Maternal intramuscular dexamethasone versus betamethasone before preterm birth (ASTEROID): a multicentre, double-blind, randomised controlled trial

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Summary

Background Antenatal corticosteroids given to women before preterm birth improve infant survival and health. However, whether dexamethasone or betamethasone have better maternal, neonatal, and childhood health outcomes remains unclear. We therefore aimed to assess whether administration of antenatal dexamethasone to women at risk of preterm birth reduced the risk of death or neurosensory disability in their children at age 2 years compared with betamethasone. We also aimed to assess whether dexamethasone reduced neonatal morbidity, had benefits for the mother, or affected childhood body size, blood pressure, behaviour, or general health compared with betamethasone.

Methods In this multicentre, double-blind, randomised controlled trial, we recruited pregnant women from 14 maternity hospitals in Australia and New Zealand that could provide care to preterm babies. Women were eligible for study inclusion if they were at risk of preterm birth before 34 weeks of gestation, had a singleton or twin pregnancy, and had no contraindications to antenatal corticosteroids. We randomly assigned women (1:1) to receive two intramuscular injections of either 12 mg dexamethasone (dexamethasone sodium phosphate) or 11·4 mg betamethasone (Celestone Chronodose), 24 h apart. The randomisation schedule used balanced, variable blocks that were stratified by hospital, gestational age, and number of fetuses (singleton or twins). We masked all participants, staff, and assessors to treatment groups. Analyses were by intention to treat. The primary outcome was death or neurosensory disability at age 2 years (corrected for prematurity). This study is registered with ANZCTR, ACTRN12608000631303.

Findings Between Jan 28, 2009, and Feb 1, 2013, we randomly assigned 1346 (78%) women who were pregnant with 1509 fetuses to groups: 679 (50%) women were assigned to receive dexamethasone and 667 (50%) women were assigned to receive betamethasone. 27 (4%) fetuses, infants, or children in the dexamethasone group and 28 (4%) fetuses, infants, or children in the betamethasone group died before age 2 years. The primary outcome of death or neurosensory disability at age 2 years was determined for 603 (79%) of 763 fetuses whose mothers received dexamethasone and 591 (79%) of 746 fetuses whose mothers received betamethasone. We found a similar incidence of death or neurosensory disability in the dexamethasone (198 [33%] of 603 infants) and betamethasone groups (192 [32%] of 591 infants; adjusted relative risk [adjRR] 0·97, 95% CI 0·83 to 1·13; p=0·66). 18 (3%) of 679 women in the dexamethasone group and 28 of 667 (4%) women in the betamethasone group reported side-effects. Discomfort at the injection site, the most frequent side-effect, was less likely in the dexamethasone group than in the betamethasone group (six [1%] women *vs* 17 [3%] women; p=0·02).

Interpretation The incidence of survival without neurosensory disability at age 2 years did not differ between dexamethasone and betamethasone treatment. Our findings indicate that either antenatal corticosteroid can be given to women before preterm birth to improve infant and child health.

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Introduction

Administration of the antenatal corticosteroids dexamethasone or betamethasone to women who are at risk of preterm birth increases the chance of their infant surviving, is associated with reduced neonatal morbidity,[1] and is recommended practice worldwide.[2–5] The choice between dexamethasone and betamethasone is affected by several factors, including opinion leaders, local availability, and cost.[6–8] A full course of dexamethasone costs approximately US$1 versus $35 for betamethasone.[7] There is a paucity of data about which corticosteroid results in better health outcomes for the mother and her infant. Retrospective studies provide conflicting results: some studies have found no differences in the risk of intraventricular haemorrhage,[9,10] periventricular leukomalacia,[10] or mortality,[9,10] but other studies report that dexamethasone is associated with an increase in periventricular leukomalacia[9] and neurosensory impairment.[11]

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Research in context

Evidence before this study

Our previous Cochrane review, which assessed the effects of different corticosteroids for women at risk of preterm birth, included ten trials (comprising 1159 women and 1213 infants, and considered at moderate risk of bias) that compared dexamethasone and betamethasone use. We searched PubMed for studies published on or before March 31, 2019, with the search terms "dexamethasone OR betamethasone OR glucocorticoids" and "pregnancy OR premature birth", with the randomised controlled trial filter applied and no language restrictions, and we found no additional trials. Although dexamethasone was associated with a lower risk of intraventricular haemorrhage than betamethasone in four trials (including 549 infants), we found no reported differences in perinatal mortality, risk of neonatal respiratory disease, or other neonatal morbidity, and long-term child outcome data were scarce. No data on maternal health outcomes were reported from any of the included trials. Indirect estimates on acceleration of fetal lung maturation from our Cochrane review suggested a higher risk of neonatal respiratory disease and maternal chorioamnionitis with dexamethasone than with betamethasone. Worldwide, substantial numbers of women at risk of preterm birth are eligible for antenatal corticosteroid treatment, so understanding the optimal drug to use is important. The summary of the evidence clearly highlighted a need for additional trials to compare dexamethasone and betamethasone use that included assessment of infant morbidity and mortality, long-term childhood health, and maternal outcomes.

Added value of this study

To our knowledge, this is the first large study to report on the comparative effects of dexamethasone and betamethasone on infant health outcomes beyond the neonatal period and into early childhood. We found no clear differences in effects of these two corticosteroids on the incidence of survival free of neurosensory disability in children at age 2 years after in-utero exposure. We have provided reliable, comparative data on the important maternal health outcomes of infectious morbidity and mode of birth that have not previously been reported. We also found that the risk of intraventricular haemorrhage with either corticosteroid is similar, which was an uncertain result in earlier, conflicting reports.

Implications of all the available evidence

There are known benefits of antenatal corticosteroid treatment being given to women at less than 35 weeks of gestation if they are at risk of preterm birth. Findings from our study provide reassurance that both dexamethasone and betamethasone have similar effects on neonatal health, including respiratory and neurological outcomes and neurodevelopmental outcomes in early childhood. We found that dexamethasone might have benefits for mothers, conferring a reduced need for caesarean birth, and for infants, conferring a lower risk of early childhood hypertension. Further research is needed to assess the effect of the different corticosteroids on mode of birth and to assess the effects of early childhood hypertension in later childhood. Our findings provide new information for pregnant women at risk of preterm birth, their families, and health practitioners to consider when making decisions as to which corticosteroid to use. Guideline developers, policy makers, and health-care funders can incorporate this new knowledge with information on availability and costs for local policy recommendations.

A systematic review[12] of ten randomised trials (which included 1159 women and 1213 infants) that compared the use of antenatal dexamethasone with betamethasone before preterm birth found no differences in the risk of neonatal mortality or respiratory distress syndrome, but a decreased risk of intraventricular haemorrhage with dexamethasone. None of the trials[1,13] reported on relevant maternal outcomes such as infectious morbidity or mode of birth (ie, vaginal or caesarean).

Although a reduction in intraventricular haemorrhage is an important outcome, it is arguably more important to attain improved long-term survival free from disability.[14] Only one randomised trial[15] has directly compared the long-term effects of dexamethasone with betamethasone: this trial followed up on children whose mothers were administered these corticosteroids, and this study reported on only 12 children up to age 18 months. Because of the inconsistent data on infant health and inadequate comparative information on child health outcomes following antenatal corticosteroid use, clinical practice guidelines have been unable to recommend one corticosteroid in preference to the other.[2–5] Investigators of cohort studies[10,11] and randomised controlled trials[16] and the authors of the Cochrane review[12] have requested further randomised trials that include outcomes relating to survival and health of infants into childhood, and that assess all relevant maternal outcomes.

The ASTEROID trial aimed to assess whether administration of antenatal dexamethasone to women at risk of preterm birth before 34 weeks of gestation reduced the risk of death or neurosensory disability in their children at age 2 years (corrected for prematurity)—the primary outcome—and whether it reduced neonatal morbidity, had benefits for the mother, or affected childhood body size, blood pressure, behaviour, or general health, compared with betamethasone.

Methods

Study design and participants

In this multicentre, double-blind, randomised controlled trial, we recruited pregnant women from 14 maternity hospitals in Australia and New Zealand that could provide care to preterm babies. Women were eligible for study inclusion if they were at risk of preterm birth before

34 weeks of gestation, had a singleton or twin pregnancy, had no contraindications to antenatal corticosteroids, and gave written informed consent. Women were ineligible if they had chorioamnionitis that necessitated urgent delivery, they had already received antenatal corticosteroids, they were in the second stage of labour, or in women with known fetal lung maturation.

The study protocol was approved by the institutional review boards at each of the participating hospitals and by the Human Research Ethics Committee at the Women's and Children's Hospital, Adelaide (REC2074/7/14). The study protocol has previously been published.[17]

Randomisation and masking

Staff who enrolled eligible women at participating hospitals randomly assigned women (1:1) to receive either dexamethasone or betamethasone by contacting a central randomisation service, to determine the treatment pack to be given. An investigator (who was not involved with clinical care and is not a co-author) used computer-generated random numbers and balanced variable blocks to produce a randomisation schedule, which was stratified by hospital, gestational age (<28 weeks or ≥28 weeks of gestation), and number of fetuses (ie, a singleton or twin pregnancy). At randomisation, the central randomisation service allocated a study number to each woman, which corresponded to a treatment pack. Treatment packs all looked identical and contained two opaque study-labelled syringes, which contained either 12 mg dexamethasone (as dexamethasone sodium phosphate, a non-sulphite containing preparation) or 11·4 mg betamethasone (Celestone Chronodose; Schering-Plough, Sydney, Australia) to be administered to participating women. We masked participants, clinical staff, study investigators, and those assessing outcomes to treatment allocations.

Procedures

Clinical staff at participating hospitals gave participating women two intramuscular injections of the study medication, 24 h apart. At weekly intervals, we assessed each woman and, if a woman had not given birth and remained at continued risk of preterm birth that warranted the use of repeat antenatal corticosteroids,[5,18] the randomisation service allocated a repeat treatment pack that could be given (to ensure the same treatment group was maintained). Repeat treatment packs contained a single syringe of the same study drug as previously administered. Women and their infants were cared for according to standard practice at each hospital. Pregnancy, birth, postnatal, and infant data were obtained from medical records by research staff.

Surviving children were assessed by a paediatrician and a psychometrist once, at age 2 years, with their age corrected for prematurity. The paediatric assessment included measurements of height, weight, head circumference, and blood pressure (with a standardised method and appropriate cuff size), and a neurological examination, which included assessment of vision and hearing. Measurements of body size were converted to Z scores specific for age and sex.[19] Blood pressure was converted to Z scores for age, height, and sex,[20] with hypertension defined as a systolic or diastolic blood pressure of more than the 95th percentile.[20] Children were considered blind if their visual acuity was less than 6/60 in both eyes. Children were considered deaf if their hearing loss was sufficient to require a hearing aid or hearing aids or worse (requiring a Cochlear implant). A diagnosis of cerebral palsy was made on the basis of a loss of motor function and abnormalities of muscle tone and power.[21] The severity of gross motor dysfunction was classified with the Gross Motor Function Classification System.[22]

The psychological assessment by the psychometrist included the cognitive, motor, and language scales of the Bayley Scales of Infant Development-III[23] (for all scales, the reference mean was 100, with a SD of 15). Children with severe developmental delay who were unable to complete the assessment were given a standardised score of 40 (ie, 4 SD below the mean). Children were considered to have a neurosensory disability if they had cerebral palsy, were blind or deaf, or showed developmental delay (defined as a score in any of the cognitive, language, and motor domains of the Bayley scales of more than 1 SD below the mean). The neurosensory disabilities imposed by the neurosensory impairments were classified as severe, moderate, or mild.[21]

To provide additional follow-up information, caregivers completed questionnaires about their child's health, including about asthma or wheezing, use of health services since birth, the child's development including in the Ages and Stages questionnaire[24] (which screens five domains: communication, gross motor, fine motor, problem solving, and personal and social skills) and the Child Behaviour Checklist[25] (which screens for behavioural and emotional problems). A minimum data form was completed by some caregivers who were not able to attend the paediatric or psychological assessments or complete the full questionnaires.

If a child was not assessed by a psychometrist, they were considered to have a cognitive delay if a difficulty with communication was reported in the questionnaire completed by the child's caregiver, if they were reported by parents to have known cognitive or language developmental delay, or if their standardised score for communication on the Ages and Stages questionnaire was more than 2 SD below the mean. If a child was not assessed by a paediatrician, they were considered to have cerebral palsy if parents reported that they had cerebral palsy, if they were unable to walk without assistance, unable to sit, or unable to control their head without support. They were considered blind or deaf if these conditions were reported by their parent or caregiver.

Outcomes

The primary outcome was a composite outcome of death or any neurosensory disability at age 2 years (corrected for prematurity), which was defined as stillbirth, death of a liveborn infant either before or after hospital discharge, or any neurosensory disability (cerebral palsy, blindness, deafness, or developmental [cognitive, language, or motor] delay, as determined in assessments by the paediatrician and psychometrist).

Secondary outcomes in the infants before hospital discharge were intraventricular haemorrhage, severe (ie, grade 3 or 4) intraventricular haemorrhage, periventricular leukomalacia, retinopathy of prematurity that required treatment, patent ductus arteriosus that required treatment, respiratory distress syndrome, severity of neonatal lung disease, chronic lung disease (defined as a need for oxygen supplementation at 36 weeks post-menstrual age or 28 days after birth, if born after 32 weeks of gestation), use of mechanical ventilation, confirmed infection within the first 48 h of life, infection after the first 48 h of life, necrotising enterocolitis, and body size at birth (weight, length, and head circumference) and at discharge from the hospital. These outcomes were assessed in liveborn infants up to the time of leaving the hospital after birth.

Secondary outcomes for the children at age 2 years (corrected for prematurity) were death or major neurosensory disability (defined as severe or moderate disability, including developmental delay with a standardised score more than 2 SD below the mean, cerebral palsy in a child who was not ambulant by age 2 years, blindness, or deafness), individual components and severity of the primary outcome, body size, general health (including use of health services since leaving the hospital after birth), childhood respiratory morbidity, blood pressure Z scores and proportion of results in hypertensive ranges, and child behaviour. We assessed these outcomes in all children whose mothers were randomly assigned to groups.

Secondary outcomes for the mothers were perinatal infectious morbidity (defined as clinical chorioamnionitis that required intrapartum antibiotics and use of postpartum antibiotics, or both). Other secondary outcomes for the mothers were induction of labour, mode of birth (ie, vaginal or caesarean), postpartum haemorrhage, and duration of postpartum hospital stay; these outcomes were prespecified in the statistical analysis plan before data analysis. We assessed these outcomes in all women randomly assigned to groups.

We also did a pre-defined sensitivity analysis, in which we used follow-up information from all sources (paediatrician, psychometrist, caregiver questionnaires and minimum data) to further examine the primary outcome. Finally, we did a post-hoc analysis to examine the rate of fetal distress on cardiotocography and the indications for caesarean birth by treatment group.

Statistical analysis

We estimated that the incidence of our primary outcome of death or neurosensory disability at age 2 years (corrected for prematurity) in children who were exposed to betamethasone antenatally would be be 27·0%.[1,21] A trial of 1499 children that allowed for 5% loss to follow-up and that had a design effect of 1·2, to allow for the clustering of babies within mothers, would have 80% power to detect a significant difference at an α level of 0·05 (two-tailed) of either a decrease in the combined outcome of death or neurosensory disability from 27·0% to 20·1% or an increase from 27·0% to 34·5% with dexamethasone compared with betamethasone.

We followed a prespecified statistical analysis plan with an intention-to-treat approach. We did unadjusted analyses first and then, as prespecified, we adjusted for the stratification factors (hospital, gestational age at entry, and number of fetuses—ie, the fixed effects). We also adjusted the analyses for 2-year outcomes, as prespecified, for language spoken at home, the mother's education, and the sex of the child. For infant outcomes, we used generalised estimating equations with exchangeable correlations to account for clustering due to twins (ie, the random effects).

Binary outcomes were analysed with log-binomial regression, in which treatment effects were expressed as relative risks, or with Fisher's exact test for rare outcomes. The effect of treatment group on continuous outcomes was expressed as differences in means by use of linear regression. Treatment effects of count outcomes were expressed as ratios of means by use of log-Poisson regression, or negative binomial regression where we found overdispersion. Ordinal outcomes were analysed with proportional odds models, in which treatment effects were expressed as odds ratios of higher severity, or with separate logistic regression for binary outcomes that were defined by different cut points, in which treatment effects were expressed as odds ratios when the proportional odds assumption was not met. We made no adjustment for multiple comparisons. We did a prespecified sensitivity analysis to examine the primary outcome, which we assessed with follow-up information from all sources (paediatrician, psychometrist, caregiver questionnaires, and minimum data). A two-sided p value of less than 0·05 was considered to indicate significance. We used SAS version 9.4 for our statistical analyses. The study was overseen by a data safety monitoring committee. No interim analyses were planned or undertaken. This study is registered with ANZCTR, ACTRN12608000631303.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Jan 28, 2009, and Feb 1, 2013, we screened 3549 women for study inclusion, of whom 1823 (51%) women were ineligible (figure). We invited 1726 (49%) eligible women to participate, of whom 380 (22%) did not provide consent to do so. We randomly assigned 1346 (78%) women pregnant with 1509 fetuses to groups: 679 (50%) women (who were pregnant with 763 fetuses) were assigned to receive dexamethasone and 667 (50%) women (who were pregnant with 746 fetuses) were assigned to receive betamethasone. 675 (99%) women in the dexamethasone group (pregnant with 758 fetuses) and 657 (99%) women in the betamethasone group (pregnant with 736 fetuses) received their allocated treatment. The main reason that women did not complete the initial treatment course (ie, did not receive a second dose) was that they gave birth: 49 women (7%) in the dexamethasone and 45 (7%) in the betamethasone group before receiving a second dose. 27 (4%) fetuses, infants, or children in the dexamethasone group died before 2 years corrected age (comprising 11 stillbirths, 14 deaths of liveborn infants before hospital discharge, and two deaths of infants after hospital discharge) and 28 (4%) fetuses, infants, or children in the betamethasone group died before 2 years corrected age (comprising nine stillbirths, 16 deaths of liveborn infants before hospital discharge, and three deaths after hospital discharge). 736 (96%) children whose mothers had received dexamethasone and 718 (96%) children whose mothers had received betamethasone were eligible for follow-up at age 2 years. 598 (81%) of eligible children in the dexamethasone group and 584 (81%) of eligible children in in the betamethasone group attended paediatric and psychometric assessments. 603 (79%) of 763 fetuses whose mothers received dexamethasone and 591 (79%) of 746 fetuses whose mothers received betamethasone provided data for the primary outcome of death or neurosensory disability at age 2 years.

The two treatment groups were similar in baseline characteristics at trial entry (table 1). The mean gestational age at entry was 29 weeks and 5 days (SD 3+1) in the dexamethasone group and 29 weeks and 6 days (3+2) in the betamethasone group. We found no differences in baseline characteristics between the participants assessed at follow-up and the total study population (appendix).

We found a similar incidence of the primary outcome—death or any neurosensory disability at age 2 years (corrected for prematurity), as assessed by a paediatrician and psychometrist—in the dexamethasone (198 [33%] of 603 infants) and betamethasone groups (192 [32%] of 591 infants; adjusted relative risk [RR] 0·97, 95% CI 0·83 to 1·13; p=0·66; table 2).

None of the birth-related secondary outcomes (ie, before hospital discharge) differed between groups, including the number of infants with respiratory distress syndrome (183 [24%] of 752 infants in the dexamethasone group *vs* 174 [24%] of 737 infants in the betamethasone group; adjusted RR 1·03, 95% CI, 0·87 to 1·23; p=0·72), the severity of lung disease, or the number with an intraventricular haemorrhage (34 [5%] infants *vs* 32 [4%] infants; 1·09, 0·67 to 1·78; p=0·72) or a severe intraventricular haemorrhage (three [<1%] infants *vs* five [1%] infants; p=0·50; table 3). Gestational age at birth and infant weight, length, and head circumference

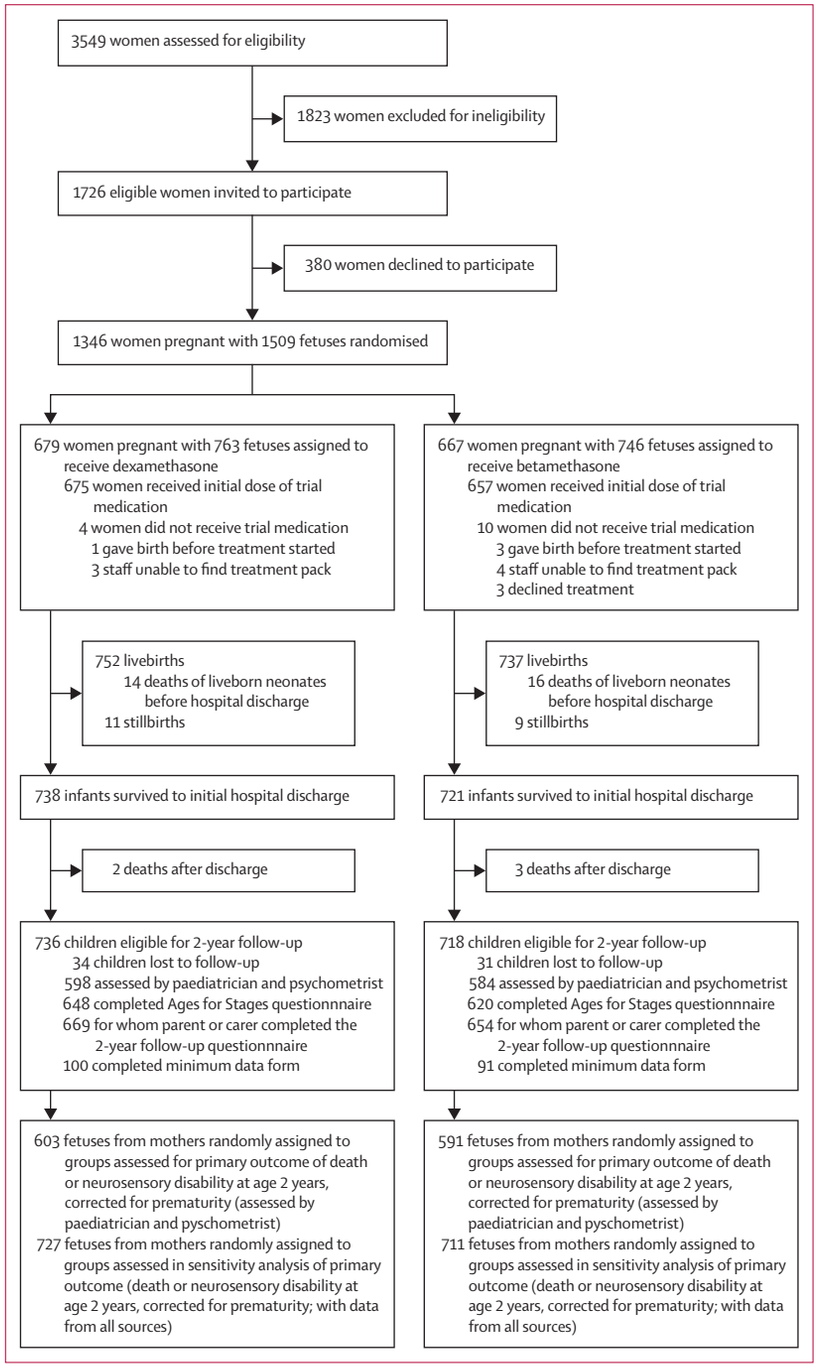

Figure: **Trial profile**

See **Online** for appendix

	Dexamethasone group (n=679)	Betamethasone group (n=667)
Maternal age, years	29·7 (6·1)	29·8 (6·3)
Parity		
Nulliparous	324 (48%)	300 (45%)
Multiparous	355 (52%)	367 (55%)
Ethnicity		
European	518 (76%)	506 (76%)
Asian	82 (12%)	93 (14%)
Aboriginal or Torres Strait Islanders	30 (4%)	19 (3%)
Polynesian	11 (2%)	10 (1%)
Maori	12 (2%)	7 (1%)
Other	26 (4%)	32 (5%)
Body mass index, kg/m²	24·4 (21·2–28·6)	24·7 (21·8–29·7)
Gestational age at entry, weeks and days	29+5 (3+1)	29+6 (3+2)
<28 weeks gestation	202 (30%)	200 (30%)
≥28 weeks gestation	477 (70%)	467 (70%)
Sex		
Female	376/763 (49%)	359/746 (48%)
Male	387/763 (51%)	387/746 (52%)
Twin pregnancy	84 (12%)	79 (12%)
Previous preterm birth (<37 weeks gestation)	121 (34%)	135 (37%)
Previous perinatal deaths (≥20 weeks gestation)	31 (9%)	37 (10%)
Main reasons for preterm birth		
Antepartum haemorrhage	157 (23%)	143 (21%)
Preterm prelabour rupture of membranes	137 (20%)	135 (20%)
Preterm labour	185 (27%)	184 (28%)
Cervical incompetence	46 (7%)	60 (9%)
Pre-eclampsia	71 (10%)	64 (10%)
Fetal compromise	60 (9%)	63 (9%)
Other	23 (3%)	18 (3%)

Data are n (%) or n/N (%), mean (SD), or median (IQR). Ethnicity was self-reported by the participant.

Table 1: **Baseline maternal and pregnancy characteristics**

did not differ between treatment groups at birth or at hospital discharge.

At 2 years corrected age, children in the dexamethasone group had lower systolic blood pressure Z scores (mean score 0·55 [SD 1·06] *vs* 0·64 [1·09]; adjusted mean difference –0·17, 95% CI –0·33 to –0·01; p=0·04) and fewer had blood pressure in the hypertensive range (115 [32%] of 356 with available data *vs* 144 [41%] of 347 with available data; adjusted RR 0·78, 95% CI 0·64 to 0·95; p=0·02) compared with those in the betamethasone group (table 2). None of the other secondary outcomes that we assessed in children at age 2 years (corrected for prematurity) differed between the treatment groups.

We found a similar incidence of maternal perinatal infectious morbidities between the treatment groups (in 125 [18%] of 679 women in the dexamethasone group *vs* 132 [20%] of 667 women in the betamethasone group; adjusted RR 0·95, 95% CI 0·77 to 1·18; p=0·65; table 4). Dexamethasone had no effect on the induction of labour, postpartum haemorrhage, need for transfusion, or length of maternal postnatal stay compared with betamethasone. However, 295 (43%) of 679 women in the dexamethasone group had a caesarean birth versus 346 (52%) of 667 women in the betamethasone group (0·84, 0·75 to 0·93; p=0·0013); the number needed to treat to benefit is 12 (95% CI 7 to 32).

18 (3%) of 679 women in the dexamethasone group and 28 of 667 (4%) women in the betamethasone group reported side-effects (table 5). Discomfort at the injection site, which was the most common side-effect, was reported less frequently in the dexamethasone group than in the betamethasone group (six [1%] women *vs* 17 [3%] women; p=0·02).

In a prespecified sensitivity analysis of the primary outcome that used follow-up information from all sources, we found that 208 (29%) of 727 infants in the dexamethasone group and 211 (30%) of 711 infants in the betamethasone group died or had a neurosensory disability at age 2 years (adjusted RR 0·94, 95% CI 0·81 to 1·10; p=0·46). In post-hoc analyses, the incidence of fetal distress (reported on cardiotocography) and the indications for the caesarean birth, including the proportion of caesarean sections done for fetal compromise, did not differ between treatment groups.

Discussion

In this multicentre, placebo-controlled randomised trial to compare dexamethasone with betamethasone given antenatally to women at risk of preterm birth, we found no significant difference in the primary outcome of death or neurosensory disability in their children at age 2 years (corrected for prematurity). Dexamethasone and betamethasone also had similar effects on infant health outcomes, including respiratory morbidity, intraventricular haemorrhage, and periventricular leukomalacia. Maternal infectious morbidity was also similar in both groups.

This trial is, to our knowledge, the largest randomised controlled comparison of the effectiveness of the two antenatal corticosteroids for accelerating fetal lung maturation that are recommended before preterm birth, and to provide data about the health of the women and their infants, including into early childhood.[12] Previous data regarding these outcomes are conflicted: some non-randomised studies suggested that dexamethasone was associated with a greater risk of periventricular leukomalacia[9] and neurosensory impairment[11] compared with betamethasone, whereas systematic reviews of relevant randomised trials showed a decreased risk of intraventricular haemorrhage[12] but also a possible greater risk of maternal chorioamnionitis.[1] Our multicentre trial recruited a similar number of women and their infants to the total number recruited in all the

trials included in our Cochrane review[12] of different corticosteroids for women at risk of preterm birth. Our results provide reassurance that none of these clinically important outcomes are significantly altered by the type of corticosteroid used. Our findings support the current guideline recommendations that either drug is appropriate for women at risk of preterm birth.[2–5]

However, we found unexpected and potentially clinically important differences in some secondary outcomes between the treatment groups. First, women receiving dexamethasone were less likely to have a caesarean birth than those receiving betamethasone, with a number needed to treat to benefit of 12. In post-hoc analyses, we found no differences between treatment groups in the indications for caesarean birth and no differences in fetal distress on cardiotocography, suggesting that known differential corticosteroid effects on fetal cardiovascular and behavioural status[12,26] do not fully explain our findings. Maternal outcomes, including mode of birth, have not been well reported in previous randomised trials,[1,12] so this finding should be examined in other settings. Our data suggest that

	Dexamethasone group	Betamethasone group	Unadjusted treatment effect (95% CI)	Unadjusted p value	Adjusted treatment effect (95% CI)	Adjusted p value
Primary outcome						
Death or any neurosensory disability	198/603 (33%)	192/591 (32%)	1·00 (0·85 to 1·19)	0·95	0·97 (0·83 to 1·13)	0·66
Secondary childhood outcomes						
Death or major neurosensory disability	93/593 (16%)	81/580 (14%)	1·11 (0·83 to 1·47)	0·48	1·13 (0·86 to 1·47)	0·38
Any death*	27/729 (4%)	28/715 (4%)	0·87 (0·50 to 1·49)	0·60	0·95 (0·56 to 1·60)	0·84
Stillbirth	11/763 (1%)	9/746 (1%)	1·01 (0·40 to 2·51)	0·99	NA	NA
Death of liveborn infant before hospital discharge*	14/752 (2%)	16/737 (2%)	0·81 (0·39 to 1·68)	0·57	0·87 (0·43 to 1·77)	0·70
Death after discharge	2/704 (<1%)	3/690 (<1%)	NA	0·68†	NA	NA
Any neurosensory disability	171/576 (30%)	164/563 (29%)	1·02 (0·84 to 1·23)	0·86	0·99 (0·84 to 1·17)	0·90
Blindness	0/614	1/613 (<1%)	NA	0·50†	NA	NA
Deafness‡	21/614 (3%)	18/613 (3%)	1·15 (0·61 to 2·17)	0·66	1·16 (0·62 to 2·16)	0·65
Cerebral palsy (definite or probable diagnosis by paediatric assessment)	15/612 (2%)	6/611 (1%)	2·47 (0·97 to 6·30)	0·06	NA	NA
Severity of cerebral palsy§						
Mild	7/612 (1%)	4/611 (1%)	2·47 (0·97 to 6·30)	0·06	NA	NA
Moderate	7/612 (1%)	1/611 (<1%)	NA	0·11†	NA	NA
Severe	1/612 (<1%)	1/611 (<1%)	NA	1·00†	NA	NA
Developmental delay						
Cognitive or language developmental delay	134/589 (23%)	134/572 (23%)	0·97 (0·78 to 1·20)	0·76	0·97 (0·78 to 1·21)	0·80
Severity of cognitive or language developmental delay¶	..	..	0·98 (0·74 to 1·30)	0·89	0·97 (0·72 to 1·31)	0·86
Mild	91/589 (15%)	100/572 (17%)	..	..	..	..
Moderate	31/589 (5%)	22/572 (4%)	..	..	..	..
Severe	12/589 (2%)	12/572 (2%)	..	..	..	..
Motor developmental delay‖	71/589 (12%)	78/577 (14%)	0·92 (0·67 to 1·25)	0·58	0·87 (0·65 to 1·18)	0·37
Severity of motor developmental delays¶	..	..	0·88 (0·61 to 1·25)	0·47	0·87 (0·60 to 1·25)	0·45
Mild	53/589 (9%)	57/577 (10%)	..	..	..	..
Moderate	10/589 (2%)	14/577 (2%)	..	..	..	..
Severe	8/589 (1%)	7/577 (1%)	..	..	..	..
BSID-III**						
Cognitive score (n=607 *vs* n=592)	100·0 (15·9)	99·5 (15·5)	0·52 (–1·32 to 2·35)	0·58	0·32 (–1·41 to 2·04)	0·72
Language score (n=587 *vs* n=573)	97·4 (18·6)	97·1 (18·1)	0·36 (–1·85 to 2·57)	0·75	0·03 (–2·02 to 2·08)	0·98
Motor score (n=585 *vs* n=575)	100·7 (15·5)	100·6 (16·7)	0·12 (–1·81 to 2·05)	0·90	–0·05 (–1·82 to 1·72)	0·96

(Table 2 continues on next page)

	Dexamethasone group	Betamethasone group	Unadjusted treatment effect (95% CI)	Unadjusted p value	Adjusted treatment effect (95% CI)	Adjusted p value
(Continued from previous page)						
Body size at 2-year follow-up						
Weight (n=599 *vs* n=609)**						
Weight, kg	13·1 (2·0)	13·1 (2·0)	0·03 (–0·21 to 0·26)	0·82	0·05 (–0·18 to 0·27)	0·69
Weight Z score	0·15 (1·28)	0·15 (1·22)	0·00 (–0·15 to 0·15)	0·98	0·00 (–0·14 to 0·15)	0·97
Height (n=591 *vs* n=596)**						
Height, cm	88·9 (5·1)	88·7 (5·2)	0·23 (–0·38 to 0·84)	0·47	0·27 (–0·30 to 0·85)	0·35
Height Z score	0·07 (1·16)	0·03 (1·13)	0·06 (–0·08 to 0·19)	0·41	0·06 (–0·08 to 0·19)	0·40
Head circumference (n=592 *vs* n=596)**						
Head circumference, cm	49·0 (1·8)	48·9 (2·4)	0·07 (–0·18 to 0·32)	0·58	0·09 (–0·14 to 0·33)	0·44
Head Z score	–0·77 (1·33)	–0·87 (1·72)	0·08 (–0·10 to 0·26)	0·39	0·07 (–0·11 to 0·25)	0·43
Use of health services since discharge						
Any hospital admission	236/669 (35%)	243/655 (37%)	0·94 (0·81 to 1·09)	0·39	0·95 (0·82 to 1·09)	0·46
Re-admission for respiratory illness	208/669 (31%)	216/655 (33%)	0·94 (0·80 to 1·10)	0·45	0·95 (0·81 to 1·11)	0·53
Physiotherapy	113/667 (17%)	129/651 (20%)	0·87 (0·68 to 1·10)	0·23	0·87 (0·70 to 1·08)	0·20
Occupational therapy	56/667 (8%)	66/652 (10%)	0·87 (0·61 to 1·23)	0·42	0·85 (0·60 to 1·20)	0·35
Speech pathology	89/667 (13%)	100/652 (15%)	0·90 (0·68 to 1·18)	0·44	0·88 (0·67 to 1·14)	0·33
Special education	8/667 (1%)	14/651 (2%)	0·66 (0·27 to 1·61)	0·36	0·59 (0·24 to 1·44)	0·24
Psychology	7/667 (1%)	13/652 (2%)	0·67 (0·26 to 1·73)	0·41	0·60 (0·23 to 1·58)	0·30
Organised play group††	34/614 (6%)	46/613 (8%)	0·71 (0·44 to 1·13)	0·15	0·71 (0·44 to 1·13)	0·15
Asthma or wheezing	136/669 (20%)	152/655 (23%)	0·90 (0·73 to 1·11)	0·31	0·90 (0·74 to 1·11)	0·34
Blood pressure						
Systolic blood pressure (n=370 *vs* n=354)**						
Mean blood pressure, mm Hg	95·3 (11·2)	95·9 (11·2)	–1·03 (–2·67 to 0·62)	0·22	–1·45 (–3·17 to 0·26)	0·10
Z score	0·55 (1·06)	0·64 (1·09)	–0·12 (–0·28 to 0·03)	0·13	–0·17 (–0·33 to –0·01)	0·04
Systolic hypertension	51/370 (14%)	66/354 (19%)	0·70 (0·49 to 0·99)	0·04	0·75 (0·54 to 1·06)	0·11
Diastolic blood pressure (n=356 *vs* n=347)**						
Mean blood pressure, mm Hg	57·9 (10·8)	58·0 (10·4)	–0·22 (–1·81 to 1·37)	0·79	–0·99 (–3·03 to 1·06)	0·34
Z score	1·14 (0·96)	1·17 (0·96)	–0·04 (–0·18 to 0·11)	0·63	–0·09 (–0·27 to 0·09)	0·32
Diastolic hypertension	99/356 (28%)	122/347 (35%)	0·78 (0·63 to 0·98)	0·03	0·80 (0·64 to 0·98)	0·03
Hypertension	115/356 (32%)	144/347 (41%)	0·77 (0·63 to 0·94)	0·01	0·78 (0·64 to 0·95)	0·02
Child behaviour checklist (n=637 *vs* n=616)						
Total score	31·4 (20·4)	31·8 (20·8)	–0·14 (–2·55 to 2·26)	0·91	0·15 (–2·20 to 2·50)	0·90
Total within clinical range	55/637 (9%)	64/616 (10%)	0·84 (0·59 to 1·19)	0·33	0·85 (0·60 to 1·20)	0·36

Drug group data are n/N with available data (%) or mean (SD). Treatment effects are relative risks (95% CI), unless otherwise indicated. Adjustments were made for study hospital, gestational age at entry, number of fetuses, the infant's sex, language spoken at home, and mother's highest education level, unless otherwise specified. BSID-III=Bayley scales of infant development-III. GMFCS=gross motor function classification system. NA=not available. *Any death and death of liveborn infant before hospital discharge were adjusted for gestational age at entry and number of fetuses only. †Calculated with Fisher's exact test. ‡Deafness was adjusted for study hospital, gestational age at entry, number of fetuses, the infant's sex, and the mother's highest education level only. §Severe cerebral palsy was defined as unlikely ever to walk (equivalent to GMFCS levels 4 and 5), moderate cerebral palsy was defined as not walking at 2 years, but likely to become ambulant (equivalent to GMFCS levels 2 or 3); and mild cerebral palsy was defined as walking at 2 years (equivalent to GMFCS level 1). Treatment effects are odds ratios (95% CI) from separate logistic models (ie, any cerebral palsy *vs* none; moderate or severe cerebral palsy *vs* none or mild; and severe cerebral palsy *vs* none, mild, or moderate). ¶Severe developmental delay was defined as a standardised BSID-III score of more than 3 SD below the mean; moderate developmental delay was defined as a standardised BSID-III score of more than 2 SD to 3 SD below the mean; and mild developmental delay was defined as a standardised BSID-III score of more than 1 SD to 2 SD below the mean. Treatment effects are odds ratios of higher severity of the given disease (95% CI). ||Motor developmental delay was adjusted for study hospital, gestational age at entry, number of fetuses, language spoken at home, and mother's highest education level only. **Treatment effects are mean differences (95% CI). ††Organised play group data were adjusted for gestational age at entry, number of fetuses, the infant's sex, language spoken at home, and mother's highest education level only.

Table 2: **Primary and secondary childhood outcomes at 2 years**

minimising the need for a caesarean section, and so minimising future reproductive risks,[27] would favour the use of dexamethasone.

Second, children exposed to dexamethasone were less likely to be hypertensive at age 2 years than those exposed to betamethasone. The clinical significance of this finding

	Dexamethasone group (n=752)	Betamethasone group (n=737)	Unadjusted treatment effect (95% CI)	Unadjusted p value	Adjusted treatment effect (95% CI)	Adjusted p value
Gestational age at birth, weeks*	34·7 (4·0)	34·5 (4·1)	0·25 (–0·19 to 0·69)	0·27	0·23 (–0·18 to 0·64)	0·27
Any intraventricular haemorrhage	34 (5%)	32 (4%)	1·12 (0·68 to 1·85)	0·64	1·09 (0·67 to 1·78)	0·72
Severe intraventricular haemorrhage (grade 3 or 4)	3 (<1%)	5 (1%)	NA	0·50†	NA	NA
Periventricular leukomalacia	2 (<1%)	2 (<1%)	NA	1·00†	NA	NA
Retinopathy of prematurity requiring treatment	0	8 (1%)	NA	0·004†	NA	NA
Patent ductus arteriosus	42 (6%)	34 (5%)	1·27 (0·80 to 2·03)	0·31	1·25 (0·81 to 1·95)	0·36
Neonatal respiratory distress syndrome	183 (24%)	174 (24%)	1·02 (0·84 to 1·24)	0·83	1·03 (0·87 to 1·23)	0·72
Severity of respiratory disease‡						
Mild	88 (12%)	88 (12%)	1·02 (0·84 to 1·24)	0·83	1·03 (0·87 to 1·23)	0·72
Moderate	60 (8%)	62 (8%)	1·08 (0·82 to 1·44)	0·58	1·08 (0·82 to 1·41)	0·58
Severe	35 (5%)	26 (4%)	1·37 (0·82 to 2·31)	0·23	1·38 (0·83 to 2·28)	0·22
Chronic lung disease	51 (7%)	54 (7%)	0·94 (0·64 to 1·37)	0·73	0·94 (0·66 to 1·34)	0·75
Mechanical ventilation	113 (15%)	118 (16%)	0·93 (0·72 to 1·19)	0·55	0·95 (0·75 to 1·19)	0·65
Duration of mechanical ventilation, h§	31·7 (151·6)	40·9 (192·7)	0·78 (0·47 to 1·28)	0·33	0·74 (0·40 to 1·37)	0·34
Proven infection in first 48 h	2 (<1%)	5 (1%)	NA	0·28†	NA	NA
Infection after the first 48 h	31 (4%)	32 (4%)	0·94 (0·58 to 1·53)	0·80	0·98 (0·61 to 1·56)	0·92
Admitted to neonatal intensive care unit	269 (36%)	257 (35%)	1·02 (0·88 to 1·18)	0·81	1·01 (0·89 to 1·15)	0·88
Length of stay in neonatal intensive care unit, days§	6·7 (18·9)	8·2 (22·4)	0·82 (0·61 to 1·09)	0·17	0·88 (0·65 to 1·19)	0·40
Body size at birth*						
Weight, g	2361 (900)	2332 (925)	28·10 (–70·30 to 126·50)	0·58	25·23 (–66·23 to 116·68)	0·59
Length, cm	45·0 (5·5)	44·9 (5·8)	0·07 (–0·56 to 0·70)	0·83	0·00 (–0·58 to 0·58)	1·00
Head circumference, cm	31·3 (3·7)	31·1 (3·7)	0·19 (–0·21 to 0·58)	0·36	0·14 (–0·23 to 0·51)	0·46
Z scores at birth						
Weight	–0·05 (1·10)	–0·05 (1·11)	–0·01 (–0·13 to 0·11)	0·86	–0·01 (–0·13 to 0·10)	0·84
Length	–0·20 (1·19)	–0·18 (1·20)	–0·03 (–0·16 to 0·10)	0·63	–0·04 (–0·17 to 0·09)	0·53
Head circumference	–0·12 (1·42)	–0·15 (1·21)	0·03 (–0·11 to 0·17)	0·64	0·03 (–0·11 to 0·17)	0·68
Body size at hospital discharge (n=738 *vs* n=721)*						
Weight, g	2779 (575)	2765 (628)	8·31 (–56·80 to 73·42)	0·80	8·78 (–52·57 to 70·13)	0·78
Length, cm	47·5 (3·6)	47·7 (3·6)	–0·20 (–0·64 to 0·24)	0·38	–0·20 (–0·62 to 0·21)	0·33
Head circumference, cm	33·8 (11·9)	33·7 (13·0)	0·12 (–1·26 to 1·50)	0·87	0·10 (–1·22 to 1·42)	0·88
Z scores at hospital discharge						
Weight	–0·70 (0·96)	–0·71 (1·07)	0·00 (–0·10 to 0·11)	0·95	0·00 (–0·10 to 0·10)	0·99
Length	–0·64 (1·45)	–0·52 (1·36)	–0·12 (–0·29 to 0·05)	0·17	–0·12 (–0·28 to 0·04)	0·15
Head circumference	0·23 (8·72)	0·21 (10·67)	0·02 (–1·06 to 1·10)	0·97	0·01 (–1·03 to 1·05)	0·99

Drug group data are n (%) or mean (SD). Treatment effects are relative risks (95% CI) unless otherwise indicated. Analyses were adjusted for study hospital, gestational age at entry, and number of fetuses. Infant analyses were adjusted for clustering within mother. Z scores were estimated with the UK–WHO growth reference.[19] NA=not available. *Treatment effects are mean differences (95% CI). †Used Fisher's exact test. ‡Treatment effects are odds ratios (95% CI) from separate logistic models (ie, any respiratory distress syndrome *vs* none; moderate or severe respiratory distress syndrome *vs* none or mild; and severe respiratory distress syndrome *vs* none, mild, or moderate), since a proportional odds assumption is not met. §Treatment effects are ratios of means (95% CI).

Table 3: **Secondary outcomes for liveborn infants assessed before hospital discharge**

is uncertain because there are few reports of childhood blood pressure after exposure to antenatal corticosteroids, and because blood pressure measurements were only available in 60% of the children. In our previous randomised trial[28] of single versus repeat courses of antenatal betamethasone (ACTORDS), 31% of children aged 2 years had hypertension, with a similar prevalence in children exposed to single and repeat courses. However, at age 6–8 years the prevalence of hypertension in that cohort had decreased to 7%, possibly reflecting, in part, the difficulty of accurate measurement of blood pressure at age 2 years or the effects of changing centiles as children age.[29] In the ASTEROID trial, the prevalence of hypertension in children exposed to dexamethasone (32%) was similar to that in the ACTORDS trial, but we found a higher prevalence (42%) in those exposed to betamethasone (ie, *vs* 31% in ACTORDS). Further follow-up will be required to determine whether these differences persist into later childhood. We acknowledge that we have performed several, planned, secondary analyses and that these two unexpected differences between treatment groups might reflect type 1 errors.

	Dexamethasone group (n=679)	Betamethasone group (n=667)	Unadjusted treatment effect (95% CI)	Unadjusted p value	Adjusted treatment effect (95% CI)	Adjusted p value
Maternal infection-related morbidities	125 (18%)	132 (20%)	0·93 (0·75 to 1·16)	0·52	0·95 (0·77 to 1·18)	0·65
Chorioamnionitis requiring intrapartum antibiotics	40 (6%)	55 (8%)	0·71 (0·48 to 1·06)	0·09	0·70 (0·48 to 1·03)	0·07
Use of postnatal antibiotics	109 (16%)	111 (17%)	0·96 (0·76 to 1·23)	0·77	0·99 (0·78 to 1·25)	0·92
Induction of labour	145 (21%)	138 (21%)	1·03 (0·84 to 1·27)	0·77	1·03 (0·84 to 1·26)	0·77
Caesarean section	295 (43%)	346 (52%)	0·84 (0·75 to 0·94)	0·0021	0·84 (0·75 to 0·93)	0·0013
Elective caesarean section	107 (16%)	129 (19%)	0·81 (0·65 to 1·03)	0·08	0·81 (0·64 to 1·02)	0·07
Emergency caesarean section	188 (28%)	216 (32%)	0·85 (0·73 to 1·01)	0·06	0·86 (0·73 to 1·00)	0·06
Main reasons for caesarean section (n=295 *vs* n=346)						
Fetal compromise	112 (38%)	144 (42%)	0·91 (0·75 to 1·11)	0·35	0·93 (0·77 to 1·12)	0·42
Haemorrhage	55 (19%)	60 (17%)	1·08 (0·77 to 1·50)	0·67	1·16 (0·84 to 1·60)	0·36
Hypertension	54 (18%)	56 (16%)	1·13 (0·80 to 1·59)	0·48	1·16 (0·83 to 1·63)	0·38
Previous caesarean section	55 (19%)	76 (22%)	0·85 (0·62 to 1·16)	0·30	0·87 (0·64 to 1·18)	0·36
Abnormal lie	54 (18%)	63 (18%)	1·01 (0·72 to 1·40)	0·97	1·00 (0·72 to 1·38)	0·99
Failure to progress	29 (10%)	25 (7%)	1·36 (0·82 to 2·27)	0·24	1·37 (0·83 to 2·27)	0·22
Prematurity	42 (14%)	36 (10%)	1·37 (0·90 to 2·08)	0·14	1·39 (0·94 to 2·07)	0·10
Postpartum haemorrhage	128 (19%)	141 (21%)	0·89 (0·72 to 1·10)	0·29	0·87 (0·71 to 1·08)	0·20
Blood transfusion required	31 (5%)	28 (4%)	1·09 (0·66 to 1·79)	0·74	1·09 (0·66 to 1·79)	0·74
Postnatal length of stay, days	4·3 (2·0)	4·4 (2·3)	0·99 (0·94 to 1·04)*	0·60	0·99 (0·94 to 1·04)*	0·58

Drug group data are n (%) or mean SD. Treatment effects are relative risks (95% CI). Analyses are adjusted for study hospital, gestational age at entry, and number of fetuses. *Data are ratios of means (95% CI).

Table 4: **Secondary maternal outcomes assessed before hospital discharge, after birth**

	Dexamethasone group (n=679)	Betamethasone group (n=667)
Use of study treatment		
Assigned treatment administered	675 (99%)	657 (99%)
Initial course not completed (only one dose given)	57 (8%)	64 (10%)
Repeat courses	176 (26%)	176 (26%)
One	103 (15%)	103 (15%)
Two	43 (6%)	48 (7%)
Three	30 (4%)	25 (4%)
Adverse effects	18 (3%)	28 (4%)
Discomfort at the injection site	6 (1%)	17 (3%)
Maternal distress	3 (<1%)	7 (1%)
Flushing	4 (1%)	1 (<1%)
Rash	0	3 (<1%)
Burning	1 (<1%)	1 (<1%)
Insomnia	1 (<1%)	1 (<1%)
Vomiting	1 (<1%)	0
Palpitations	0	1 (<1%)

Data are n (%).

Table 5: **Use of study treatment and adverse events**

The major strengths of our trial are that it is considerably larger than previous randomised trials[12] and, for this reason, we might have been able to detect differences that smaller studies were not able to identify. Even so, a larger sample size would be required to detect more marginal differences in death and neurosensory disability. Our trial assessed important outcomes with assessors masked to treatment group, including perinatal outcomes that were previously not well reported, for women and for infants beyond the neonatal period. Earlier, retrospective studies[9–11] that compared dexamethasone and betamethasone have provided conflicting results on neonatal morbidity and a paucity of data on childhood neurodisability outcomes. Systematic reviews of the randomised trials alone[1,12] and those also including cohort studies[30] have highlighted the sparsity of comparative data available on neurodevelopmental outcomes, including cerebral palsy, after antenatal corticosteroid exposure before preterm birth. Only one previous randomised trial[15] reported health outcomes following antenatal treatment with dexamethasone compared with betamethasone beyond the neonatal period, and this study was restricted to a sample of 12 children (11% of those recruited) who were assessed at age 18 months.

A possible weakness of our trial is that data were not collected on the use of postnatal corticosteroids, which could have affected outcomes if usage differed between the treatment groups. However, since the incidence of severe neonatal lung disease, chronic lung disease, and requirement for mechanical ventilation were all low and similar in the two groups, such a difference is unlikely.

When two possible treatments have similar efficacy and safety, selection of the lower cost option is normally preferred. Dexamethasone is 3% of the cost of betamethasone,[7] is more readily available,[7] and it is listed on WHO's Essential Medicines List.[31] A formal economic analysis would help to clarify the importance of these differences and could inform future policy guidance.

Although our study was done in 14 hospitals in two high-income countries with well coordinated, publicly funded, health-care systems, the results will be of relevance in other health-care settings. The lower cost and greater accessibility of dexamethasone means that it is the antenatal corticosteroid most often used in low-income and middle-income countries.[6,8,32] However, experience has shown that the risks and benefits of antenatal corticosteroids can differ in resource-limited settings.[13]

Clinicians who are using dexamethasone in their practice will be reassured by our findings of similar neonatal outcomes, a similar likelihood of survival free of neurosensory disability in early childhood, a similar risk of maternal infectious morbidity, and less maternal pain on injection when using a less expensive drug. In view of the higher use of caesarean section observed with betamethasone, the higher risk of hypertension in exposed children, and greater drug costs, clinicians who are using betamethasone might wish to confirm our findings in subsequent randomised controlled trials. Assessing any change in drug choice in clinical practice and monitoring short-term and long-term health outcomes will be important.

In conclusion, antenatal dexamethasone and betamethasone use provided similar likelihoods of survival free of neurosensory disability at age 2 years, and either can be given to women at risk of preterm birth to improve infant and child health. The incidence of neonatal respiratory morbidity and serious neonatal outcomes, including intraventricular haemorrhage, and of maternal infectious morbidity were similar in both groups. Fewer women randomly assigned to receive dexamethasone reported pain at the injection site, fewer gave birth by caesarean section, and dexamethasone-exposed children were less likely to be hypertensive at a 2-year follow-up than those exposed to betamethasone. These results can be used to aid decisions on the choice of corticosteroid to use for women at risk of preterm birth.

Contributors

CAC and PFM conceived the study and developed the study design with CCA, LWD, JSR, and JEH. CAC, PA, CCA, LWD, and JEH acquired the data. TT analysed the data. CAC wrote the initial draft of the manuscript and all authors contributed to interpretation of the data and critical revision of the manuscript and approved the final version.

Declaration of interests

We declare no competing interests.

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Data sharing statement

A de-identified dataset and a data dictionary used in the analyses can be requested 6 months after publication of this Article by contacting the Maternal and Perinatal Research Hub at the Liggins Institute, University of Auckland. Data will be shared with researchers who provide a methodologically sound proposal and have appropriate ethical approval, where necessary, to achieve the research aims in the approved proposal. Data requestors will be required to sign a Data Access Agreement before data are released.

To contact the **Maternal and Perinatal Research Hub** email: researchhub@auckland.ac.nz

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