat	t), 188 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0).75 p=0.5				
05 In babies exposed to r	repeat corticosteroids a	t a minimum interval betv	veen 8 and 14 days		
Subtotal (95% CI)	0	0	,	0.0	Not estimable
Total events: 0 (Repeat), (0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
06 In babies exposed to r	repeat corticosteroids a	t a minimum interval of >	14 days		
Subtotal (95% CI)	0	0	,	0.0	Not estimable
Total events: 0 (Repeat), (0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		
					()

Favours repeat Favours single (Continued . . .)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
07 In babies exposed to or	ne repeat course of pr	enatal corticosteroids		. ,	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0		-			
Test for heterogeneity: not	/				
Test for overall effect: not a					
08 In babies exposed to tv		renatal corticosteroids 0		0.0	Not estimable
Subtotal (95% CI) Total events: 0 (Repeat), 0	(Single)	U		0.0	Not estimable
Test for heterogeneity: not	/				
Test for overall effect: not a	• •				
09 In babies exposed to th	·	•			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	, ,				
Test for heterogeneity: not					
Test for overall effect: not a	аррисаріе				
10 In babies exposed to fo	our or more repeat cou	urses of prenatal corticost	eroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	/				
Test for heterogeneity: not					
Test for overall effect: not a	applicable				
I I In babies where planne	d dose per treatment	course 12 mg or less of be	etamethasone or equivalent		
Crowther 2006	173/567	188/577	-	100.0	0.94 [0.79, 1.11]
Subtotal (95% CI)	567	577	•	100.0	0.94 [0.79, 1.11]
Total events: 173 (Repeat),		3//		100.0	0.74 [0.77, 1.11]
Test for heterogeneity: not	/				
Test for overall effect z=0.7					
			or less of betamethasone or equivaler		N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	, ,				
Test for heterogeneity: not					
Test for overall effect: not a	аррисавіе				
13 In babies where planne	d dose per treatment	course > 24 mg of betam	ethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	/				
Test for heterogeneity: not					
Test for overall effect: not a	applicable				
14 In babies where planne	d repeat drug exposur	e was 12 mg or less/week	of betamethasone or equivalent		
Crowther 2006	173/567	188/577	<u></u>	100.0	0.94 [0.79, 1.11]
Subtotal (95% CI)	567	577	+	100.0	0.94 [0.79, 1.11]
Total events: 173 (Repeat),		<u></u>		. 00.0	5.7 . [5.7 7, 1.1 1]
Test for heterogeneity: not	, ,				
			<u> </u>		
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		(Continued)
					,

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Test for overall effect z=	0.75 p=0.5				
15 In babies where planr	ned repeat drug exposur	re was > 12 mg/week to	24 mg/week of betamethasone or equ	uivalent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: n	ot applicable				
Test for overall effect: no	t applicable				
16 In babies where planr	ned repeat drug exposur	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: n	ot applicable				
Test for overall effect: no	t applicable				
			0.1 0.2 0.5 2 5 10		

Analysis 01.38. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 38 Proven infection while in the neonatal intensive care unit

Favours repeat Favours single

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 38 Proven infection while in the neonatal intensive care unit

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed) 95% CI
	n/N	n/N	95% CI	(%)	
01 In all babies					_
Aghajafari 2002	1/9	2/7		2.2	0.39 [0.04, 3.47]
Crowther 2006	70/567	72/577	•	69.9	0.99 [0.73, 1.35]
Guinn 2002	13/255	10/245	+	10.0	1.25 [0.56, 2.80]
Wapner 2006	11/250	18/242		17.9	0.59 [0.29, 1.23]
Subtotal (95% CI)	1801	1071	•	100.0	0.93 [0.71, 1.21]
Total events: 95 (Repeat),	102 (Single)				
Test for heterogeneity chi-	-square=2.76 df=3 p=0	0.43 I ² =0.0%			
Test for overall effect z=0	.53 p=0.6				
02 In babies where pregna	ancy complicated by pr	eterm prelabour rupture	e of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.01 0.1 1 10 100		
			Favours repeat Favours single		(Continued)

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI	
03 In babies exposed to re	epeat corticosteroids a	s betamethasone				
Aghajafari 2002	1/9	2/7		2.2	0.39 [0.04, 3.47]	
Crowther 2006	70/567	72/577	•	69.9	0.99 [0.73, 1.35]	
Guinn 2002	13/255	10/245	-	10.0	1.25 [0.56, 2.80]	
Wapner 2006	11/250	18/242	-	17.9	0.59 [0.29, 1.23]	
Subtotal (95% CI) Total events: 95 (Repeat), Test for heterogeneity chi- Test for overall effect z=0.	square=2.76 df=3 p=	107 l 0.43 l² =0.0%	•	100.0	0.93 [0.71, 1.21]	
04 In babies exposed to re	epeat corticosteroids a	at a minimum interval of 7 d	ays or less			
Aghajafari 2002	1/9	2/7	, <u> </u>	2.2	0.39 [0.04, 3.47]	
Crowther 2006	70/567	72/577	•	69.9	0.99 [0.73, 1.35]	
Guinn 2002	13/255	10/245	-	10.0	1.25 [0.56, 2.80]	
Wapner 2006	11/250	18/242	-	17.9	0.59 [0.29, 1.23]	
Subtotal (95% CI) Total events: 95 (Repeat),	1081 102 (Single)	1071	•	100.0	0.93 [0.71, 1.21]	
Test for heterogeneity chi- Test for overall effect z=0.	53 p=0.6		20 0 20 14 14 12			
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	it a minimum interval betwe	erro and 14 days	0.0	Not estimable	
06 In babies exposed to re Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	at a minimum interval of > I	4 days	0.0	Not estimable	
07 In babies exposed to o Subtotal (95% CI) Total events: 0 (Repeat), 0	0	renatal corticosteroids 0		0.0	Not estimable	
Test for heterogeneity: not Test for overall effect: not						
08 In babies exposed to to Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	orenatal corticosteroids 0		0.0	Not estimable	
09 In babies exposed to th	nree repeat courses of	prenatal corticosteroids				
			0.01 0.1 10 100 Favours repeat Favours single		(Continued)	

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI	
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	t applicable	0		0.0	Not estimable	
10 In babies exposed to fo Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	urses of prenatal cortico 0	steroids	0.0	Not estimable	
II In babies where planne	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent			
Crowther 2006	70/567	72/577	<u>*</u>	100.0	0.99 [0.73, 1.35]	
Subtotal (95% CI) Total events: 70 (Repeat), Test for heterogeneity: nor Test for overall effect z=0.	t applicable	577	•	100.0	0.99 [0.73, 1.35]	
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 m	ng or less of betamethasone or equivale	nt		
Aghajafari 2002	1/9	2/7		7.3	0.39 [0.04, 3.47]	
Guinn 2002	13/255	10/245	-	33.2	1.25 [0.56, 2.80]	
Wapner 2006	11/250	18/242	-	59.5	0.59 [0.29, 1.23]	
Subtotal (95% CI)	514	494	•	100.0	0.79 [0.48, 1.33]	
Total events: 25 (Repeat), Test for heterogeneity chi- Test for overall effect z=0.	square=2.25 df=2 p=0	0.32 2 = . %				
I 3 In babies where planne Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	course > 24 mg of betar 0	nethasone or equivalent	0.0	Not estimable	
14 In babies where planne	ed repeat drug exposur	re was 12 mg or less/wee	ek of betamethasone or equivalent			
Crowther 2006	70/567	72/577	<u> </u>	100.0	0.99 [0.73, 1.35]	
Subtotal (95% CI) Total events: 70 (Repeat), Test for heterogeneity: nor Test for overall effect z=0.	t applicable	577	•	100.0	0.99 [0.73, 1.35]	
15 In babies where planne	ed repeat drug exposur	re was > 12 mg/week to	24 mg/week of betamethasone or equ	ivalent		
Aghajafari 2002	1/9	2/7		7.3	0.39 [0.04, 3.47]	
Guinn 2002	13/255	10/245	+	33.2	1.25 [0.56, 2.80]	
Wapner 2006	11/250	18/242	-	59.5	0.59 [0.29, 1.23]	
Subtotal (95% CI)	514	494	+	100.0	0.79 [0.48, 1.33]	
			0.01 0.1 10 100			
			Favours repeat Favours single		(Continued)	



Study	Repeat	Single	Relative F	Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	959	% CI	(%)	95% CI
Total events: 25 (Repeat)	, 30 (Single)					
Test for heterogeneity ch	i-square=2.25 df=2 p=0	0.32 2 = . %				
Test for overall effect z=0	0.87 p=0.4					
16 In babies where plann	ed repeat drug exposur	re was > 24 mg/week of	betamethasone or	equivalent		
Subtotal (95% CI)	0	0			0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)					
Test for heterogeneity: no	ot applicable					
Test for overall effect: no	t applicable					
			0.01 0.1	1 10 100		
			Favours repeat	Favours single		

Analysis 01.39. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 39 Admission to the neonatal intensive care unit

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease Comparison: 01 Repeat doses of corticosteroids versus single course Outcome: 39 Admission to the neonatal intensive care unit Study Relative Risk (Fixed) Relative Risk (Fixed) Repeat Single Weight n/N n/N 95% CI (%) 95% CI 01 In all babies Crowther 2006 407/567 399/577 100.0 1.04 [0.96, 1.12] Subtotal (95% CI) 577 100.0 1.04 [0.96, 1.12] Total events: 407 (Repeat), 399 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.97 p=0.3 02 In babies where pregnancy complicated by preterm prelabour rupture of membranes at trial entry Subtotal (95% CI) 0.0 Not estimable Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 03 In babies exposed to repeat corticosteroids as betamethasone Crowther 2006 407/567 399/577 100.0 1.04 [0.96, 1.12] Subtotal (95% CI) 567 577 100.0 1.04 [0.96, 1.12] Total events: 407 (Repeat), 399 (Single) Test for heterogeneity: not applicable Test for overall effect z=0.97 p=0.3 04 In babies exposed to repeat corticosteroids at a minimum interval of 7 days or less 0.1 0.2 0.5 5 10 (Continued ...) Favours repeat Favours single

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% Cl	
Crowther 2006	407/567	399/577	•	100.0	1.04 [0.96, 1.12]	
Subtotal (95% CI) Total events: 407 (Repeat), Test for heterogeneity: not	, ,	577	•	100.0	1.04 [0.96, 1.12]	
Test for overall effect z=0.9	7 p=0.3					
05 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 (0	a minimum interval betw 0	veen 8 and 14 days	0.0	Not estimable	
Test for heterogeneity: not Test for overall effect: not a	applicable					
06 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0	0	a minimum interval of >	14 days	0.0	Not estimable	
Test for heterogeneity: not Test for overall effect: not a						
07 In babies exposed to on Subtotal (95% CI) Total events: 0 (Repeat), 0 (0	enatal corticosteroids 0		0.0	Not estimable	
Test for heterogeneity: not Test for overall effect: not a	applicable					
08 In babies exposed to tw Subtotal (95% CI) Total events: 0 (Repeat), 0 I Test for heterogeneity: not Test for overall effect: not a	0 (Single) applicable	0		0.0	Not estimable	
09 In babies exposed to the Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not	0 (Single) applicable	prenatal corticosteroids 0		0.0	Not estimable	
Test for overall effect: not a 10 In babies exposed to for Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not Test for overall effect: not a	ur or more repeat cou 0 (Single) applicable	orses of prenatal corticost	eroids	0.0	Not estimable	
		ourse 12 mg or less of b 399/577	etamethasone or equivalent	100.0	1.04 [0.96, 1.12]	
			Ţ			
Subtotal (95% CI) Total events: 407 (Repeat), Test for heterogeneity: not Test for overall effect z=0.9	applicable	577		100.0	1.04 [0.96, 1.12]	
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		(Continued)	

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
12 In babies where plann	ed dose per treatment o	ourse > 12 mg to 24 m	g or less of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
13 In babies where plann	ed dose per treatment o	ourse > 24 mg of betar	nethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
14 In babies where plann	ed repeat drug exposun	e was 12 mg or less/wee	k of betamethasone or equivalent		
Crowther 2006	407/567	399/577	+	100.0	1.04 [0.96, 1.12]
Subtotal (95% CI)	567	577	•	100.0	1.04 [0.96, 1.12]
Total events: 407 (Repeat	t), 399 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0).97 p=0.3				
15 In babies where plann	ed repeat drug exposun	e was > 12 mg/week to	24 mg/week of betamethasone or equival	lent	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
16 In babies where plann	ed repeat drug exposun	e was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				

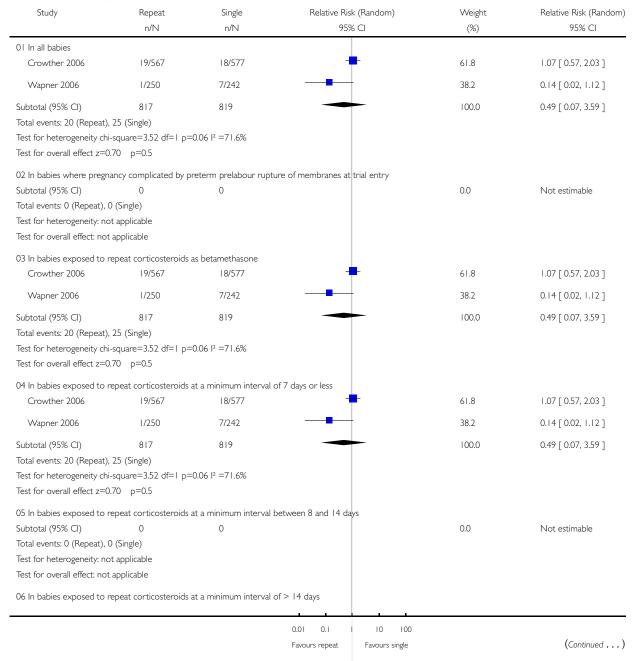
0.1 0.2 0.5 2 5 10 Favours repeat Favours single

Analysis 01.40. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 40 Air leak syndrome

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 40 Air leak syndrome



Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% Cl	Weight (%)	Relative Risk (Random 95% CI
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
07 In babies exposed to or	ne repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
08 In babies exposed to tw	o repeat courses of	prenatal corticosteroid	5		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
09 In babies exposed to th	ree repeat courses o	f prenatal corticosteroi	ds		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
10 In babies exposed to for	ur or more repeat co	ourses of prenatal corti	costeroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
I I In babies where planned	d dose per treatment	course 12 mg or less of	of betamethasone or equivalent		
Crowther 2006	19/567	18/577		100.0	1.07 [0.57, 2.03]
Subtotal (95% CI)	567	577	+	100.0	1.07 [0.57, 2.03]
Total events: 19 (Repeat), 1	8 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.2	2 p=0.8				
12 In babies where planned	d dose per treatment	course > 12 mg to 24	mg or less of betamethasone or equivale	ent	
Wapner 2006	1/250	7/242		100.0	0.14 [0.02, 1.12]
Subtotal (95% CI)	250	242		100.0	0.14 [0.02, 1.12]
Total events: I (Repeat), 7	(Single)				
Test for heterogeneity: not					
Test for overall effect z=1.8	86 p=0.06				
13 In babies where planned	d dose per treatment	course > 24 mg of be	tamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
			0.01 0.1 10 100		

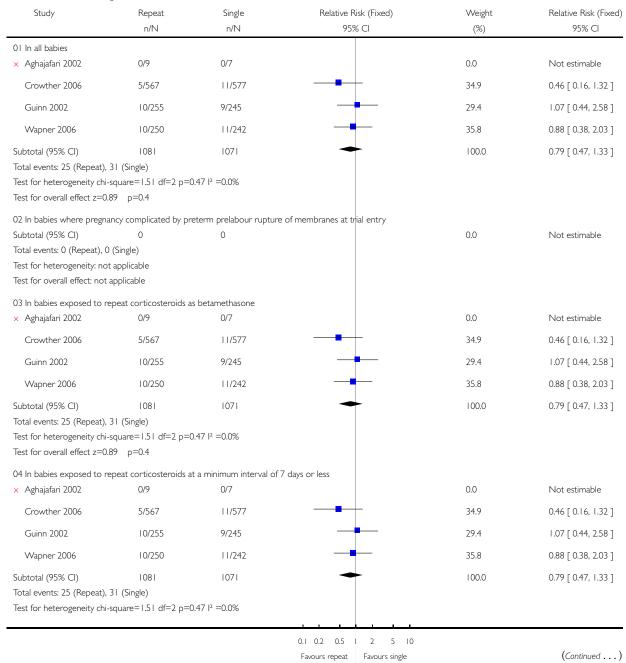
Study	Repeat	Single	Relative Risk (Random)	Weight	Relative Risk (Random
	n/N	n/N	95% CI	(%)	95% CI
14 In babies where planne	ed repeat drug exposi	ure was 12 mg or less/v	veek of betamethasone or equivalent		
Crowther 2006	19/567	18/577	-	100.0	1.07 [0.57, 2.03]
Subtotal (95% CI)	567	577	+	100.0	1.07 [0.57, 2.03]
Total events: 19 (Repeat),	18 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0	.22 p=0.8				
15 In babies where planne	ed repeat drug exposi	ure was > 12 mg/week	to 24 mg/week of betamethasone or ed	quivalent	
Wapner 2006	1/250	7/242	-	100.0	0.14 [0.02, 1.12]
Subtotal (95% CI)	250	242		100.0	0.14 [0.02, 1.12]
Total events: (Repeat), 7	7 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.86 p=0.06				
16 In babies where planne	ed repeat drug exposi	ure was > 24 mg/week	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.01 0.1 10 100		
			Favours repeat Favours single		

Analysis 01.41. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 41 Necrotising enterocolitis

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 41 Necrotising enterocolitis



Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed
Test for overall effect z=0.	89 p=0.4				
05 In babies exposed to re	epeat corticosteroids a	at a minimum interval bet	ween 8 and 14 days		
Subtotal (95% CI)	0	0	,	0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	, ,				
Test for overall effect: not	• •				
06 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0	,	0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	(0)				
Test for overall effect: not					
07 In babies exposed to o	one repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	, -,				
Test for overall effect: not					
08 In babies exposed to to	wo repeat courses of r	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: not	. 0 /				
Test for overall effect: not					
09 In babies exposed to th	hree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	, -,				
Test for overall effect: not	• •				
10 In babies exposed to fo	our or more repeat co	urses of prenatal corticos	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: no	` 0 /				
Test for overall effect: not					
I I In babies where planne	ed dose per treatment	course 12 mg or less of t	petamethasone or equivalent		
Crowther 2006	5/567	11/577		100.0	0.46 [0.16, 1.32]
Subtotal (95% CI)	567	577		100.0	0.46 [0.16, 1.32]
Total events: 5 (Repeat), I		• •			[,
Test for heterogeneity: no	, -,				
Test for overall effect z=1.	• •				
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 m	g or less of betamethasone or equivale	nt	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Guinn 2002	10/255	9/245		45.1	1.07 [0.44, 2.58]
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Wapner 2006	10/250	11/242	-	54.9	0.88 [0.38, 2.03]
Subtotal (95% CI)	514	494	-	100.0	0.96 [0.53, 1.77]
Total events: 20 (Repeat),	20 (Single)				
Test for heterogeneity chi-	-square=0.10 df=1 p=	0.76 l² =0.0%			
Test for overall effect z=0.	.12 p=0.9				
13 In babies where planne	ed dose per treatment	course > 24 mg of betai	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	5/567	11/577	-	100.0	0.46 [0.16, 1.32]
Subtotal (95% CI)	567	577		100.0	0.46 [0.16, 1.32]
Total events: 5 (Repeat), I	I (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.	.44 p=0.2				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equi	valent	
× Aghajafari 2002	0/9	0/7		0.0	Not estimable
Guinn 2002	10/255	9/245		45.1	1.07 [0.44, 2.58]
Wapner 2006	10/250	11/242	_	54.9	0.88 [0.38, 2.03]
Subtotal (95% CI)	514	494	-	100.0	0.96 [0.53, 1.77]
Total events: 20 (Repeat),	20 (Single)				
Test for heterogeneity chi-	/	0.76 l² =0.0%			
Test for overall effect z=0.	.12 p=0.9				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0	'	0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no					
Test for overall effect: not					
			01 02 05 1 2 5 10		

0.1 0.2 0.5 1 2 5 10

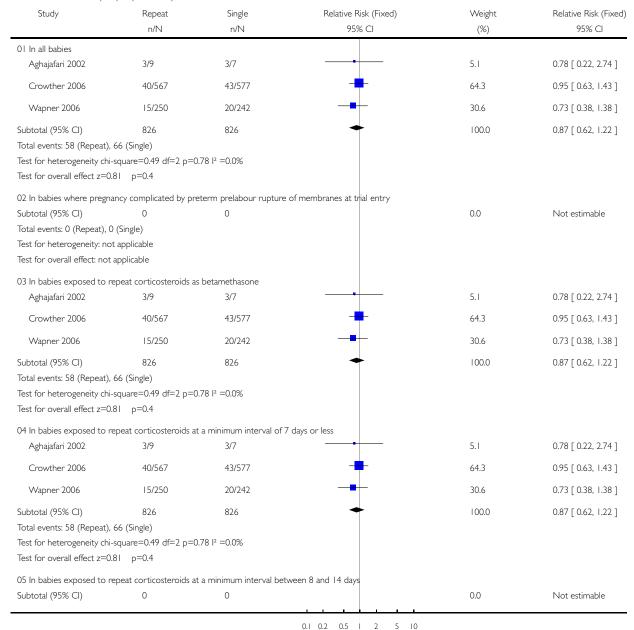
Favours repeat Favours single

Analysis 01.42. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 42 Retinopathy of prematurity

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 42 Retinopathy of prematurity



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours repeat

Favours single

(Continued ...)

					(continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not a	applicable					
06 In babies exposed to re	epeat corticosteroids a	t a minimum interval of	> 14 days			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
07 In babies exposed to or	ne repeat course of pr	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
08 In babies exposed to tv	wo repeat courses of p	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
09 In babies exposed to th	nree repeat courses of	prenatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
10 In babies exposed to fo	our or more repeat co	urses of prenatal corticos	steroids			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
I I In babies where planne	d dose per treatment	course 12 mg or less of I	petamethasone or equivalent			
Crowther 2006	40/567	43/577	+	100.0	0.95 [0.63, 1.43]	
Subtotal (95% CI)	567	577	+	100.0	0.95 [0.63, 1.43]	
Total events: 40 (Repeat),	43 (Single)					
Test for heterogeneity: not	applicable					
Test for overall effect z=0.2	26 p=0.8					
12 In babies where planne	d dose per treatment	course > 12 mg to 24 m	g or less of betamethasone or equivaler	nt		
Aghajafari 2002	3/9	3/7		14.2	0.78 [0.22, 2.74]	
Wapner 2006	15/250	20/242		85.8	0.73 [0.38, 1.38]	
Subtotal (95% CI)	259	249		100.0	0.73 [0.41, 1.31]	
Total events: 18 (Repeat), 2	23 (Single)					
Test for heterogeneity chi-	square=0.01 df=1 p=0	0.92 l² =0.0%				
Test for overall effect z=1.0	05 p=0.3					
			0.1 0.2 0.5 1 2 5 10		,	
			Favours repeat Favours single		(Continued	

(%) 0.0	95% CI Not estimable
	Not estimable
	Not estimable
ut.	
*	
IL .	
100.0	0.95 [0.63, 1.43]
100.0	0.95 [0.63, 1.43]
or equivalent	
14.2	0.78 [0.22, 2.74]
85.8	0.73 [0.38, 1.38]
100.0	0.73 [0.41, 1.31]
0.0	Not estimable
	0.0

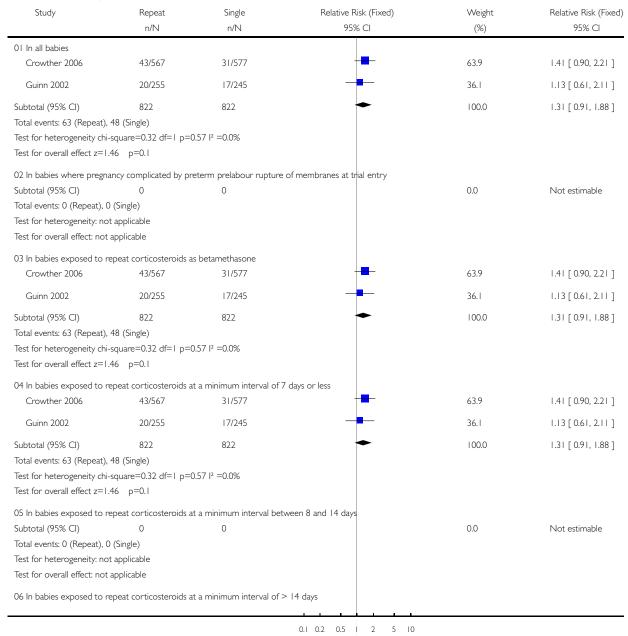
0.1 0.2 0.5 | 2 5 10 Favours repeat Favours single

Analysis 01.43. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 43 Use of postnatal steroids

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 43 Use of postnatal steroids



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours repeat Favours single

(Continued ...)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed 95% Cl	
	n/N	n/N	95% CI	(%)		
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	applicable					
Test for overall effect: not a	applicable					
07 In babies exposed to or	ne repeat course of p	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	, ,					
Test for overall effect: not a						
08 In babies exposed to tv	vo repeat courses of r	prenatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0		-				
Test for heterogeneity: not						
Test for overall effect: not a	• •					
09 In babies exposed to th	uree repeat courses of	Enrenatal continenteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0		0		0.0	THOE ESTIMABLE	
Test for heterogeneity: not						
Test for overall effect: not a	• •					
rest for overall effect. Not a	аррисаріе					
10 In babies exposed to fo	·	•	steroids			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not a	applicable					
I I In babies where planne	d dose per treatment	course 12 mg or less of t	petamethasone or equivalent			
Crowther 2006	43/567	31/577	+	100.0	1.41 [0.90, 2.21]	
Subtotal (95% CI)	567	577	•	100.0	1.41 [0.90, 2.21]	
Total events: 43 (Repeat),	31 (Single)					
Test for heterogeneity: not	applicable					
Test for overall effect z=1.5	51 p=0.1					
12 In babies where planne	d dose per treatment	course > 12 mg to 24 m	g or less of betamethasone or equivaler	nt		
Guinn 2002	20/255	17/245	-	100.0	1.13 [0.61, 2.11]	
Subtotal (95% CI)	255	245		100.0	1.13 [0.61, 2.11]	
Total events: 20 (Repeat),		213		100.0	1.15 [0.01, 2.11]	
Test for heterogeneity: not	, ,					
Test for overall effect z=0.3						
	•					
13 In babies where planne		G	methasone or equivalent	_		
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0						
Test for heterogeneity: not						
Test for overall effect: not a	applicable					
			0.1 0.2 0.5 2 5 10		(5	
			Favours repeat Favours single		(Continued	

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
14 In babies where planne	d repeat drug exposu	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	43/567	31/577	+	100.0	1.41 [0.90, 2.21]
Subtotal (95% CI)	567	577	•	100.0	1.41 [0.90, 2.21]
Total events: 43 (Repeat), 3	31 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=1.5	51 p=0.1				
15 In babies where planne	d repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent	
Guinn 2002	20/255	17/245	-	100.0	1.13 [0.61, 2.11]
Subtotal (95% CI)	255	245	-	100.0	1.13 [0.61, 2.11]
Total events: 20 (Repeat),	17 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.3	39 p=0.7				
16 In babies where planne	d repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				

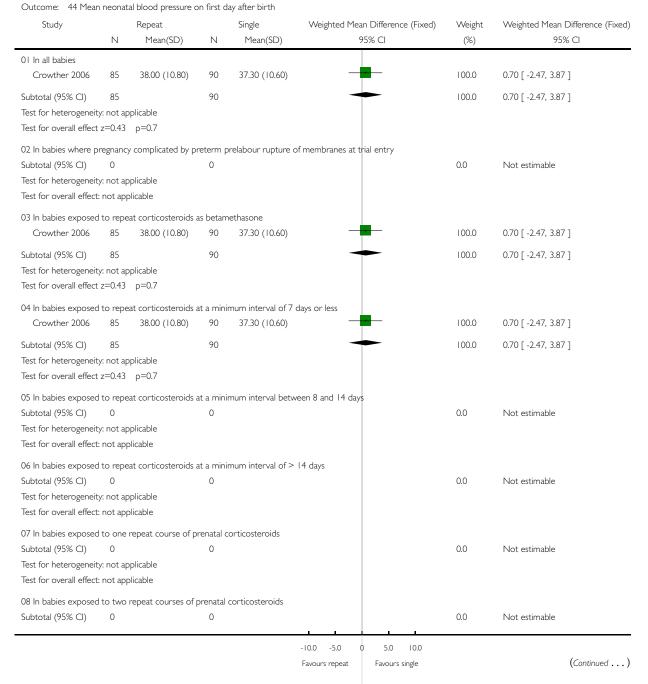
0.1 0.2 0.5 I 2 5 I 0

Favours repeat Favours single

Analysis 01.44. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 44 Mean neonatal blood pressure on first day after birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course



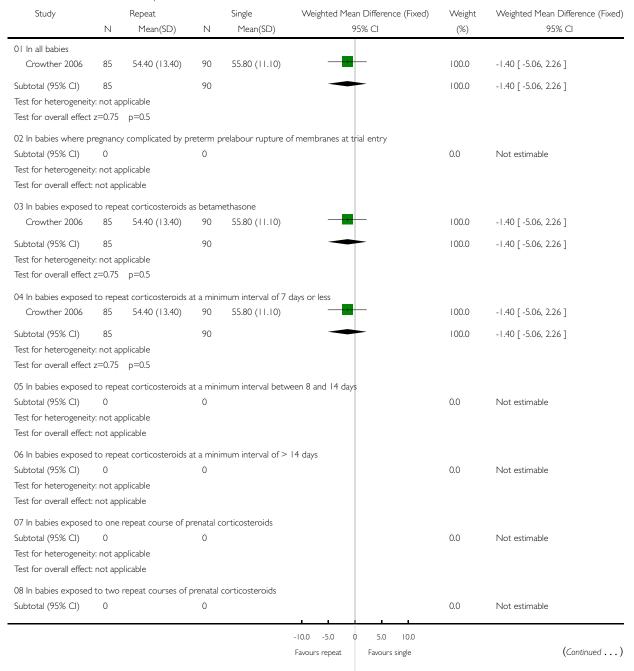
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
-	Ν	Mean(SD)	N	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity Test for overall effect:							
09 In babies exposed	to thre	e repeat courses o	f prenata	l corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	/: not ap	oplicable					
Test for overall effect:	not app	plicable					
10 In babies exposed	to four	or more repeat co	ourses of	prenatal corticost	eroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity Test for overall effect:							
				10 1 61			
Crowther 2006	anned o	dose per treatment 38.00 (10.80)	course 90	12 mg or less of be 37.30 (10.60)	etamethasone or equivalent	100.0	0.70 [-2.47, 3.87]
		30.00 (10.00)		37.30 (10.00)	I		
Subtotal (95% CI) Test for heterogeneity	85	anlicable	90			100.0	0.70 [-2.47, 3.87]
Test for overall effect							
		•		> 12 mag to 24 mag	an lass of historical horange on an involved		
Subtotal (95% CI)	anned o	ose per treatment	course .	> 12 mg to 24 mg	or less of betamethasone or equivalent	0.0	Not estimable
Test for heterogeneity		oplicable	Ü			0.0	1 voc estimable
Test for overall effect:							
13 In babies where pl	anned o	dose per treatment	course	> 24 mg of betam	ethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not app	plicable					
14 In babies where pl	anned r	repeat drug exposu	ire was I	2 mg or less/week	of betamethasone or equivalent		
Crowther 2006	85	38.00 (10.80)	90	37.30 (10.60)		100.0	0.70 [-2.47, 3.87]
Subtotal (95% CI)	85		90			100.0	0.70 [-2.47, 3.87]
Test for heterogeneity							
Test for overall effect	z=0.43	p=0./					
		repeat drug exposu		> 12 mg/week to 2	4 mg/week of betamethasone or equiv		
Subtotal (95% CI) Test for heterogeneity	0	anlicable	0			0.0	Not estimable
Test for overall effect:							
				24 mag/, male of b	etamethasone or equivalent		
Subtotal (95% CI)	anned r 0	chear ains exhorr	re was -	Z T THE WEEK OF D	Ctarriculasone of equivalent	0.0	Not estimable
Test for heterogeneity	/: not ap	oplicable					
Test for overall effect:	not app	plicable					
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.45. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 45 Mean neonatal blood pressure 6 weeks after birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 45 Mean neonatal blood pressure 6 weeks after birth



							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity Test for overall effect:							
			_				
09 In babies exposed Subtotal (95% CI)	to thre	e repeat courses o	f prenata 0	l corticosteroids		0.0	Not estimable
Test for heterogeneity		oplicable	U			0.0	NOT ESTIMABLE
Test for overall effect:							
10 In babies exposed	to four	or more repeat co	ourses of	prenatal corticost	eroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:							
II In babies where pl Crowther 2006	anned o		course 90	-	etamethasone or equivalent	100.0	140 [504 224]
		54.40 (13.40)		55.80 (11.10)			-1.40 [-5.06, 2.26]
Subtotal (95% CI) Test for heterogeneity	85	anlicable	90			100.0	-1.40 [-5.06, 2.26]
Test for overall effect							
12 In habies where pl	anned o	dose per treatment	course :	> 12 mg to 24 mg	or less of betamethasone or equivalent	+	
Subtotal (95% CI)	0	aoso per a caament	0	1211,510 2111,5	or ress or became rasone or equivalent	0.0	Not estimable
Test for heterogeneity	/: not ap	oplicable					
Test for overall effect:	not app	plicable					
		dose per treatment		> 24 mg of betam	ethasone or equivalent		
Subtotal (95% CI) Test for heterogeneity	0	anlicable	0			0.0	Not estimable
Test for overall effect:							
14 In babies where pl	anned r	reneat drug exposu	ıre was I	2 mg or less/week	of betamethasone or equivalent		
Crowther 2006	85	54.40 (13.40)	90	55.80 (11.10)		100.0	-1.40 [-5.06, 2.26]
Subtotal (95% CI)	85		90			100.0	-1.40 [-5.06, 2.26]
Test for heterogeneity	/: not ap	oplicable					
Test for overall effect	z=0.75	p=0.5					
15 In babies where pl	anned r	repeat drug exposu	ire was >	→ 12 mg/week to 2	4 mg/week of betamethasone or equiv	alent	
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity Test for overall effect:							
				24 mag/, male of b	etamethasone or equivalent		
Subtotal (95% CI)	0	epeat drug expost	0 0	24 mg/week or b	etametriasone or equivalent	0.0	Not estimable
Test for heterogeneity	/: not ap	oplicable					
Test for overall effect:	not app	plicable					
							_
					-10.0 -5.0 0 5.0 10.0 Favours repeat Favours single		
					ravours repeat ravours single		

Analysis 01.46. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 46 Neonatal cardiac hypertrophy as measured by interventricular septal thickness (IVSd)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 46 Neonatal cardiac hypertrophy as measured by interventricular septal thickness (IVSd)

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies Crowther 2006	85	2.95 (0.86)	90	2.94 (0.83)	•	100.0	0.01 [-0.24, 0.26]
Subtotal (95% CI) Test for heterogeneity Test for overall effect	85 : not app	blicable	90	2.71 (0.03)	Ţ	100.0	0.01 [-0.24, 0.26]
02 In babies where properties of Subtotal (95% CI) Test for heterogeneity, Test for overall effect:	0 : not app	blicable	reterm p	relabour rupture	of membranes at trial entry	0.0	Not estimable
03 In babies exposed							
Crowther 2006	85	2.95 (0.86)	90	2.94 (0.83)		100.0	0.01 [-0.24, 0.26]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			90			100.0	0.01 [-0.24, 0.26]
04 In babies exposed Crowther 2006	to repea 85	t corticosteroids 2.95 (0.86)	at a mini 90	mum interval of 2.94 (0.83)	7 days or less	100.0	0.01 [-0.24, 0.26]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			90		•	100.0	0.01 [-0.24, 0.26]
05 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	at a mini 0	mum interval bet	ween 8 and 14 days	0.0	Not estimable
06 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	at a mini 0	mum interval of	> 14 days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	blicable	renatal c	orticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI)	to two r	epeat courses of	prenatal 0	corticosteroids		0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0 Favours repeat Favours single		(Continued)
					Tarour Single		(00.10.1000)

							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity							
Test for overall effect:	not appl	icable					
09 In babies exposed		repeat courses o	f prenata	l corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	ıcable					
10 In babies exposed		or more repeat co		prenatal corticos	steroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appi	icable					
·				_	petamethasone or equivalent		
Crowther 2006	85	2.95 (0.86)	90	2.94 (0.83)	•	100.0	0.01 [-0.24, 0.26]
Subtotal (95% CI)	85		90		•	100.0	0.01 [-0.24, 0.26]
Test for heterogeneity	/: not app	olicable					
Test for overall effect	z=0.08	p=0.9					
12 In babies where pl	anned do	ose per treatment	course	> 12 mg to 24 m	g or less of betamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	/: not app	olicable					
Test for overall effect:	not appl	icable					
13 In babies where pl	anned do	ose per treatment	course	> 24 mg of betar	nethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity	/: not app	olicable					
Test for overall effect:	not appl	icable					
14 In babies where pl	anned re	peat drug exposi	ıre was I	2 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	85	2.95 (0.86)	90	2.94 (0.83)	•	100.0	0.01 [-0.24, 0.26]
Subtotal (95% CI)	85		90		•	100.0	0.01 [-0.24, 0.26]
Test for heterogeneity		olicable					[,]
Test for overall effect	z=0.08	p=0.9					
15 In habies where n	anned re	neat drug exnosi	ire was 2	> 12 mg/week to	24 mg/week of betamethasone or equiva	alent	
Subtotal (95% CI)	0	pear arag expose	0	12 mg week to	21 mg/week of Betained abone of equivi	0.0	Not estimable
Test for heterogeneity	/: not app	olicable					
Test for overall effect:	not appl	icable					
16 In babies where of	anned re	neat drug exnosi	ire was 3	> 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	r - 11 0, 06 0xp030	0		2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	0.0	Not estimable
Test for heterogeneity		olicable					
Test for overall effect:	not appl	icable					
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.47. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 47 Neonatal cardiac hypertrophy as measured by left ventricular wall thickness in diastole

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 47 Neonatal cardiac hypertrophy as measured by left ventricular wall thickness in diastole

Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
01 In all babies							
Crowther 2006	85	3.02 (0.86)	90	3.06 (0.71)	•	100.0	-0.04 [-0.27, 0.19]
Subtotal (95% CI)	85		90		•	100.0	-0.04 [-0.27, 0.19]
Test for heterogeneity:	not app	olicable					
Test for overall effect z	=0.33	p=0.7					
02 In babies where pre	egnancy	complicated by p	reterm p	relabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity:							
Test for overall effect:	not appl	icable					
03 In babies exposed t	o repea	t corticosteroids	as betam	ethasone	<u></u>		
Crowther 2006	85	3.02 (0.86)	90	3.06 (0.71)	•	100.0	-0.04 [-0.27, 0.19]
Subtotal (95% CI)	85		90		†	100.0	-0.04 [-0.27, 0.19]
Test for heterogeneity:	not app	olicable					
Test for overall effect z	=0.33	p=0.7					
04 In babies exposed t	o repea	t corticosteroids	at a mini	mum interval of	7 days or less		
Crowther 2006	85	3.02 (0.86)	90	3.06 (0.71)	•	100.0	-0.04 [-0.27, 0.19]
Subtotal (95% CI)	85		90		+	100.0	-0.04 [-0.27, 0.19]
Test for heterogeneity:	not app	olicable					
Test for overall effect z	=0.33	p=0.7					
05 In babies exposed t	o repea	t corticosteroids	at a mini	mum interval bet	ween 8 and 14 days		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity:							
Test for overall effect:	not appl	icable					
06 In babies exposed t		t corticosteroids		mum interval of	> 14 days		
Subtotal (95% CI)	0	P 11	0			0.0	Not estimable
Test for heterogeneity: Test for overall effect:							
07 In babies exposed t		epeat course of p		orticosteroids		0.0	NL c C LL
Subtotal (95% CI) Test for heterogeneity:	0	dicable	0			0.0	Not estimable
Test for neterogeneity:							
08 In babies exposed t Subtotal (95% CI)	o two n 0	epeat courses of	prenatal 0	corticosteroids		0.0	Not estimable
JUDIULAI (73/0 CI)	U		U			0.0	I NOT ESTILIADIE

							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	-	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity Test for overall effect:							
09 In babies exposed	to three	repeat courses o	f prenata	l corticosteroids			
Subtotal (95% CI) Test for heterogeneity Test for overall effect:			0			0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	ourses of 0	prenatal corticos	steroids	0.0	Not estimable
II In babies where pla	anned do	ose per treatment	course	12 mg or less of I	petamethasone or equivalent		
Crowther 2006	85	3.02 (0.86)	90	3.06 (0.71)	•	100.0	-0.04 [-0.27, 0.19]
Subtotal (95% CI) Test for heterogeneity Test for overall effect 2			90			100.0	-0.04 [-0.27, 0.19]
12 In babies where pla	anned do	ose per treatment	: course	> 12 mg to 24 m	g or less of betamethasone or equivale	ent	
Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	0			0.0	Not estimable
13 In babies where pla	anned do	ose per treatment	: course	> 24 mg of betar	nethasone or equivalent		
Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	0	Ü	·	0.0	Not estimable
14 In babies where pla	anned re	neat drug exnosi	ire was I	2 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	85	3.02 (0.86)	90	3.06 (0.71)	• equivalent	100.0	-0.04 [-0.27, 0.19]
Subtotal (95% CI) Test for heterogeneity Test for overall effect 2			90		•	100.0	-0.04 [-0.27, 0.19]
15 In babies where pla	anned re	peat drug exposi	ire was >	12 mg/week to	24 mg/week of betamethasone or equ	ıivalent	
Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	olicable	0	Ü		0.0	Not estimable
16 In babies where pla	anned re	peat drug exposu	ıre was >	24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	blicable	0	-		0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.48. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 48 Mean basal cortisol concentrations (nmol/L) at birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 48 Mean basal cortisol concentrations (nmol/L) at birth

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies Crowther 2006	34	60.10 (43.00)	33	105.00 (88.60)		100.0	-44.90 [-78.41, -11.39]
Subtotal (95% CI) Test for heterogeneity Test for overall effect	34 y: not ap	pplicable	33	103.00 (00.00)	-	100.0	-44.90 [-78.41, -11.39]
02 In babies where p Subtotal (95% CI) Test for heterogeneit Test for overall effect:	0 y: not ap	pplicable	reterm p	orelabour rupture o	f membranes at trial entry	0.0	Not estimable
03 In babies exposed Crowther 2006	to repe	at corticosteroids 60.10 (43.00)	as betan 33	nethasone 105.00 (88.60)	-	100.0	-44.90 [-78.41, -11.39]
Subtotal (95% CI) Test for heterogeneit; Test for overall effect			33		-	100.0	-44.90 [-78.41, -11.39]
04 In babies exposed Crowther 2006	to repe	at corticosteroids 60.10 (43.00)	at a mini 33	imum interval of 7 o	days or less	100.0	-44.90 [-78.41, -11.39]
Subtotal (95% CI) Test for heterogeneit Test for overall effect			33			100.0	-44.90 [-78.41, -11.39]
05 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect:	0 y: not ap	pplicable	at a mini 0	imum interval betwe	een 8 and 14 days	0.0	Not estimable
06 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect:	0 y: not ap	pplicable	at a mini 0	imum interval of >	14 days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogeneit Test for overall effect:	0 y: not ap	pplicable	renatal o	corticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI)	to two	repeat courses of	prenatal 0	corticosteroids		0.0	Not estimable

-100.0 -50.0 0 50.0 100.0

Favours single Favours repeat (Continued . . .)

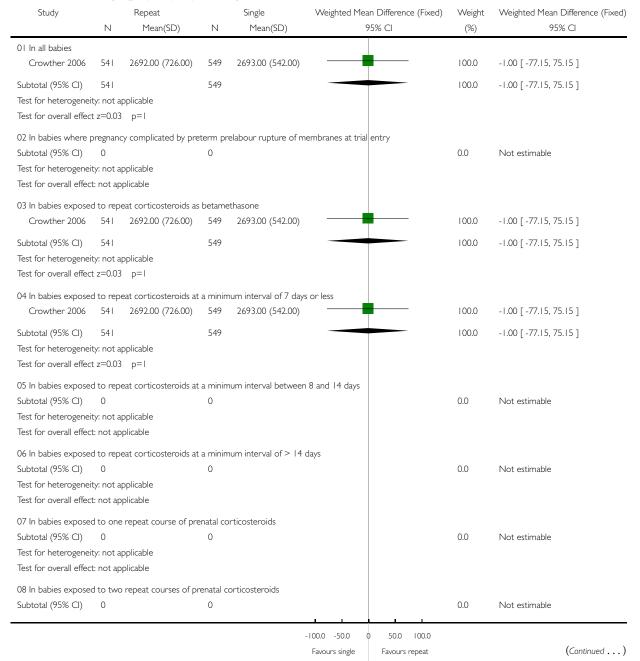
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneit	y: not a	pplicable					
Test for overall effects	not ap	plicable					
09 In babies exposed	to thre	e repeat courses o	of prenata	al corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not ap	pplicable					
Test for overall effect:	not ap	plicable					
10 In babies exposed	to four	or more repeat co	ourses of	prenatal corticost	eroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit	y: not ap	pplicable					
Test for overall effect:	not ap	plicable					
II In babies where p	lanned o	dose per treatment	t course	12 mg or less of be	etamethasone or equivalent		
Crowther 2006	34	60.10 (43.00)	33	105.00 (88.60)	-	100.0	-44.90 [-78.41, -11.39]
Subtotal (95% CI)	34		33		-	100.0	-44.90 [-78.41, -11.39]
Test for heterogeneit		pplicable					
Test for overall effect	z=2.63	p=0.009					
12 In habies where n	lanned (dose per treatment	course	> 12 mg to 24 mg	or less of betamethasone or equivalent		
Subtotal (95% CI)	0	aose per treatment	0	- IZING to ZITING	or less of betainethasone or equivalent	0.0	Not estimable
Test for heterogeneit		pplicable	Ü			0.0	1 tot estimasie
Test for overall effect:	not ap	plicable					
13 In habies where n	lanned (dose ner treatment	t course	> 24 mg of hetam	ethasone or equivalent		
Subtotal (95% CI)	0	aoso per a caamen	0	z mg or octam	outuserie et equivalent	0.0	Not estimable
Test for heterogeneit	y: not a	pplicable					
Test for overall effects	not ap	plicable					
14 In babies where p	lanned i	reneat drug exposi	ıre was	2 mg or less/week	of betamethasone or equivalent		
Crowther 2006	34	60.10 (43.00)	33	105.00 (88.60)		100.0	-44.90 [-78.41, -11.39]
Cultural (0F9/ CI)	34	, ,	33	, ,		100.0	-
Subtotal (95% CI) Test for heterogeneit		policable	33			100.0	-44.90 [-78.41, -11.39]
Test for overall effect							
		•		. 12 / 1 / 2			
	lanned i	repeat drug exposi	ure was 2 0	> 12 mg/week to 2	4 mg/week of betamethasone or equival	ent 0.0	Not estimable
Subtotal (95% CI) Test for heterogeneit		pplicable	U			0.0	NOT estimable
Test for overall effect:							
		•		24			
16 In babies where p Subtotal (95% CI)	lanned i 0	repeat drug exposi	ure was > 0	> 24 mg/week of b	etamethasone or equivalent	0.0	Not estimable
Test for heterogeneit		onlicable	U			0.0	I NOT ESTILITABLE
Test for overall effects							
					-100.0 -50.0 0 50.0 100.0		
					Favours single Favours repeat		

Analysis 01.49. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 49 Mean weight (g) at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 49 Mean weight (g) at primary hospital discharge



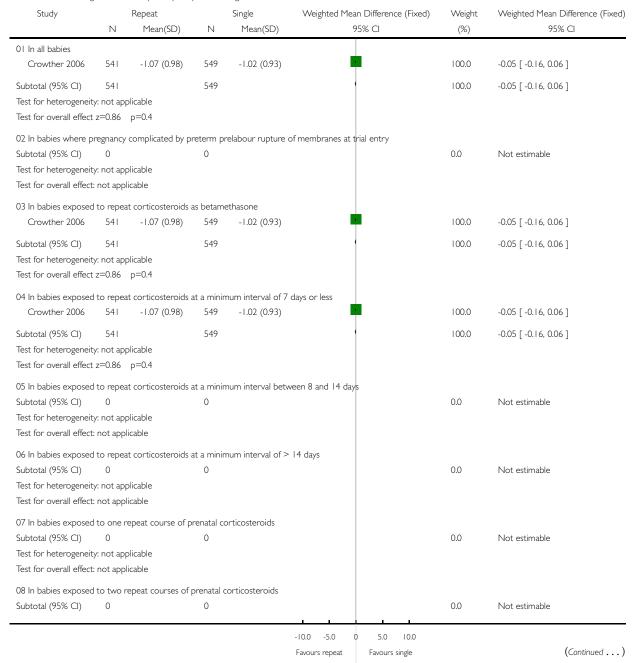
							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Test for heterogeneit			14	r-leari(3D)	73% CI	(/0)	73/6 CI
Test for overall effect	,	•					
09 In habies exposed	to the	ee repeat courses of	nrenatal	continosteroids			
Subtotal (95% CI)	0	00 100000 0001505 01	0	cor deostororas		0.0	Not estimable
Test for heterogeneit	ty: not a	applicable					
Test for overall effect	t: not ap	pplicable					
10 In babies exposed	d to fou	r or more repeat cou	irses of p	orenatal corticostero	pids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effect	•	• •					
Crowther 2006	olanned 541	2692.00 (726.00)	ourse 1 549	2 mg or less of betain 2693.00 (542.00)	methasone or equ <mark>i</mark> valent ————————————————————————————————————	100.0	-1.00 [-77.15, 75.15]
		2072.00 (720.00)		2073.00 (3 12.00)			
Subtotal (95% CI) Test for heterogeneit	541	applicable	549			100.0	-1.00 [-77.15, 75.15]
Test for overall effect	,						
12 In habies where r	olanned	dose per treatment o	ourse >	12 mg to 24 mg or	less of betamethasone or equivalent		
Subtotal (95% CI)	0	dose per a dan neme	0	12 mg to 2 mg or	ioss of sourmentastric or equivalent	0.0	Not estimable
Test for heterogeneit	ty: not a	applicable					
Test for overall effect	t: not ap	pplicable					
13 In babies where p	lanned	dose per treatment o	ourse >	24 mg of betameth	asone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effect							
14 In babies where p Crowther 2006	olanned 541	repeat drug exposun 2692.00 (726.00)	e was 12 549	2 mg or less/week of 2693.00 (542.00)	betamethasone or equivalent	100.0	-1.00 [-77.15, 75.15]
		2072.00 (720.00)		2073.00 (3 12.00)			
Subtotal (95% CI) Test for heterogeneit	541	applicable	549			100.0	-1.00 [-77.15, 75.15]
Test for overall effect	•	• •					
15 In habies where r	olanned	reneat drug exposum	e was >	12 mg/week to 24 r	ng/week of betamethasone or equivaler	nt	
Subtotal (95% CI)	0	repeat drug exposur	0	12 mg week to 211	ing week of betamentations of equivalen	0.0	Not estimable
Test for heterogeneit	ty: not a	applicable					
Test for overall effect	t: not ap	pplicable					
16 In babies where p	olanned	repeat drug exposur	e was >	24 mg/week of beta	methasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for everall effect	•						
Test for overall effect	.: not ap	pplicable					
					-100.0 -50.0 0 50.0 100.0		
					Favours single Favours repeat		

Analysis 01.50. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 50 Weight Z scores at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 50 Weight Z scores at primary hospital discharge



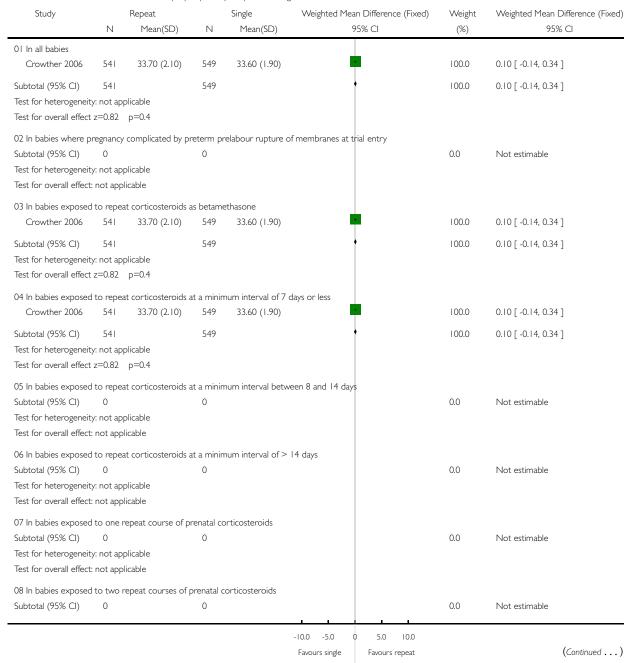
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity Test for overall effect:							
09 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 y: not app	licable	prenatal 0	corticosteroids		0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 y: not app	licable	urses of p	orenatal corticost	eroids	0.0	Not estimable
I I In babies where pl Crowther 2006	lanned do 541	se per treatment -1.07 (0.98)	course I 549	2 mg or less of be -1.02 (0.93)	etamethasone or equivalent	100.0	-0.05 [-0.16, 0.06]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549			100.0	-0.05 [-0.16, 0.06]
12 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 y: not app	licable	course >	12 mg to 24 mg	or less of betamethasone or equivalent	0.0	Not estimable
13 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 y: not app	licable	course > 0	24 mg of betame	ethasone or equivalent	0.0	Not estimable
14 In babies where pl	lanned rep	oeat drug exposu	re was 12	! mg or less/week	of betamethasone or equivalent		
Crowther 2006	541	-1.07 (0.98)	549	-1.02 (0.93)	•	100.0	-0.05 [-0.16, 0.06]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549			100.0	-0.05 [-0.16, 0.06]
15 In babies where pl	lanned rep	oeat drug exposu	re was >	12 mg/week to 2	4 mg/week of betamethasone or equiva	lent	
Subtotal (95% CI) Test for heterogeneity Test for overall effect:			0			0.0	Not estimable
I 6 In babies where pl	lanned rep	oeat drug exposu	re was >	24 mg/week of b	etamethasone or equivalent		
Subtotal (95% CI) Test for heterogeneity Test for overall effect:			0			0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.51. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 51 Mean head circumference (cm) at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 51 Mean head circumference (cm) at primary hospital discharge



							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity							
Test for overall effect:	not appl	icable					
09 In babies exposed	to three	repeat courses of	prenatal	corticosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	ıcable					
10 In babies exposed	to four c	or more repeat co	urses of p	orenatal corticoste	eroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	icable					
		•		-	etamethasone or equivalent		
Crowther 2006	541	33.70 (2.10)	549	33.60 (1.90)	•	100.0	0.10 [-0.14, 0.34]
Subtotal (95% CI)	541		549		†	100.0	0.10 [-0.14, 0.34]
Test for heterogeneity	: not app	olicable					
Test for overall effect	z=0.82	p=0.4					
12 In babies where pl	anned do	ose per treatment	course >	12 mg to 24 mg	or less of betamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	icable					
13 In babies where pl	anned do	ose per treatment	course >	24 mg of betame	ethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	icable					
14 In babies where pl	anned re	peat drug exposu	re was 12	mg or less/week	of betamethasone or equivalent		
Crowther 2006	541	33.70 (2.10)	549	33.60 (1.90)	•	100.0	0.10 [-0.14, 0.34]
Subtotal (95% CI)	541		549		•	100.0	0.10 [-0.14, 0.34]
Test for heterogeneity							
Test for overall effect	z=0.82	p=0.4					
15 In babies where pl	anned re	peat drug exposui	re was >	12 mg/week to 2	4 mg/week of betamethasone or equiva	alent	
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	icable					
16 In babies where pl	anned re	peat drug exposu	re was >	24 mg/week of b	etamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appl	ıcable					
					100 50 0		
					-10.0 -5.0 0 5.0 10.0		
					Favours single Favours repeat		

Analysis 01.52. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 52 Head circumference Z scores at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 52 Head circumference Z scores at primary hospital discharge

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies							
Crowther 2006	541	-0.19 (1.12)	549	-0.15 (1.06)		100.0	-0.04 [-0.17, 0.09]
Subtotal (95% CI) Test for heterogeneit	541 y: not app	olicable	549			100.0	-0.04 [-0.17, 0.09]
Test for overall effect	z=0.61	p=0.5					
02 In babies where p	regnancy	complicated by pr	eterm pn	elabour rupture o	of membranes at trial entry		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect:	not appl	icable					
03 In babies exposed	to repea	t corticosteroids a	s betame	thasone	<u></u>		
Crowther 2006	541	-0.19 (1.12)	549	-0.15 (1.06)	•	100.0	-0.04 [-0.17, 0.09]
Subtotal (95% CI)	541		549			100.0	-0.04 [-0.17, 0.09]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.61	p=0.5					
04 In babies exposed	to repea	t corticosteroids a	t a minim	num interval of 7	days or less		
Crowther 2006	541	-0.19 (1.12)	549	-0.15 (1.06)		100.0	-0.04 [-0.17, 0.09]
Subtotal (95% CI)	541		549			100.0	-0.04 [-0.17, 0.09]
Test for heterogeneit	y: not app	olicable					
Test for overall effect	z=0.61	p=0.5					
05 In babies exposed	to repea	t corticosteroids a	t a minim	num interval betw	veen 8 and 14 days		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit							
Test for overall effect:	not appl	icable					
06 In babies exposed		t corticosteroids a		num interval of >	14 days		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity Test for overall effects							
07 In babies exposed		epeat course of pi		rticosteroids			
Subtotal (95% CI)	0	ali an la la	0			0.0	Not estimable
Test for heterogeneity Test for overall effects							
08 In babies exposed Subtotal (95% CI)	to two n	epeat courses of p	orenatal co	orticosteroids		0.0	Not estimable
343 (7370 CI)						0.0	1 VOE CSUITADIC
					-10.0 -5.0 0 5.0 10.0		
					Favours single Favours repeat		(Continued)

								(Continued)
Study	Re N	peat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Differenc	, ,	/eight (%)	Weighted Mean Difference (Fixed) 95% CI
Test for heterogeneity Test for overall effect:							,	
09 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	prenatal 0	corticosteroids		0.4	0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	urses of p	orenatal corticost	eroids	0.4	0	Not estimable
II In babies where pl Crowther 2006		per treatment -0.19 (1.12)	course 12 549	2 mg or less of be	etamethasone or equivalent	10	0.00	-0.04 [-0.17, 0.09]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549			IC	0.00	-0.04 [-0.17, 0.09]
12 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	course > 0	12 mg to 24 mg	or less of betamethasone or	equivalent 0.1	0	Not estimable
13 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	course > 0	24 mg of betam	ethasone or equivalent	0.0	0	Not estimable
14 In babies where pl Crowther 2006		t drug exposu -0.19 (1.12)	~e was 12 549	mg or less/week -0.15 (1.06)	of betamethasone or equival		0.00	-0.04 [-0.17, 0.09]
Subtotal (95% CI) Test for heterogeneity Test for overall effect	541 : not applica	ble	549	` /			0.00	-0.04 [-0.17, 0.09]
15 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	re was >	12 mg/week to 2	4 mg/week of betamethasone	e or equivalent 0.1	0	Not estimable
16 In babies where pl Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not applica	ble	re was >	24 mg/week of b	etamethasone or equivalent	0.0	0	Not estimable
					-10.0 -5.0 0 5.0 Favours single Favours r	10.0 repeat		

Analysis 01.53. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 53 Mean length (cm) at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 53 Mean length (cm) at primary hospital discharge

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all babies Crowther 2006	541	47.40 (4.30)	549	47.40 (4.00)	-	100.0	0.00 [-0.49, 0.49]
Subtotal (95% CI) Test for heterogeneity Test for overall effect	541 v: not app	olicable	549	()	•	100.0	0.00 [-0.49, 0.49]
02 In babies where pr Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 not app	olicable	eterm pr 0	elabour rupture c	f membranes at trial entry	0.0	Not estimable
03 In babies exposed						100.0	000 0 0 40 0 40 1
Crowther 2006 Subtotal (95% CI) Test for heterogeneity Test for overall effect			549 549	47.40 (4.00)	Ī	100.0	0.00 [-0.49, 0.49]
04 In babies exposed Crowther 2006	to repea 541	t corticosteroids a 47.40 (4.30)	it a minim 549	num interval of 7 (47.40 (4.00)	days or less	100.0	0.00 [-0.49, 0.49]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549		•	100.0	0.00 [-0.49, 0.49]
05 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	olicable	t a minim 0	num interval betw	een 8 and 14 days	0.0	Not estimable
06 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 : not app	olicable	t a minim 0	num interval of >	14 days	0.0	Not estimable
07 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 v: not app	ilicable	renatal co	rticosteroids		0.0	Not estimable
08 In babies exposed Subtotal (95% CI)	to two re	epeat courses of p	orenatal c	orticosteroids		0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0 Favours single Favours repeat		(Continued)

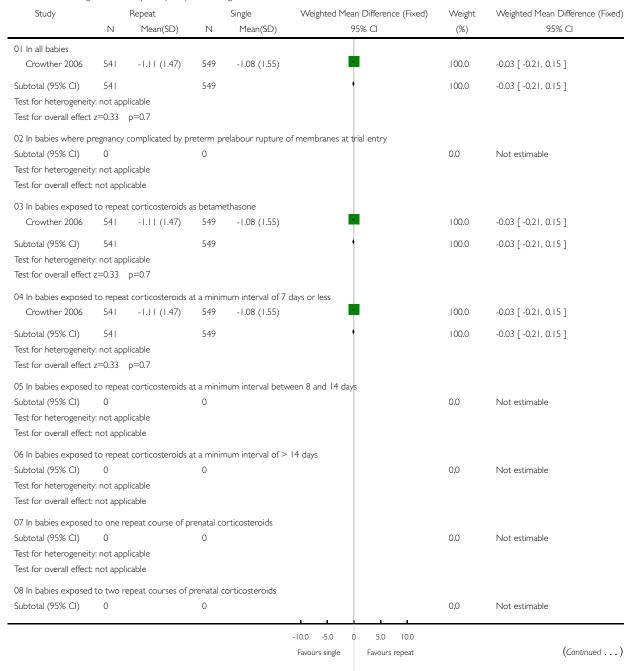
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity							
Test for overall effect:							
09 In babies exposed	to three 0	repeat courses of	f prenatal 0	corticosteroids		0.0	Not estimable
Subtotal (95% CI) Test for heterogeneity		olicable	U			0.0	Not estimable
Test for overall effect:							
10 In babies exposed	to four c	or more repeat co	urses of p	orenatal corticost	eroids		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appli	ıcable					
I I In babies where place Crowther 2006	anned do 541		course 1:	-	etamethasone or equivalent	100.0	0.00 [0.40 0.40]
		47.40 (4.30)		47.40 (4.00)	Ţ		0.00 [-0.49, 0.49]
Subtotal (95% CI) Test for heterogeneity	541	dicable	549		Ĭ	100.0	0.00 [-0.49, 0.49]
Test for overall effect							
12 In babies where pl	anned do	ose per treatment	course >	· 12 mg to 24 mg	or less of betamethasone or equivalen	t	
Subtotal (95% CI)	0	'	0	0 0	· ·	0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appli	icable					
		se per treatment		24 mg of betame	ethasone or equivalent	0.0	No. 2 II
Subtotal (95% CI) Test for heterogeneity	0 c not app	olicable.	0			0.0	Not estimable
Test for overall effect:							
14 In babies where pla	anned re	peat drug exposu	re was 12	2 mg or less/week	of betamethasone or equivalent		
Crowther 2006	541	47.40 (4.30)	549	47.40 (4.00)	•	100.0	0.00 [-0.49, 0.49]
Subtotal (95% CI)	541		549		•	100.0	0.00 [-0.49, 0.49]
Test for heterogeneity							
Test for overall effect	z=0.00	p=I					
		peat drug exposu		12 mg/week to 2	4 mg/week of betamethasone or equiv		
Subtotal (95% CI) Test for heterogeneity	0 r not ann	dicable	0			0.0	Not estimable
Test for overall effect:							
16 In babies where pl	anned re	peat drug exposu	re was >	24 mg/week of b	etamethasone or equivalent		
Subtotal (95% CI)	0	. 0 1	0	Ü		0.0	Not estimable
Test for heterogeneity							
Test for overall effect:	not appli	icable					
					-10.0 -5.0 0 5.0 10.0		
					Favours single Favours repeat		

Analysis 01.54. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 54 Length Z score at primary hospital discharge

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 54 Length Z score at primary hospital discharge



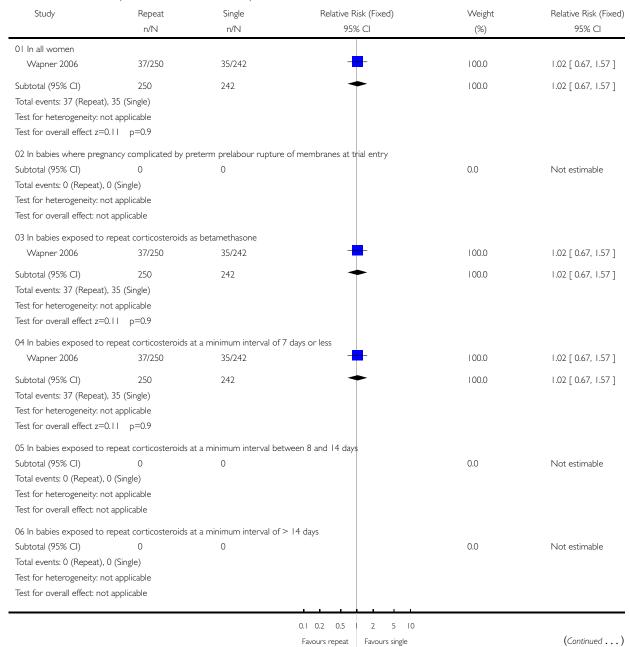
							(Continued)
Study		Repeat		Single	Weighted Mean Difference (Fixed)	Weight	Weighted Mean Difference (Fixed)
	Ν	Mean(SD)	Ν	Mean(SD)	95% CI	(%)	95% CI
Test for heterogeneity Test for overall effect:							
09 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	prenatal 0	corticosteroids		0.0	Not estimable
10 In babies exposed Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	urses of p	orenatal corticost	eroids	0.0	Not estimable
II In babies where pla	anned do	se per treatment	course I	2 mg or less of be	etamethasone or equivalent		
Crowther 2006	541	-1.11 (1.47)	549	-1.08 (1.55)	•	100.0	-0.03 [-0.21, 0.15]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549			100.0	-0.03 [-0.21, 0.15]
12 In babies where place Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	course >	12 mg to 24 mg	or less of betamethasone or equivalent	0.0	Not estimable
13 In babies where pl. Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	course >	24 mg of betame	ethasone or equivalent	0.0	Not estimable
14 In babies where pl	anned rep	oeat drug exposu	re was 12	mg or less/week	of betamethasone or equivalent		
Crowther 2006	541	-1.11 (1.47)	549	-1.08 (1.55)	<u>•</u>	100.0	-0.03 [-0.21, 0.15]
Subtotal (95% CI) Test for heterogeneity Test for overall effect			549			100.0	-0.03 [-0.21, 0.15]
15 In babies where pl. Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	re was > 0	12 mg/week to 2	4 mg/week of betamethasone or equiva	lent 0.0	Not estimable
16 In babies where pl. Subtotal (95% CI) Test for heterogeneity Test for overall effect:	0 r: not app	licable	re was > 0	24mg/week of be	etamethasone or equivalent	0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0 Favours single Favours repeat		

Analysis 01.55. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 55 Prelabour rupture of membranes after trial entry

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 55 Prelabour rupture of membranes after trial entry



Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
07 In babies exposed to on	e repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (/				
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
08 In babies exposed to tw	o repeat courses of	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 ((Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
09 In babies exposed to thr	ree repeat courses o	f prenatal corticosteroids	6		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
IO la babias avasas de fav		af amountal continue	.atauaida		
10 In babies exposed to fou Subtotal (95% CI)	or more repeat co	0	steroids	0.0	Not estimable
Total events: 0 (Repeat), 0 (O		0.0	Not estimable
Test for heterogeneity: not					
Test for overall effect: not a					
rest for overall effect flot a	ppiicabie				
		-	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
12 In babies where planned	dose per treatment	course > 12 mg to 24 n	ng or less of betame <mark>t</mark> hasone or equivalen	t	
Wapner 2006	37/250	35/242		100.0	1.02 [0.67, 1.57]
Subtotal (95% CI)	250	242	+	100.0	1.02 [0.67, 1.57]
Total events: 37 (Repeat), 3	5 (Single)				
Test for heterogeneity: not					
Test for overall effect z=0.1	I p=0.9				
13 In babies where planned	dose per treatment	course > 24 mg of heta	methasone or equivalent		
Subtotal (95% CI)	0	0	inethasone of equivalent	0.0	Not estimable
Total events: 0 (Repeat), 0 (Ü		0.0	1 VOC CSUITIABLE
Test for heterogeneity: not					
Test for overall effect: not a	• •				
·	•				
		_	ek of betamethasone or equivalent	0.5	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 (
Test for heterogeneity: not a					
Test for overall effect: not a	phiicable				
			01 02 05 2 5 10		
			0.1 0.2 0.5 2 5 10		(Continued)
			Favours repeat Favours single		(Conunued)



Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% Cl	Weight (%)	Relative Risk (Fixed) 95% CI
15 In babies where plann			to 24 mg/week of betamethasone or		7370 CI
Wapner 2006	37/250	35/242	+	100.0	1.02 [0.67, 1.57]
Subtotal (95% CI)	250	242	•	100.0	1.02 [0.67, 1.57]
Total events: 37 (Repeat)	, 35 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=0).II p=0.9				
16 In babies where plann	ed repeat drug exposi	ure was > 24 mg/week o	f betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.56. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 56 Hypertension (variously defined by the authors)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 56 Hypertension (variously defined by the authors)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all women					
Crowther 2006	62/489	67/493	+	89.1	0.93 [0.68, 1.29]
Wapner 2006	15/250	8/242		10.9	1.82 [0.78, 4.20]
Subtotal (95% CI)	739	735	+	100.0	1.03 [0.76, 1.39]
Total events: 77 (Repeat),	75 (Single)				
Test for heterogeneity chi	-square=2.11 df=1 p=0	0.15 l² =52.6%			
Test for overall effect z=0	.19 p=0.9				
02 In babies where pregn	ancy complicated by pr	reterm prelabour ruptur	e of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids a	s betamethasone			
Crowther 2006	62/489	67/493	+	89.1	0.93 [0.68, 1.29]
Wapner 2006	15/250	8/242	-	10.9	1.82 [0.78, 4.20]
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued)

					(Continued)	
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI	
Subtotal (95% CI)	739	735	+	100.0	1.03 [0.76, 1.39]	
Total events: 77 (Repeat),	75 (Single)					
Test for heterogeneity chi-	square=2.11 df=1 p=0).15 l² =52.6%				
Test for overall effect z=0.	19 p=0.9					
04 In babies exposed to re	epeat corticosteroids a	t a minimum interval of	7 days or less			
Crowther 2006	62/489	67/493		89.1	0.93 [0.68, 1.29]	
Wapner 2006	15/250	8/242		10.9	1.82 [0.78, 4.20]	
Subtotal (95% CI)	739	735	•	100.0	1.03 [0.76, 1.39]	
Total events: 77 (Repeat),					[,]	
Test for heterogeneity chi-	, -,).15 l² =52.6%				
Test for overall effect z=0.						
05 In babies exposed to re	epeat corticosteroids a	t a minimum interval be	tween 8 and 14 days			
Subtotal (95% CI)	0	0	·	0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
06 In babies exposed to re	epeat corticosteroids a	t a minimum interval of	> 14 days			
Subtotal (95% CI)	0	0	,	0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
07 In babies exposed to o	ne repeat course of pr	enatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
08 In babies exposed to tv	wo repeat courses of p	renatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
09 In babies exposed to th	nree repeat courses of	prenatal corticosteroids				
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not	t applicable					
Test for overall effect: not	applicable					
10 In babies exposed to fo	our or more repeat co	urses of prenatal cortico	steroids			
Subtotal (95% CI)	0	0		0.0	Not estimable	
Total events: 0 (Repeat), 0	(Single)					
Test for heterogeneity: not						
Test for overall effect: not	applicable					
			0.1 0.2 0.5 2 5 10		(= : : : : : : : : : : : : : : : : : : :	
			Favours repeat Favours single		(Continued)	

					(Conunued
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
II In babies where planne	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Crowther 2006	62/489	67/493	-	100.0	0.93 [0.68, 1.29]
Subtotal (95% CI)	489	493	+	100.0	0.93 [0.68, 1.29]
Total events: 62 (Repeat),	67 (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect z=0.	42 p=0.7				
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 n	ng or less of betamethasone or equivalen	t	
Wapner 2006	15/250	8/242	 	100.0	1.82 [0.78, 4.20]
Subtotal (95% CI)	250	242		100.0	1.82 [0.78, 4.20]
Total events: 15 (Repeat),	8 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.	39 p=0.2				
13 In babies where planne	ed dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/we	ek of betamethasone or equivalent		
Crowther 2006	62/489	67/493	-	100.0	0.93 [0.68, 1.29]
Subtotal (95% CI)	489	493	+	100.0	0.93 [0.68, 1.29]
Total events: 62 (Repeat),	67 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=0.	42 p=0.7				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent	
Wapner 2006	15/250	8/242	 	100.0	1.82 [0.78, 4.20]
Subtotal (95% CI)	250	242		100.0	1.82 [0.78, 4.20]
Total events: 15 (Repeat),	8 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.	39 p=0.2				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		

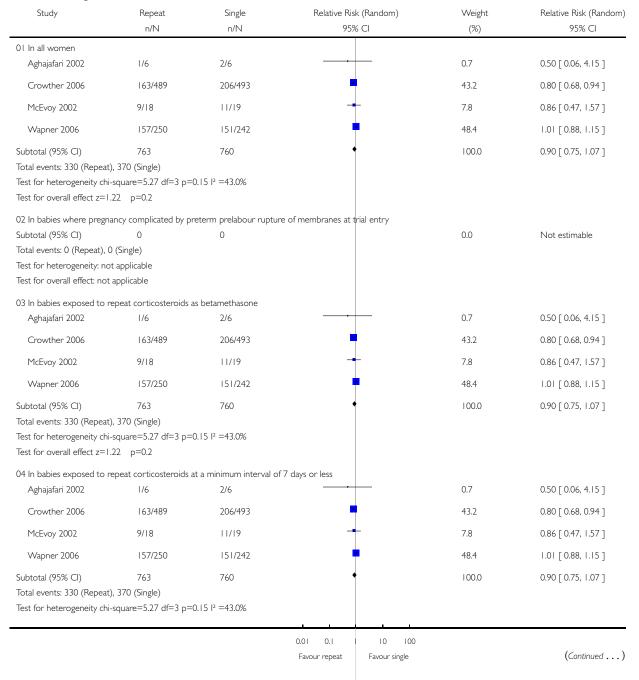
0.1 0.2 0.5 | 2 5 | 10 Favours repeat | Favours single

Analysis 01.57. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 57 Vaginal birth

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 57 Vaginal birth



p=0.2 peat corticosteroids 0 Single) applicable	at a minimum interval be	stygen 8 and 14 days	* *	
0 Single)		stugen 8 and 14 days		
0 Single)		ctarcetto atio it adyp		
		,	0.0	Not estimable
ιρρικαυικ				
pplicable				
eat corticosteroids	at a minimum interval of	> 14 days		
0	0		0.0	Not estimable
Single)				
applicable				
e repeat course of p	renatal corticosteroids			
0	0		0.0	Not estimable
Single)				
o repeat courses of	prenatal corticosteroids			
0	0		0.0	Not estimable
Single)				
- /				
ee repeat courses o	f prenatal corticosteroid	s		
0	0		0.0	Not estimable
Single)				
r or more repeat co	urses of prenatal cortice	osteroids		
0	0		0.0	Not estimable
Single)				
dose per treatment	course 12 mg or less of	betamethasone or equivalent		
163/489	206/493	•	100.0	0.80 [0.68, 0.94]
489	493	•	100.0	0.80 [0.68, 0.94]
206 (Single)				
dose per treatment	course > 12 mg to 24 r	ng or less of betamethasone or equiv	alent	
1/6	2/6		0.4	0.50 [0.06, 4.15]
9/18	11/19	+	4.9	0.86 [0.47, 1.57]
****			***	1.11 [01.11, 1.10,]
		0.01 0.1 10 100		
		Favour repeat Favour single		(Continued
	O (Single) applicable e repeat course of p O (Single) applicable or repeat courses of p O (Single) applicable ere repeat courses or O (Single) applicable ere reatment E (63/489 489 206 (Single) applicable ere reatment ere of O (Single) applicable ere of O (Single) appl	O O O Single) applicable e repeat course of prenatal corticosteroids O O O O O O O O O O O O O O O O O O O	Single) applicable poplicable e repeat course of prenatal corticosteroids 0 0 Single) applicable poplicable poplicable or repeat courses of prenatal corticosteroids 0 0 0 Single) applicable poplicable poplicable poplicable ree repeat courses of prenatal corticosteroids 0 0 Single) applicable poplicable ur or more repeat courses of prenatal corticosteroids 0 0 Single) applicable poplicable loose per treatment course 12 mg or less of betamethasone or equivalent 163/489 206/493 489 493 206 (Single) applicable 2 p=0.007 Idose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent 1/6 2/6 9/18 11/19	O O O O O O O O O O O O O O O O O O O

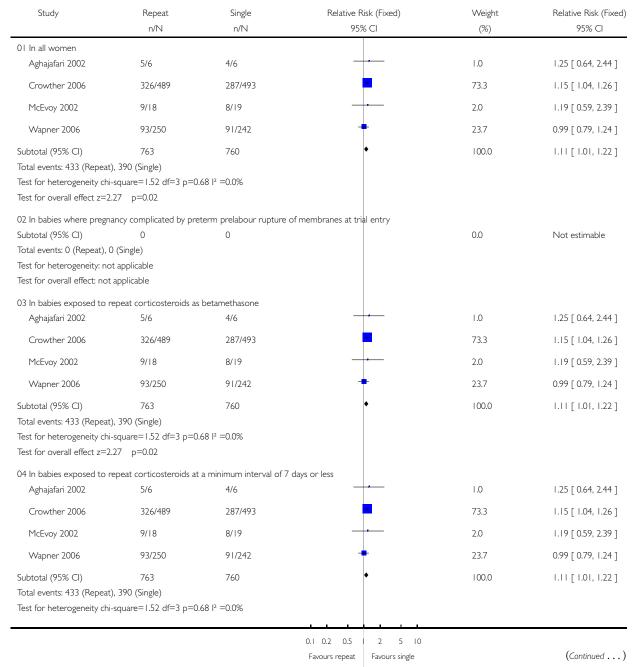
					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% Cl	Weight (%)	Relative Risk (Random) 95% CI
Wapner 2006	157/250	151/242	•	94.7	1.01 [0.88, 1.15]
Subtotal (95% CI) Total events: 167 (Repeat) Test for heterogeneity chi- Test for overall effect z=0.0	square=0.65 df=2 p=	267 0.72 ² =0.0%		100.0	1.00 [0.87, 1.14]
13 In babies where planne	ed dose per treatment	course > 24 mg of beta	amethasone or equivalent		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	0		0.0	Not estimable
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/we	eek of betamethasone or equivalent		
Crowther 2006	163/489	206/493	•	100.0	0.80 [0.68, 0.94]
Subtotal (95% CI) Total events: 163 (Repeat) Test for heterogeneity: not Test for overall effect z=2.	t applicable	493	•	100.0	0.80 [0.68, 0.94]
15 In babies where planne	d repeat drug exposu	re was > 12 mg/week to	o 24 mg/week of betamethasone or equ	iivalent	
Aghajafari 2002	1/6	2/6		0.4	0.50 [0.06, 4.15]
McEvoy 2002	9/18	11/19	+	4.9	0.86 [0.47, 1.57]
Wapner 2006	157/250	151/242	-	94.7	1.01 [0.88, 1.15]
Subtotal (95% CI) Total events: 167 (Repeat) Test for heterogeneity chi- Test for overall effect z=0.0	square=0.65 df=2 p=	267 0.72 ² =0.0%	•	100.0	1.00 [0.87, 1.14]
16 In babies where planne	d repeat drug exposu	re was > 24 mg/week o	f betamethasone or equivalent		
Subtotal (95% CI) Total events: 0 (Repeat), 0 Test for heterogeneity: not Test for overall effect: not	0 (Single) t applicable	0		0.0	Not estimable
			0.01 0.1 10 100 Favour repeat Favour single		

Analysis 01.58. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 58 Caesarean section

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 58 Caesarean section



					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for overall effect z=2	.27 p=0.02				
05 In babies exposed to r	reneat continueteroids a	t a minimum interval het	ween 8 and 14 days		
Subtotal (95% CI)	0	0	weem o and in days	0.0	Not estimable
Total events: 0 (Repeat), (-			
Test for heterogeneity: no	, - ,				
Test for overall effect: not					
06 In babies exposed to r	reneat continueteroids a	t a minimum interval of 3	> 14 days		
Subtotal (95% CI)	0	0	1 T days	0.0	Not estimable
Total events: 0 (Repeat), (Ŭ		0.0	1 VOC CSUITIABLE
Test for heterogeneity: no	` 0 /				
Test for overall effect: not					
07 In babies exposed to c				0.0	No. of the
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0					
Test for heterogeneity: no					
Test for overall effect: not	аррисаріе				
08 In babies exposed to t	wo repeat courses of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
09 In babies exposed to t	hree repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
10 In babies exposed to f	our or more repeat cou	urses of prenatal corticos	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (O (Single)				
Test for heterogeneity: no	, ,				
Test for overall effect: not	applicable				
I I In habies where planne	ed dose per treatment	course 12 mg or less of h	petamethasone or equivalent		
Crowther 2006	326/489	287/493	+	100.0	1.15 [1.04, 1.26]
Subtotal (95% CI)	489	493	•	100.0	1.15 [1.04, 1.26]
Total events: 326 (Repeat	, , ,				
Test for heterogeneity: no					
Test for overall effect z=2	./2 p=0.006				
12 In babies where planne	ed dose per treatment	course > 12 mg to 24 m	g or less of betamethasone or equivaler	nt	
Aghajafari 2002	5/6	4/6	+	3.8	1.25 [0.64, 2.44]
McEvoy 2002	9/18	8/19	+	7.5	1.19 [0.59, 2.39]
			0.1 0.2 0.5 2 5 10		
					(Continued)
			Favours repeat Favours single		(Con

					(Contantaed
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed 95% CI
Wapner 2006	93/250	91/242	-	88.7	0.99 [0.79, 1.24]
Subtotal (95% CI)	274	267	+	100.0	1.01 [0.82, 1.25]
Total events: 107 (Repeat	;), 103 (Single)				
Test for heterogeneity chi	-square=0.61 df=2 p=	0.74 l ² =0.0%			
Test for overall effect z=0	n.13 p=0.9				
13 In babies where planne	ed dose per treatment	course > 24 mg of betar	methasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/wee	ek of betamethasone or equivalent		
Crowther 2006	326/489	287/493	<u>-</u>	100.0	1.15 [1.04, 1.26]
Subtotal (95% CI)	489	493	•	100.0	1.15 [1.04, 1.26]
Total events: 326 (Repeat), 287 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=2	.72 p=0.006				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	alent	
Aghajafari 2002	5/6	4/6	- • -	3.8	1.25 [0.64, 2.44]
McEvoy 2002	9/18	8/19	-	7.5	1.19 [0.59, 2.39]
Wapner 2006	93/250	91/242	#	88.7	0.99 [0.79, 1.24]
Subtotal (95% CI)	274	267	+	100.0	1.01 [0.82, 1.25]
Total events: 107 (Repeat), 103 (Single)				
Test for heterogeneity chi	-square=0.61 df=2 p=	0.74 l ² =0.0%			
Test for overall effect z=0	.13 p=0.9				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week of	betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
			0.1 0.2 0.5 2 5 10		

0.1 0.2 0.5 2 5 10

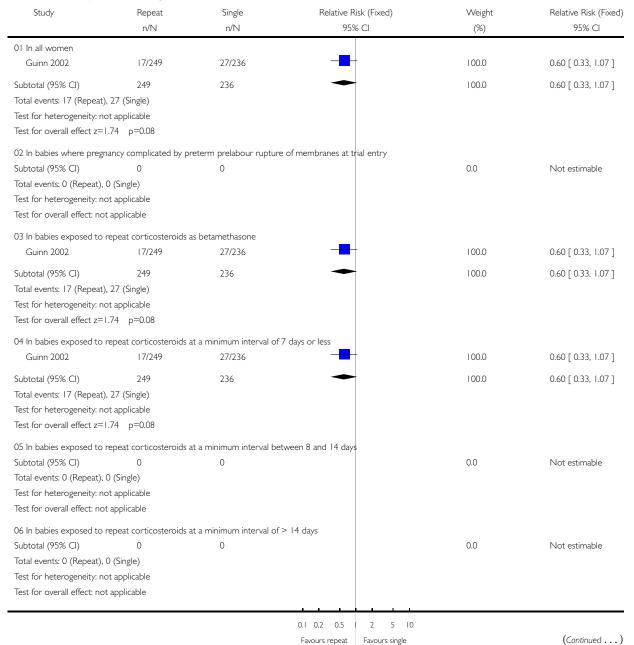
Favours repeat Favours single

Analysis 01.59. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 59 Postpartum haemorrhage

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 59 Postpartum haemorrhage



Study Repeat Single Relative Risk (Fixed) n/N n/N 95% CI 07 In babies exposed to one repeat course of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable 88 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable Test for overall effect not applicable Test for overall effect: not applicable Test for heterogeneity, not applicable Test for overall effect: not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect: not applicable Test for heterogeneity, not applicable Test for heterogeneity, not applicable Test for overall effect: not applicable Test for heterogeneity, not applicable	Weight (%) 0.0 0.0	Relative Risk (Fixed) 95% CI Not estimable Not estimable
O7 In babies exposed to one repeat course of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for Neterogeneity: not applicable Test for Overall effect: not applicable Test for Neterogeneity: not applicable Test for heterogeneity: not applicable	0.0	Not estimable
Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable		
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for Neterogeneity: not applicable		
Test for heterogeneity: not applicable Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for levens: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for levens: 0 (Repeat), 0 (Single) Test for Repeat), 0 (Single) Test for heterogeneity: not applicable Test for levens: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for levens: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	Not estimable
Test for overall effect: not applicable 08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for leterogeneity: not applicable	0.0	Not estimable
08 In babies exposed to two repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity, not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	Not estimable
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Total events: 0 (Repeat), 0 (Single) Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable	0.0	Not estimable
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable	0.0	Not estimable
Test for heterogeneity: not applicable Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable		
Test for overall effect: not applicable 09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
09 In babies exposed to three repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for heterogeneity: not applicable Test for overall effect: not applicable		
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I I In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Test for heterogeneity: not applicable Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 11 In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	Not estimable
Test for overall effect: not applicable 10 In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable Il In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I2 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
IO In babies exposed to four or more repeat courses of prenatal corticosteroids Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I2 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I I In babies where planned dose per treatment course I 2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I 2 In babies where planned dose per treatment course > I 2 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 I7/249 27/236 Subtotal (95% CI) 249 236 Total events: I 7 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I I In babies where planned dose per treatment course I 2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I 2 In babies where planned dose per treatment course > I 2 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: I 7 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable II In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I2 In babies where planned dose per treatment course > I2 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: I7 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	Not estimable
Test for heterogeneity: not applicable Test for overall effect: not applicable I I In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable I2 In babies where planned dose per treatment course > I2 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 I7/249 27/236 Subtotal (95% CI) 249 236 Total events: I7 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	1 VOE CSGITIABIC
Test for overall effect: not applicable II In babies where planned dose per treatment course I2 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable I2 In babies where planned dose per treatment course > I2 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 I7/249 27/236 Subtotal (95% CI) 249 236 Total events: I7 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Il In babies where planned dose per treatment course 12 mg or less of betamethasone or equivalent Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Total events: 0 (Repeat), 0 (Single) Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Test for heterogeneity: not applicable Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	0.0	Not estimable
Test for overall effect: not applicable 12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
12 In babies where planned dose per treatment course > 12 mg to 24 mg or less of betamethasone or equivalent Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Guinn 2002 17/249 27/236 Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Subtotal (95% CI) 249 236 Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable		
Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	100.0	0.60 [0.33, 1.07]
Total events: 17 (Repeat), 27 (Single) Test for heterogeneity: not applicable	100.0	0.60 [0.33, 1.07]
Test for example effect $z=1.74$, $z=0.00$		
lest for overall effect 2–1.74 p=0.06		
13 In babies where planned dose per treatment course > 24 mg of betamethasone or equivalent		
Subtotal (95% CI) 0 0	0.0	Not estimable
Total events: 0 (Repeat), 0 (Single)		
Test for heterogeneity: not applicable		
Test for overall effect: not applicable		
···		
14 In babies where planned repeat drug exposure was 12 mg or less/week of betamethasone or equivalent Subtotal (95% CI) 0 0	0.0	Not estimable
Subtotal (95% CI) 0 0 Total events: 0 (Repeat), 0 (Single)	0.0	i not estimable
Test for heterogeneity: not applicable		
Test for overall effect: not applicable		
rest for overall effect flot applicable		
0.1 0.2 0.5 2 5 10		
Favours repeat Favours single		(Continued)
1 avours repeat 1 avours strigte		(-011011000)

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
15 In babies where plann	ed repeat drug exposi	ıre was > 12 mg/week t	o 24 mg/week of betamethasone or equiv	valent	
Guinn 2002	17/249	27/236	-	100.0	0.60 [0.33, 1.07]
Subtotal (95% CI)	249	236	•	100.0	0.60 [0.33, 1.07]
Total events: 17 (Repeat)	, 27 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.74 p=0.08				
16 In babies where plann	ed repeat drug exposu	ure was > 24 mg/week o	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.60. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 60 Postnatal pyrexia (variously defined by authors)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 60 Postnatal pyrexia (variously defined by authors)

Study Repeat Single Odds Ratio (Fixed) Weight Odds Ratio (Fixed)

n/N n/N 95% CI (%) 95% CI

Study	Repeat	Single	Odds Ratio (Fixed)	Weight	Odds Ratio (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
01 In all women					
Crowther 2006	32/489	37/493	-	100.0	0.86 [0.53, 1.41]
Subtotal (95% CI)	489	493	•	100.0	0.86 [0.53, 1.41]
Total events: 32 (Repeat),	37 (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect z=0.	59 p=0.6				
02 In babies where pregna	ancy complicated by pr	eterm prelabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
03 In babies exposed to re	epeat corticosteroids a	s betamethasone			
Crowther 2006	32/489	37/493	-	100.0	0.86 [0.53, 1.41]
Subtotal (95% CI)	489	493	•	100.0	0.86 [0.53, 1.41]
Total events: 32 (Repeat),	37 (Single)				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		(Continued)

					(Continued)	
Study	Repeat n/N	Single n/N	Odds Ratio (Fixed) 95% CI	Weight (%)	Odds Ratio (Fixed) 95% CI	
Test for heterogeneity: not a						
04 In babies exposed to rep	oeat corticosteroids a	t a minimum interval of 7	days or less			
Crowther 2006	32/489	37/493	· —	100.0	0.86 [0.53, 1.41]	
Subtotal (95% CI) Total events: 32 (Repeat), 3 Test for heterogeneity: not a Test for overall effect z=0.5	applicable	493	+	100.0	0.86 [0.53, 1.41]	
05 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	0 (Single) applicable	t a minimum interval betv 0	veen 8 and 14 days	0.0	Not estimable	
06 In babies exposed to rep Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	0 (Single) applicable	t a minimum interval of > 0	· 14 days	0.0	Not estimable	
07 In babies exposed to on Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not	re repeat course of pr 0 (Single) applicable	renatal corticosteroids 0		0.0	Not estimable	
Test for overall effect: not all 08 In babies exposed to two Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	o repeat courses of p 0 (Single) applicable	orenatal corticosteroids 0		0.0	Not estimable	
09 In babies exposed to thr Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	ree repeat courses of 0 (Single) applicable	prenatal corticosteroids 0		0.0	Not estimable	
10 In babies exposed to fou Subtotal (95% CI) Total events: 0 (Repeat), 0 (Test for heterogeneity: not a Test for overall effect: not a	ur or more repeat cou 0 (Single) applicable	urses of prenatal corticost O	teroids	0.0	Not estimable	
II In babies where plannec	dose per treatment	course 12 mg or less of b	etamethasone or equivalent			
Crowther 2006	32/489	37/493	-	100.0	0.86 [0.53, 1.41]	
Crowther 2006			l l			

					(Continued
Study	Repeat	Single	Odds Ratio (Fixed)	Weight	Odds Ratio (Fixed
	n/N	n/N	95% CI	(%)	95% CI
Total events: 32 (Repeat), 3	37 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.5	59 p=0.6				
12 In babies where planned	d dose per treatment	course > 12 mg to 24 mg	g or less of betamethasone or equivalent	t	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
3 In babies where planned	d dose per treatment	course > 24 mg of betam	nethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
otal events: 0 (Repeat), 0	(Single)				
est for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
14 In babies where planned	d repeat drug exposur	re was 12 mg or less/wee	k of betamethasone or equivalent		
Crowther 2006	32/489	37/493	+	100.0	0.86 [0.53, 1.41]
Subtotal (95% CI)	489	493	•	100.0	0.86 [0.53, 1.41]
Total events: 32 (Repeat), 3	37 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=0.5	59 p=0.6				
15 In babies where planned	d repeat drug exposur	re was > 12 mg/week to 3	24 mg/week of betamethasone or equiv	alent	
Subtotal (95% CI)	0	0		0.0	Not estimable
otal events: 0 (Repeat), 0	(Single)				
est for heterogeneity: not	applicable				
est for overall effect: not a	applicable				
6 In babies where planned	d repeat drug exposur	re was > 24 mg/week of l	petamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
			0.1 0.2 0.5 2 5 10		

Favours repeat Favours single

Analysis 01.61. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 61 Length of postnatal hospitalisation (days)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 61 Length of postnatal hospitalisation (days)

Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
01 In all women Guinn 2002	249	2.60 (1.20)	236	2.60 (1.30)		100.0	0.00 [-0.22, 0.22]
Subtotal (95% CI) Test for heterogeneit Test for overall effect	,		236		•	100.0	0.00 [-0.22, 0.22]
02 In women where Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	blicable	preterm p	orelabour rupture	e of membranes at trial entry	0.0	Not estimable
03 In women given n							
Guinn 2002	249	2.60 (1.20)	236	2.60 (1.30)	Ī	100.0	0.00 [-0.22, 0.22]
Subtotal (95% CI) Test for heterogeneit Test for overall effect			236			100.0	0.00 [-0.22, 0.22]
04 In women given n Guinn 2002	epeat cor 249	ticosteroids at a r 2.60 (1.20)	minimum 236	interval of 7 days 2.60 (1.30)	or less	100.0	0.00 [-0.22, 0.22]
Subtotal (95% CI) Test for heterogeneit Test for overall effect			236		•	100.0	0.00 [-0.22, 0.22]
05 In women given in Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	blicable	minimum 0	interval between	8 and 14 days	0.0	Not estimable
06 In women given n Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	blicable	minimum 0	interval of > 14 c	days	0.0	Not estimable
07 In women given of Subtotal (95% CI) Test for heterogeneit Test for overall effect	0 y: not app	blicable	tal corticc 0	osteroids		0.0	Not estimable
08 In women given t Subtotal (95% CI)	wo repea	t courses of pren	atal cortic	osteroids		0.0	Not estimable
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		(Continued)

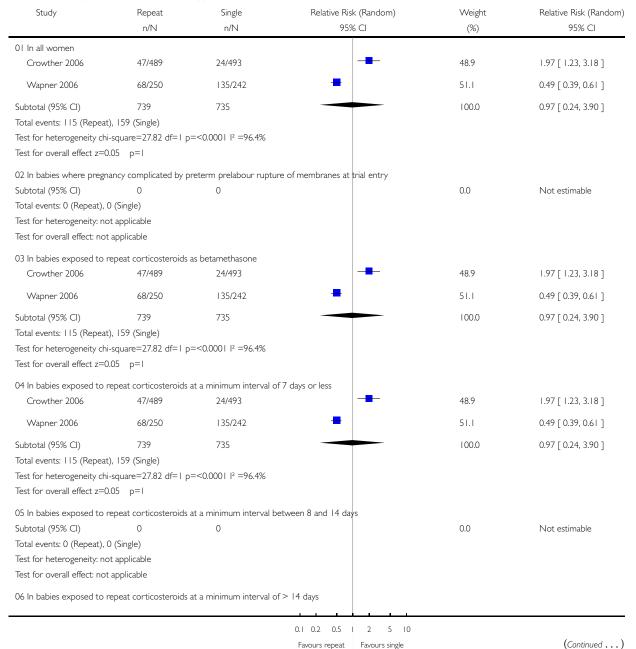
							(Continued)
Study	Ν	Repeat Mean(SD)	Ν	Single Mean(SD)	Weighted Mean Difference (Fixed) 95% CI	Weight (%)	Weighted Mean Difference (Fixed) 95% CI
Test for heterogeneit	y: not app	, ,				. ,	
Test for overall effect	: not appl	icable					
09 In women given th	nree repe	at courses of pre	natal cort	icosteroids			
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effect							
10 In women given for			s of props	atal carticactora	ide		
Subtotal (95% CI)	0	re repeat course	0	ital col ticostero	ids	0.0	Not estimable
Test for heterogeneit	y: not app	olicable					
Test for overall effect	: not appl	icable					
		dose per treatme		12 mg or less of	f betamethasone or equivalent		
Subtotal (95% CI)	0	licable	0			0.0	Not estimable
Test for heterogeneit Test for overall effect							
12 In women where	planned c	lose per treatme	nt course	> 12 mg to 24 i	mg or less of betamethasone or equivalen	t	
Guinn 2002	249	2.60 (1.20)	236	2.60 (1.30)	•	100.0	0.00 [-0.22, 0.22]
Subtotal (95% CI)	249		236		•	100.0	0.00 [-0.22, 0.22]
Test for heterogeneit							
Test for overall effect	z=0.00	p=I					
		dose per treatme		> 24 mg of beta	amethasone or equivalent	0.0	No. of the
Subtotal (95% CI) Test for heterogeneit	0 v: not add	olicable	0			0.0	Not estimable
Test for overall effect							
14 In women where	planned r	epeat drug expo	sure was	12 mg or less/we	eek of betamethasone or equivalent		
Subtotal (95% CI)	0		0			0.0	Not estimable
Test for heterogeneit Test for overall effect							
				. 12 / 1 .			
Guinn 2002	planned r 249	epeat drug expo 2.60 (1.20)	sure was 2 236	> 12 mg/week to 2.60 (1.30)	o 24 mg/week of betamethasone or equiv	alent 100.0	0.00 [-0.22, 0.22]
Subtotal (95% CI)	249	()	236	()	•	100.0	0.00 [-0.22, 0.22]
Test for heterogeneit		olicable	230			100.0	0.00 [-0.22, 0.22]
Test for overall effect	z=0.00	p=I					
16 In women where	planned r	epeat drug expo	sure was	> 24 mg/week o	f betamethasone or equivalent		
Subtotal (95% CI)	0	E 11	0			0.0	Not estimable
Test for heterogeneit Test for overall effect	, , ,						
					-10.0 -5.0 0 5.0 10.0		
					Favours repeat Favours single		

Analysis 01.62. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 62 Any maternal side-effects of therapy

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 62 Any maternal side-effects of therapy



Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Randor 95% Cl
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	/				
Test for overall effect: not a					
07 In babies exposed to or	ne repeat course of p	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
08 In babies exposed to tw	o repeat courses of	prenatal corticosteroids	3		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	pplicable				
09 In babies exposed to th	ree repeat courses o	of prenatal corticosteroid	ds		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
10 In babies exposed to for	•		costeroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	, ,				
Test for heterogeneity: not					
Test for overall effect: not a	pplicable				
		-	of betamethasone or equivalent	100.0	10751222103
Crowther 2006	47/489	24/493	-	100.0	1.97 [1.23, 3.18]
Subtotal (95% CI)	489	493	-	100.0	1.97 [1.23, 3.18]
Total events: 47 (Repeat), 2	/				
Test for heterogeneity: not					
Test for overall effect z=2.8					
12 In babies where planned Wapner 2006	d dose per treatmen 68/250	t course > 12 mg to 24 135/242	mg or less of betamethasone or equivale	ent 100.0	0.49 [0.39, 0.61]
	250	242	•	100.0	0.49 [0.39, 0.61]
Subtotal (95% CI) Fotal events: 68 (Repeat), I		ZTZ	-	100.0	0.47 [0.37, 0.61]
Test for heterogeneity: not	, ,				
Test for overall effect z=6.0					
	•				
l 3 In babies where planned Subtotal (95% CI)	d dose per treatmen 0	t course > 24 mg of bet 0	amethasone or equivalent	0.0	Not estimable
Fotal events: 0 (Repeat), 0		V		0.0	I AOF CZELLIADIG
Test for heterogeneity: not					
Test for overall effect: not a					
2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2. 2.	rr -==				
			0.1 0.2 0.5 1 2 5 10		
			Favours repeat Favours single		(Continued

Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% Cl	Weight (%)	Relative Risk (Random) 95% CI
14 In babies where plann	ed repeat drug exposi	ure was 12 mg or less/v	veek of betamethasone or equivalent		
Crowther 2006	47/489	24/493	-	100.0	1.97 [1.23, 3.18]
Subtotal (95% CI)	489	493	•	100.0	1.97 [1.23, 3.18]
Total events: 47 (Repeat),	24 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=2	.80 p=0.005				
15 In babies where plann	ed repeat drug exposi	ure was > 12 mg/week	to 24 mg/week of betamethasone or equi	valent	
Wapner 2006	68/250	135/242		100.0	0.49 [0.39, 0.61]
Subtotal (95% CI)	250	242	•	100.0	0.49 [0.39, 0.61]
Total events: 68 (Repeat),	135 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=6	.07 p<0.00001				
16 In babies where plann	ed repeat drug exposi	ure was > 24 mg/week	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				

0.1 0.2 0.5 I 2 5 I0

Favours repeat Favours single

Analysis 01.63. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 63 Maternal hyperglycaemia (variously defined by authors)

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course
Outcome: 63 Maternal hyperglycaemia (variously defined by authors)

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 In all women					
Wapner 2006	50/250	37/242	-	100.0	1.31 [0.89, 1.93]
Subtotal (95% CI)	250	242	•	100.0	1.31 [0.89, 1.93]
Total events: 50 (Repeat)	, 37 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.36 p=0.2				
02 In babies where pregn	nancy complicated by p	reterm prelabour rupture	of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
03 In babies exposed to 1	repeat corticosteroids	as betamethasone			
Wapner 2006	50/250	37/242		100.0	1.31 [0.89, 1.93]
Subtotal (95% CI)	250	242	•	100.0	1.31 [0.89, 1.93]
Total events: 50 (Repeat)	, 37 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=1	.36 p=0.2				
04 In babies exposed to 1	repeat corticosteroids	at a minimum interval of 7	days or less		
Wapner 2006	50/250	37/242	, -	100.0	1.31 [0.89, 1.93]
Subtotal (95% CI)	250	242	•	100.0	1.31 [0.89, 1.93]
Total events: 50 (Repeat)	, 37 (Single)				
Test for heterogeneity: no	, ,				
Test for overall effect z=1	.36 p=0.2				
05 In babies exposed to a	repeat corticosteroids	at a minimum interval bet	ween 8 and 14 days		
Subtotal (95% CI)	0	0	<i>,</i>	0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	, ,				
Test for overall effect: not					
06 In babies exposed to	repeat corticosteroids	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	, ,				
Test for overall effect: not					
			0.1 0.2 0.5 2 5 10		

Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease (Review) Copyright © 2007 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd

Favours repeat

Favours single

(Continued . . .)

					(Continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% Cl	Weight (%)	Relative Risk (Fixed) 95% CI
07 In babies exposed to d	one repeat course of n			()	
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (-			
Test for heterogeneity: no	. 0 /				
Test for overall effect: not					
08 In babies exposed to t	•	•		0.0	N
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0 Test for heterogeneity: no	, ,				
Test for overall effect: not					
lest for overall effect. Hot	аррисавіе				
09 In babies exposed to t	hree repeat courses o	f prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
10 In babies exposed to f	our or more repeat co	ourses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
I I In habies where plann	ed dose per treatment	course 12 mg or less of	betamethasone or equivalent		
Subtotal (95% CI)	0	0	betametrasone or equivalent	0.0	Not estimable
Total events: 0 (Repeat), (o .		0.0	1 Vot estimable
Test for heterogeneity: no					
Test for overall effect: not					
		10			
			ng or less of betamethasone or equivaler		1211000 1021
Wapner 2006	50/250	37/242	_	100.0	1.31 [0.89, 1.93]
Subtotal (95% CI)	250	242	•	100.0	1.31 [0.89, 1.93]
Total events: 50 (Repeat),	37 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.36 p=0.2				
13 In babies where plann	ed dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0	·	0.0	Not estimable
Total events: 0 (Repeat), () (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
14 In habies where plann	ed reneat drug evnosi	ire was 12 mg or less/we	ek of betamethasone or equivalent		
Subtotal (95% CI)	o o repeat drug expost	0 0	ch of octamical asome of equivalent	0.0	Not estimable
Total events: 0 (Repeat), (· ·		0.0	i vot estillable
Test for heterogeneity: no	/				
Test for overall effect: not					
	The same of				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		(Continued
					(

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
15 In babies where plann	ned repeat drug exposi	ire was > 12 mg/week t	o 24 mg/week of betamethasone or equ	iivalent	
Wapner 2006	50/250	37/242		100.0	1.31 [0.89, 1.93]
Subtotal (95% CI)	250	242	•	100.0	1.31 [0.89, 1.93]
Total events: 50 (Repeat)	, 37 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=	1.36 p=0.2				
16 In babies where plann	ned repeat drug exposu	ıre was > 24 mg/week o	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: no	t applicable				
			0.1 0.2 0.5 2 5 10		
			Favours repeat Favours single		

Analysis 01.64. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 64 Insomnia

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 64 Insomnia

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	N n/N	95% CI	(%)	95% CI
01 In all women					
Crowther 2006	3/489	0/493	-	8.9	7.06 [0.37, 136.26]
Wapner 2006	11/250	5/242	-	91.1	2.13 [0.75, 6.04]
Subtotal (95% CI)	739	735	•	100.0	2.57 [0.98, 6.77]
Total events: 14 (Repeat),	5 (Single)				
Test for heterogeneity chi	-square=0.57 df=1 p=	0.45 I ² =0.0%			
Test for overall effect z=1	.91 p=0.06				
02 In babies where pregn	ancy complicated by pi	reterm prelabour ruptu	re of membranes at trial entry		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
03 In babies exposed to r	repeat corticosteroids a	as betamethasone			
Crowther 2006	3/489	0/493	-	8.9	7.06 [0.37, 136.26]
Wapner 2006	11/250	5/242	-	91.1	2.13 [0.75, 6.04]
			0.001 0.01 0.1 10 100 1000		
					(Continued)
			Favours repeat Favours single		(Continued)

					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
Subtotal (95% CI)	739	735	•	100.0	2.57 [0.98, 6.77]
Total events: 14 (Repeat),	5 (Single)				
Test for heterogeneity chi-	-square=0.57 df=1 p=	0.45 l ² =0.0%			
Test for overall effect $z=1$.	.91 p=0.06				
04 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	7 days or less		
Crowther 2006	3/489	0/493	,	8.9	7.06 [0.37, 136.26]
Wapner 2006	11/250	5/242	-	91.1	2.13 [0.75, 6.04]
Subtotal (95% CI)	739	735	•	100.0	2.57 [0.98, 6.77]
Total events: 14 (Repeat),	5 (Single)				
Test for heterogeneity chi-	,	0.45 l ² =0.0%			
Test for overall effect z=1.	.91 p=0.06				
05 In babies exposed to re	epeat corticosteroids a	at a minimum interval be	tween 8 and 14 days		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not					
06 In babies exposed to re	epeat corticosteroids a	at a minimum interval of	> 14 days		
Subtotal (95% CI)	0	0	,	0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: not	. 0 /				
Test for overall effect: not					
07 In babies exposed to o	one repeat course of p	renatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
08 In babies exposed to to	wo repeat courses of p	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
09 In babies exposed to th	hree repeat courses of	prenatal corticosteroids	;		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
10 In babies exposed to fo	our or more repeat co	urses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0) (Single)				
Test for heterogeneity: not	t applicable				
Test for overall effect: not	applicable				
			0.001 0.01 0.1 10 100 1000		(6)
			Favours repeat Favours single		(Continued)

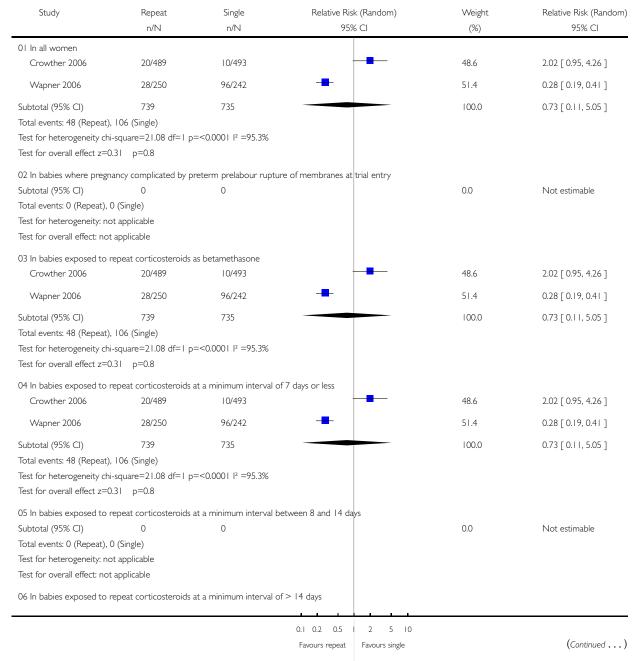
					(Continued)
Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
I I In babies where planne	ed dose per treatment	course 12 mg or less of	of betamethasone or equivalent		
Crowther 2006	3/489	0/493	 	100.0	7.06 [0.37, 136.26]
Subtotal (95% CI)	489	493		100.0	7.06 [0.37, 136.26]
Total events: 3 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=1.	29 p=0.2				
12 In babies where planne	ed dose per treatment	course > 12 mg to 24	mg or less of betamethasone or equivale	ent	
Wapner 2006	11/250	5/242	=	100.0	2.13 [0.75, 6.04]
Subtotal (95% CI)	250	242	•	100.0	2.13 [0.75, 6.04]
Total events: 11 (Repeat),	5 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.	42 p=0.2				
13 In babies where planne	ed dose per treatment	course > 24 mg of bet	tamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/w	reek of betamethasone or equivalent		
Crowther 2006	3/489	0/493	 	100.0	7.06 [0.37, 136.26]
Subtotal (95% CI)	489	493		100.0	7.06 [0.37, 136.26]
Total events: 3 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=1.	29 p=0.2				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week	to 24 mg/week of betamethasone or equ	uivalent	
Wapner 2006	11/250	5/242		100.0	2.13 [0.75, 6.04]
Subtotal (95% CI)	250	242	•	100.0	2.13 [0.75, 6.04]
Total events: 11 (Repeat),	5 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect $z=1$.	42 p=0.2				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				
			0.001 0.01 0.1 1 10 100 1000		
			Favours repeat Favours single		

Analysis 01.65. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 65 Pain at injection site

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 65 Pain at injection site



Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% Cl	Weight (%)	Relative Risk (Random 95% CI
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	/				
Test for overall effect: not a					
07 In babies exposed to or	ne repeat course of p	orenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
08 In babies exposed to tw	vo repeat courses of	prenatal corticosteroid	S		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
09 In babies exposed to th	ree repeat courses o	of prenatal corticosteroi	ds		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
10 In babies exposed to fo	ur or more repeat co	ourses of prenatal corti	costeroids		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	/				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
I I In babies where planned	d dose per treatmen	t course 12 mg or less	of betamethasone or equivalent		
Crowther 2006	20/489	10/493		100.0	2.02 [0.95, 4.26]
Subtotal (95% CI)	489	493	-	100.0	2.02 [0.95, 4.26]
Total events: 20 (Repeat),	10 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect $z=1.8$	34 p=0.07				
12 In babies where planned	d dose per treatmen	t course > 12 mg to 24	mg or less of betamethasone or equivale	ent	
Wapner 2006	28/250	96/242		100.0	0.28 [0.19, 0.41]
Subtotal (95% CI)	250	242	•	100.0	0.28 [0.19, 0.41]
Total events: 28 (Repeat), 9	96 (Single)				
Test for heterogeneity: not	applicable				
Test for overall effect z=6.4	19 p<0.00001				
13 In babies where planner	d dose per treatmen	t course > 24 mg of be	tamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: not	applicable				
Test for overall effect: not a	applicable				
			0.1 0.2 0.5 2 5 10		15
			Favours repeat Favours single		(Continued

Study	Repeat n/N	Single n/N	Relative Risk (Random) 95% CI	Weight (%)	Relative Risk (Random) 95% CI
14 In babies where planne	ed repeat drug exposu	re was 12 mg or less/v	veek of betamethasone or equivalent		
Crowther 2006	20/489	10/493	-	100.0	2.02 [0.95, 4.26]
Subtotal (95% CI)	489	493	-	100.0	2.02 [0.95, 4.26]
Total events: 20 (Repeat),	10 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=I	.84 p=0.07				
15 In babies where planne	ed repeat drug exposu	re was > 12 mg/week	to 24 mg/week of betamethasone or equ	ivalent	
Wapner 2006	28/250	96/242		100.0	0.28 [0.19, 0.41]
Subtotal (95% CI)	250	242	•	100.0	0.28 [0.19, 0.41]
Total events: 28 (Repeat),	96 (Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect z=6	.49 p<0.00001				
16 In babies where planne	ed repeat drug exposu	re was > 24 mg/week	of betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	(Single)				
Test for heterogeneity: no	t applicable				
Test for overall effect: not	applicable				

0.1 0.2 0.5 2 5 10 Favours repeat Favours single

Analysis 01.66. Comparison 01 Repeat doses of corticosteroids versus single course, Outcome 66 Bruising at injection site

Review: Repeat doses of prenatal corticosteroids for women at risk of preterm birth for preventing neonatal respiratory disease

Comparison: 01 Repeat doses of corticosteroids versus single course

Outcome: 66 Bruising at injection site

Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% Cl	Weight (%)	Relative Risk (Fixed
01 In all women					
Wapner 2006	13/250	33/242	-	100.0	0.38 [0.21, 0.71]
Subtotal (95% CI) Total events: 13 (Repeat), Test for heterogeneity: no Test for overall effect z=3.	t applicable	242	-	100.0	0.38 [0.21, 0.71]
	·	estama analaba un mustuma	of accordance at this least w		
Subtotal (95% CI) Total events: 0 (Repeat), C Test for heterogeneity: no Test for overall effect: not	0) (Single) t applicable	o O	of membranes at trial entry	0.0	Not estimable
03 In babies exposed to n	epeat corticosteroids	as betamethasone			
Wapner 2006	13/250	33/242	-	100.0	0.38 [0.21, 0.71]
Subtotal (95% CI) Total events: 13 (Repeat), Test for heterogeneity: no Test for overall effect z=3:	t applicable	242	-	100.0	0.38 [0.21, 0.71]
04 In babies exposed to n	epeat corticosteroids	at a minimum interval of 7	7 days or less		
Wapner 2006	13/250	33/242	, <u> </u>	100.0	0.38 [0.21, 0.71]
Subtotal (95% CI) Total events: 13 (Repeat), Test for heterogeneity: no Test for overall effect z=3.	t applicable	242		100.0	0.38 [0.21, 0.71]
05 In babies exposed to n	epeat corticosteroids	at a minimum interval bet	ween 8 and 14 days		
Subtotal (95% CI) Total events: 0 (Repeat), C Test for heterogeneity: no Test for overall effect: not	0) (Single) t applicable	0		0.0	Not estimable
06 In babies exposed to n	epeat corticosteroids	at a minimum interval of	> 14 days		
Subtotal (95% CI) Total events: 0 (Repeat), C Test for heterogeneity: no Test for overall effect: not	t applicable	0		0.0	Not estimable

0.1 0.2 0.5 | 2 5 10

Favours repeat Favours single

(Continued \dots)

					(continued)
Study	Repeat n/N	Single n/N	Relative Risk (Fixed) 95% CI	Weight	Relative Risk (Fixed) 95% CI
		•	93% CI	(%)	95% CI
07 In babies exposed to o				0.0	No. of the
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), (Test for heterogeneity: no					
Test for overall effect: not					
lest for overall effect; not	. аррисаріе				
08 In babies exposed to t	wo repeat courses of	prenatal corticosteroids			
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	/				
Test for heterogeneity: no					
Test for overall effect: not	applicable				
09 In babies exposed to t	hree repeat courses o	f prenatal corticosteroids	;		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat), 0	O (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
10 In babies exposed to f	our or more repeat or	ourses of prenatal cortico	steroids		
Subtotal (95% CI)	0	0	5.61.61.63	0.0	Not estimable
Total events: 0 (Repeat), (-			
Test for heterogeneity: no					
Test for overall effect: not					
		12 1 6			
•	ed dose per treatment 0	course 12 mg or less of	betamethasone or equivalent	0.0	Not estimable
Subtotal (95% CI) Total events: 0 (Repeat), (U		0.0	NOL ESTIMADIE
Test for heterogeneity: no					
Test for overall effect: not					
	• •				
			ng or less of betamethasone or equivalen		0005001.0713
Wapner 2006	13/250	33/242		100.0	0.38 [0.21, 0.71]
Subtotal (95% CI)	250	242	-	100.0	0.38 [0.21, 0.71]
Total events: 13 (Repeat),	33 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=3	.06 p=0.002				
13 In babies where planne	ed dose per treatment	course > 24 mg of beta	methasone or equivalent		
Subtotal (95% CI)	0	0	·	0.0	Not estimable
Total events: 0 (Repeat), (
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	applicable				
14 la babisa ubana alama	ad was act dw. z a. za a.		al, af hatamathasan an an involent		
Subtotal (95% CI)	ea repeat arug exposi 0	ire was 12 mg or less/we	ek of betamethasone or equivalent	0.0	Not estimable
Total events: 0 (Repeat), (O		0.0	Not estimable
Test for heterogeneity: no	(0 /				
Test for overall effect: not					
			0,1 0,2 0,5 1 2 5 10		
					(Continued)
			1.200.3 35.180		(======================================
			0.1 0.2 0.5 2 5 10 Favours repeat Favours single		

Study	Repeat	Single	Relative Risk (Fixed)	Weight	Relative Risk (Fixed)
	n/N	n/N	95% CI	(%)	95% CI
15 In babies where plann	ed repeat drug exposu	re was > 12 mg/week to	24 mg/week of betamethasone or equiv	valent	
Wapner 2006	13/250	33/242		100.0	0.38 [0.21, 0.71]
Subtotal (95% CI)	250	242	•	100.0	0.38 [0.21, 0.71]
Total events: 13 (Repeat)	, 33 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect z=3	3.06 p=0.002				
16 In babies where plann	ed repeat drug exposu	re was > 24 mg/week o	f betamethasone or equivalent		
Subtotal (95% CI)	0	0		0.0	Not estimable
Total events: 0 (Repeat),	0 (Single)				
Test for heterogeneity: no	ot applicable				
Test for overall effect: not	t applicable				
			_ , , , , , , ,		