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Papers

Antenatal exposure to betamethasone: psychological functioning and health related quality of life 31 years after inclusion in randomised controlled trial

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Abstract

Objectives To determine if antenatal exposure to betamethasone for the prevention of neonatal respiratory distress syndrome alters psychological functioning and health related quality of life in adulthood.

Design Follow-up of the first and largest double blind, placebo controlled, randomised trial of a single course of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome.

Setting Tertiary obstetric hospital in Auckland, New Zealand.

Participants 192 adult offspring, mean age 31 years, of mothers who took part in a randomised controlled trial of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome (87 exposed to betamethasone and 105 exposed to placebo).

Interventions Mothers received two doses of betamethasone or placebo 24 hours apart.

Main outcome measures Cognitive functioning assessed with Wechsler abbreviated scale of intelligence; working memory and attention assessed with Benton visual retention test, paced auditory serial addition test, and Brown attention deficit disorder scale; psychiatric morbidity assessed with Beck depression inventory II, state-trait anxiety inventory, and schizotypy traits questionnaire; handedness assessed with Edinburgh handedness inventory; health related quality of life assessed with short form 36 health survey.

Results No differences were found between groups exposed to betamethasone and placebo in cognitive functioning, working memory and attention, psychiatric morbidity, handedness, or health related quality of life.

Conclusions Prenatal exposure to a single course of betamethasone does not alter cognitive functioning, working memory and attention, psychiatric morbidity, handedness, or health related quality of life in adulthood. Obstetricians should continue to use a single course of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome.

Introduction

A single course of antenatal glucocorticoids is recommended in the management of preterm labour for the prevention of neonatal respiratory distress syndrome.[1] The use of glucocorticoids results in considerable reduction in mortality and morbidity, as well as costs, in infants born preterm.[1 2] Follow-up studies of development into childhood suggest that no adverse effects occur through early childhood.[3] However, information about long term psychological functioning and health related quality of life into adulthood after antenatal glucocorticoids remains scarce.

Other perinatal exposure to glucocorticoids has been associated with adverse neurodevelopmental outcomes. Repeated antenatal courses of glucocorticoids cause decreased fetal brain growth and myelination in sheep.[4] Non-randomised studies in humans have reported decreased neonatal head circumference after repeated courses of antenatal glucocorticoids,[5] with increased risk of hyperactivity in childhood.[6] Furthermore, school age children exposed to postnatal glucocorticoids for neonatal chronic lung disease have lower IQ scores.[7] To date the data on psychological functioning in adulthood after exposure to antenatal glucocorticoids are limited to one small follow-up study of a randomised controlled trial. No difference in cognitive functioning or self report of psychoneuroticism was found between groups in 81 participants aged 20.[8] Conversely, a non-randomised cohort of 130 children at age 14 suggested better cognitive functioning in those exposed to glucocorticoids.[9]

Given the above concerns, we followed a cohort of neonatal survivors from the first and largest randomised controlled trial of antenatal glucocorticoids (the Auckland steroid trial, conducted by Liggins and Howie[10]) to assess the long term effects on psychological functioning and health related quality of life in adulthood.

Methods

Protocol

Auckland steroid trial

The Auckland steroid trial and childhood follow-up have been described previously.[3 10] Briefly, between December 1969 and February 1974 all women expected to deliver between 24 and 36 weeks at the National Women's Hospital, Auckland, New Zealand, were eligible for enrolment unless immediate delivery was indicated. Women were randomised to an intramuscular injection of 6 mg short acting betamethasone phosphate and 6 mg long acting betamethasone acetate or an identical looking placebo of 6 mg cortisone acetate with a 70th of the glucocorticoid potency (trial 1). The allocated treatment was repeated 24 hours later if delivery had not occurred. If possible, labour was arrested with tocolytics for 48 hours. After the first 717 women had enrolled, the dose of betamethasone was doubled (trial 2). A total of 1142 women were enrolled and delivered 1218 babies.

Primary endpoints were neonatal respiratory distress syndrome and perinatal death.

Follow-up in adulthood
Between February 2002 and December 2003 attempts were made to trace those "babies," now adults, who survived the neonatal period. Those located were invited to enter a follow-up study of adult cardiovascular and respiratory status,[11] including collection of information about medical history and socioeconomic status. Between February 2003 and March 2004 we invited the subgroup of those who had participated in the cardiorespiratory follow-up who lived in the greater Auckland area to participate in the current study, which involved a structured assessment by a researcher in psychology (VKL). We obtained written informed consent from each participant.

Outcome measures and definitions

Cognitive functioning
We used the Wechsler abbreviated scale of intelligence to assess cognitive functioning.[12] This comprises four subtests giving scales for full IQ, verbal IQ, and performance IQ.

Working memory and attention
We used the Benton visual retention test,[13] the paced auditory serial addition test,[14] and the Brown attention deficit disorder scale to assess working memory and attention.[15] The Benton visual retention test assesses visual perception, visual memory, and visuoconstructive abilities by asking participants to copy from memory 10 increasingly difficult designs. Results are expressed as number of correct designs and a total error score.

The paced auditory serial addition test assesses sustained attention by asking participants to add 61 consecutive digits. As each digit is presented, the participant must sum that digit with the digit presented beforehand. The test is repeated with decreasing intervals between digits: 2.4 seconds, 2.0 seconds, 1.6 seconds, and 1.2 seconds. Results are expressed as a score of correct digits at each time interval. The Brown attention deficit disorder scale is a 40 item self completed questionnaire that measures symptoms of attention deficit disorder, with a total score out of 120. We defined probable attention deficit disorder as a score of >39.

Psychiatric morbidity
We used the Beck depression inventory II,[16] the trait portion of the state-trait anxiety inventory,[17] and the schizotypy traits questionnaire to assess psychiatric morbidity.[18] The Beck depression inventory II is a 21 item self completed questionnaire that measures presence and severity of depression symptoms as listed in the *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition. We defined probable depression as a score of >13. The trait portion of the state-trait anxiety inventory is a 20 item self completed questionnaire that measures individual differences in proneness to anxiety. We defined probable anxiety as a score above the 80th centile. The schizotypy traits questionnaire is a 37 item self completed questionnaire that measures the minor manifestations of a psychotic disorder. Results are expressed as a total score and three subscales—magical ideation, unusual perceptual experiences, and paranoid ideation and suspiciousness.

Handedness
We used the Edinburgh handedness inventory to assess handedness.[19] This is a 10 item self completed questionnaire that measures hand preference for 10 everyday activities. Results are expressed as a laterality quotient, where right handedness is +30 to +100, ambidextrous is −30 to +30, and left handedness is −100 to −30.

Health related quality of life
We assessed health related quality of life by using the Australasian version of the short form 36 health survey (SF-36), which has been validated in 7862 New Zealanders.[20] This is a 36 item self completed questionnaire that measures eight multi-item domains of perceived health related quality of life. Scores range from 0 (worst) to 100 (best) for all domains. Five domains (physical functioning, role limitation due to physical problems, bodily pain, social functioning, role limitation due to emotional problems) define health status by absence of disability, and the maximum score is achieved when no disability is reported. Three domains (general health perception, vitality, and mental health) define both positive and negative health status, and a score of 50 indicates neither positive nor negative status. We also asked participants questions to determine the presence of visual, hearing, and speech abnormalities.

Assignment
The chief pharmacist used random number tables to generate randomisation and held the randomisation key. The study drug was supplied in identical numbered ampoules.

Masking
Staff who enrolled mothers and who cared for and assessed participants in the neonatal period were blind to study group allocation. Adult participants and all members of the study team involved in tracing, recruitment, assessment and analysis were also unaware of the participants' in utero exposure.

Participant flow and follow-up
Of the 988 neonatal survivors from the Auckland steroid trial, 713 (72%) were successfully traced at 30 years. Of these, 534 completed the cardiorespiratory follow-up—56% of those presumed to be alive and 80% of those traced and known to be alive.[11] Of these, 280 were eligible for the current study (that is, lived in the greater Auckland area), of whom 192 (69%) participated (figure).

Analyses
We used SAS version 8.02 (SAS Institute, Cary, NC) to analyse data on an intention to treat basis. We compared continuous variables with unpaired t tests or Mann-Whitney tests and categorical data with χ^2 tests as appropriate. We log transformed variables with skewed distributions. If the distribution remained skewed, we present data as medians. Primary analyses were unadjusted. Secondary analyses used multiple linear regression to adjust for confounding by sex, birth weight, gestational age, and socioeconomic status decided a priori. We explored further confounders by using the change in estimates technique at the 10% level.[21] We created birth weight standard deviation (z) scores by using data from all New Zealand deliveries in 1990-1. We assigned New Zealand socioeconomic index scores from occupational data.[11]

Results

Recruitment
Eighty seven participants exposed to betamethasone and 105 participants exposed to placebo took part (66% v 71% of those eligible; $P=0.36$). Mean (SD) age at follow-up was 31.2 (1.1) and 31.1 (1.1) years in the two groups.

Background characteristics

Those who participated in this study were more likely to have had respiratory distress syndrome but had otherwise similar perinatal characteristics to the entire cohort of non-participants presumed to be alive at age 30 (table 1). Those who participated were less likely to have been from a multiple pregnancy, to have obtained fewer than four years of high school education, or to be in the lowest socioeconomic group but had otherwise similar perinatal and adult characteristics to those who were eligible for this study (lived in the Auckland area) but declined participation (table 1). No significant differences in perinatal or adult characteristics existed between the betamethasone and placebo exposed participants who took part (table 2).

Previous psychiatric diagnosis

A previous psychiatric diagnosis was reported by six (7%) betamethasone exposed and six (6%) placebo exposed participants (relative risk 1.2, 95% confidence interval 0.40 to 3.6; P = 0.74). One placebo exposed participant had schizophrenia. The other diagnoses were affective and anxiety conditions.

Psychological functioning

No difference existed between groups in measures of cognitive functioning, working memory and attention, depression, anxiety, schizotypy, or handedness (table 3). Adjustment for previous psychiatric diagnosis did not change the depression, anxiety, or schizotypy results.

Health related quality of life

We found no difference between groups in the eight domains of the SF-36 (table 3). No difference existed between groups in the numbers reporting visual or hearing difficulties. However, betamethasone exposed participants reported significantly fewer speech difficulties. All participants with speech difficulties reported a mild impairment, in that they were partially understood when speaking to strangers but completely understood when speaking to those who knew them well.

Multivariate analysis

Adjustment for sex, birth weight, gestational age, and socioeconomic status did not change the results.

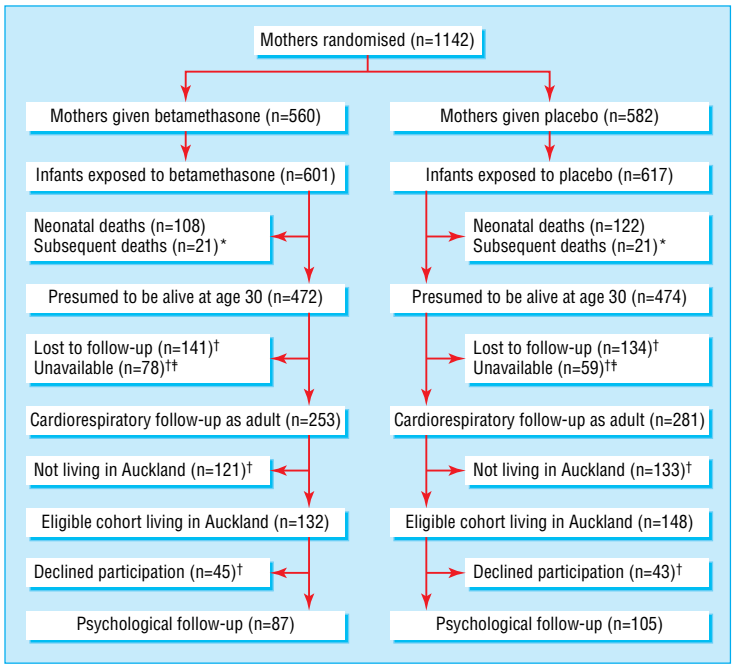
Discussion

We studied 192 neonatal survivors at 31 years of age from the first and largest randomised controlled trial of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome. We found that antenatal exposure to betamethasone did not alter cognitive functioning, working memory and attention, psychiatric morbidity, handedness, or health related quality of life at age 31.

The only other report of outcome in adulthood after a randomised controlled trial of antenatal glucocorticoids involved 81 participants at a mean age of 20 and found no differences in cognitive functioning, handedness, or psychopathology.[8] Our study is the first to report health related quality of life into adulthood after exposure to antenatal glucocorticoids.

Comparison with other studies

Our findings are consistent with previous childhood follow-up studies from both the Auckland steroid trial and other randomised trials of antenatal glucocorticoids.[3 22] MacArthur et al followed 258 children at age 4 and 250 children at age 6 from the first 318 neonatal survivors of the Auckland steroid trial (trial 1).[3] They reported no overall differences in cognition between the two groups. However, betamethasone exposed children had lower scores on the Raven's progressive matrices test (a test of non-verbal reasoning) and two of the visual subsets of the Illinois test of psycholinguistic abilities at age 6. These differences were thought to be unimportant, and this is consistent with our findings of no difference between groups in the Benton visual retention test and the matrix subtest of the Wechsler abbreviated scale of intelligence (a test of non-verbal reasoning). The authors of the second largest randomised trial of antenatal glucocorticoids



Participant flow to psychological follow-up in adulthood. *Details published elsewhere.[11] †Non-participants presumed to be alive at age 30. ‡Traced but declined participation in cardiorespiratory adult follow-up or residing overseas and not returning to New Zealand within timeframe of study

Table 1 Characteristics of infants who participated in this study compared with those who were eligible but declined participation and with all non-participants presumed to be alive at age 30. Values are numbers (percentages) unless stated otherwise

		Eligible for participation but declined (n=88)		Non-participants presumed to be alive at age 30* (n=754)	
Characteristic	**Participants (n=192)**	**Values**	**P value†**	**Values**	**P value†**
Maternal characteristics					
Multiple pregnancy	22 (11)	19 (22)	0.03	91 (12)	0.82
Unplanned premature labour	159 (83)	68 (77)	0.27	625 (83)	0.98
Hypertension	16 (8.3)	8 (9.1)	0.83	51 (6.8)	0.45
Gestational diabetes	3 (1.6)	3 (3.4)	0.38	10 (1.3)	0.73
Haemolytic disease	8 (4.2)	5 (5.7)	0.58	33 (4.4)	0.90
Median (IQR) gestational age at entry (days)	231 (216-242)	235 (213-244)	0.63	232 (217-244)	0.52
Median (IQR) entry/delivery interval (days)	4.8 (1.7-36)	3.3 (1.4-29)	0.20	4.4 (1.8-38)	0.95
Trial 1	120 (63)	49 (56)	0.28	465 (62)	0.83
Betamethasone treatment	87 (45)	45 (51)	0.36	385 (51)	0.16
Neonatal characteristics					
Male sex	99 (52)	44 (50)	0.81	424 (56)	0.25
Median (IQR) gestational age at delivery (days)	245 (234-266)	245 (231-259)	0.20	248 (236-266)	0.44
Term delivery	66 (34)	23 (26)	0.17	268 (36)	0.76
Mean (SD) birth weight (g)	2403 (796)	2243 (801)	0.12	2416 (722)	0.83
Mean (SD) birth weight z score	–0.32 (0.98)	–0.39 (1.16)	0.58	–0.40 (0.97)	0.33
Birth weight <10th centile	27 (14)	18 (20)	0.18	127 (17)	0.35
Fetal distress	27 (14)	12 (14)	0.92	105 (14)	0.96
5 min Apgar >7	148 (77)	69 (78)	0.81	599 (79)	0.47
RDS	21 (11)	9 (10)	0.86	48 (6.4)	0.03
RDS (moderate or severe)	17 (8.9)	6 (6.8)	0.56	32 (4.2)	0.01
Adult characteristics					
Ethnicity:					
European	144 (75)	62 (70)	0.34		
Maori	35 (18)	23 (26)			
Pacific	12 (6.3)	3 (3.4)			
Other	1 (0.5)	0 (0)			
Tobacco use:					
Non-smoker	102 (53)	42 (48)	0.12		
Former smoker	38 (20)	12 (14)			
Current smoker	52 (27)	34 (39)			
Alcohol use‡:					
Non-drinker	46 (24)	24 (27)	0.82		
Social drinker	118 (61)	51 (58)			
Heavy drinker	28 (15)	13 (15)			
Marital status:					
Single	62 (32)	33 (38)	0.20		
Separated/divorced/widowed	6 (3.1)	6 (6.8)			
Married or living with partner	124 (65)	49 (56)			
Education level:					
High school <4 years	35 (18)	35 (40)	<0.001		
High school ≥4 years	48 (25)	19 (22)			
Polytechnic	62 (32)	23 (26)			
University	47 (24)	11 (13)			
Socioeconomic status§:					
1	9 (4.7)	4 (4.7)	0.05		
2	34 (18)	14 (16)			
3	61 (32)	13 (15)			
4	45 (24)	30 (35)			
5	28 (15)	14 (16)			
6	14 (7.3)	11 (13)			

IQR=interquartile range; RDS=respiratory distress syndrome.
*Includes infants eligible for participation but who declined (see figure).
†For differences compared with participants.
‡Based on standard units of alcohol consumption, adjusted for sex.[11]
§Based on occupation: 1=highest socioeconomic group.[11] Occupation could not be coded for one participant and two people who were eligible for participation but declined.

followed 339 infants at 36 months of age and reported no difference in cognitive outcome.[22]

Post hoc calculations indicate that our study had 80% power ($\alpha = 0.05$) to detect a difference between treatment groups of 5% for IQ, 7% for Brown attention deficit disorder scale total scores, 3% for state-trait anxiety inventory scores, and 10% for SF-36 mental health scores. Thus clinicians can be confident that the relatively small fetal glucocorticoid exposure resulting from a single course of antenatal betamethasone for the prevention of neonatal respiratory distress syndrome has no clinically detectable effect on cognitive functioning, working memory and attention, or psychiatric morbidity into adulthood. This

Table 2 Characteristics of participants exposed to betamethasone and placebo. Values are numbers (percentages) unless stated otherwise

Characteristic	Betamethasone (n=87)	Placebo (n=105)	P value
Maternal characteristics			
Multiple pregnancy	12 (14)	10 (10)	0.36
Unplanned premature labour	71 (82)	88 (84)	0.69
Hypertension	10 (11)	6 (5.7)	0.15
Gestational diabetes	1 (1.2)	2 (1.9)	1.00
Haemolytic disease	3 (3.4)	5 (4.8)	0.73
Median (IQR) gestational age at entry (days)	231 (212-240)	232 (217-242)	0.50
Median (IQR) entry/delivery interval (days)	4.6 (1.9-39)	5.6 (1.6-36)	0.56
Trial 1	55 (63)	65 (62)	0.85
Neonatal characteristics			
Male sex	46 (53)	53 (50)	0.74
Median (IQR) gestational age at delivery (days)	245 (235-266)	248 (232-266)	0.83
Term delivery	27 (31)	39 (37)	0.38
Mean (SD) birth weight (g)	2369 (817)	2432 (782)	0.59
Mean (SD) birth weight z score	−0.40 (0.93)	−0.25 (1.01)	0.31
Birth weight <10th centile	15 (17)	12 (11)	0.25
Fetal distress	9 (10)	18 (17)	0.18
5 min Apgar >7	70 (80)	78 (74)	0.31
RDS	8 (9.2)	13 (12)	0.48
RDS (moderate or severe)	7 (8.0)	10 (9.5)	0.72
Adult characteristics			
Ethnicity:			
European	67 (77)	77 (73)	0.70
Maori	14 (16)	21 (20)	
Pacific	6 (6.9)	6 (5.7)	
Other	0	1 (1.0)	
Tobacco use:			
Non-smoker	46 (53)	56 (53)	0.61
Former smoker	15 (17)	23 (22)	
Current smoker	26 (30)	26 (25)	
Alcohol use*:			
Non-drinker	24 (28)	22 (21)	0.52
Social drinker	50 (57)	68 (65)	
Heavy drinker	13 (15)	15 (14)	
Marital status:			
Single	28 (32)	34 (32)	0.97
Separated/divorced/widowed	3 (3.4)	3 (2.9)	
Married or living with partner	56 (64)	68 (65)	
Education level:			
High school <4 years	19 (22)	16 (15)	0.52
High school ≥4 years	22 (25)	26 (25)	
Polytechnic	24 (28)	38 (36)	
University	22 (25)	25 (24)	
Socioeconomic status†:			
1	3 (3.4)	6 (5.8)	0.62
2	17 (20)	17 (16)	
3	23 (26)	38 (37)	
4	22 (25)	23 (22)	
5	14 (16)	14 (13)	
6	8 (9.2)	6 (5.8)	

IQR=interquartile range; RDS=respiratory distress syndrome.
*Based on standard units of alcohol consumption, adjusted for sex.[11]
†Based on occupation: 1=highest socioeconomic group.[11]

confidence cannot be extrapolated to other situations of much larger glucocorticoid exposures in the perinatal period. Animal studies and non-randomised evidence suggest possible adverse psychological sequelae after repeated courses of antenatal glucocorticoids.[4 5] Long term follow-up of recent randomised controlled trials is essential to clarify the clinical relevance of these effects. Follow-up of 146 school age children from a randomised controlled trial of much larger doses of glucocorticoids for treatment of neonatal chronic lung disease also found poorer cognitive functioning in those exposed to glucocorticoids.[7]

We found that participants exposed to betamethasone reported a lower incidence of speech difficulties than those exposed to placebo. The self reported speech impairment described was clinically mild, but the difference between groups cannot be explained by cerebral palsy, cognitive functioning, or ethnicity. MacArthur et al reported no difference between groups in incidence of stammering, stutter, or intelligibility of speech at 4 and 6 years of age.[3] The differences between groups in adulthood must be interpreted with caution in light of the multiple comparisons done in the analysis and hence the possibility of a type I error.

Limitations

Our study has several limitations. Only 69% of the eligible cohort of neonatal survivors living in the Auckland region participated in this study. Although this obviously introduces the potential for selection bias, the likely direction of such bias remains uncertain.[23 24] However, lack of complete follow-up would bias our results only if the association between exposure to betamethasone and psychological and health related quality of life outcomes differed between those who did and those who did not participate. As the original trial was randomised, we have no reason to think that this might be the case. Furthermore, the Auckland steroid trial is particularly suited to long term follow-up, as very few mothers were not considered for randomisation and similar numbers of neonatal survivors with similar perinatal morbidity were available from both treatment groups.

Further potential for selection bias is introduced by the geographical restriction of study participants to those living in the Auckland region, for logistic and funding reasons. However, once again, this would bias our results only if the association between betamethasone exposure and psychological and health related quality of life outcomes differed between those living in Auckland and those living elsewhere. This seems unlikely given the randomised nature of the original trial, the similar proportion of the survivors from each treatment group who were eligible for the study, and the similar proportion who took part from among those eligible. Furthermore, the only difference in perinatal variables between the participants and the total cohort of neonatal survivors presumed to be alive at age 30 was the higher incidence of neonatal respiratory distress syndrome in participants.

Implications

The applicability of our findings to current clinical practice is less clear cut. Our study only included nine infants born <30 weeks' gestation. However, the expected neonatal outcome for these very premature infants today is similar to that of our more mature cohort 30 years ago. Furthermore, most preterm babies are born after 30 weeks' gestation, and this group is most similar to the cohort reported in this study. Nevertheless, further follow-up studies of more recent randomised trial cohorts will be helpful in clarifying any possible long term effects of exposure to antenatal betamethasone at much earlier gestations than was the case in this study.

Conclusions

We conclude that antenatal exposure to a single course of betamethasone does not alter cognitive functioning, working memory and attention, psychiatric morbidity, handedness, or health related quality of life in adulthood. Obstetricians should

Table 3 Psychological functioning and health related quality of life outcomes in groups exposed to betamethasone and placebo

Outcome	Measured outcome				
	Measurement	Betamethasone (n=87)	Placebo (n=105)	Difference (95% CI)	P value
Cognitive functioning					
Full IQ	Mean (SD)	102.6 (12.5)	103.7 (13.5)	–1.0 (–4.8 to 2.7)	0.58
Verbal IQ	Mean (SD)	97.6 (11.9)	98.3 (12.8)	–0.8 (–4.3 to 2.8)	0.67
Performance IQ	Mean (SD)	107.2 (13.8)	108.3 (14.7)	–1.1 (–5.2 to 3.0)	0.59
Working memory and attention					
Benton: total correct score	Mean (SD)	7.0 (1.7)	7.2 (1.8)	–0.1 (–0.6 to 0.4)	0.59
Benton: total number of errors	Mean (SD)	3.8 (2.6)	3.7 (3.0)	–0.1 (–0.7 to 0.9)	0.89
Paced auditory serial addition test, correct score at:					
2.4 second	Median (IQR)	41 (27-49)	43 (28-49)	–1 (–5 to 3)	0.72
2.0 second	Median (IQR)	37 (27-46)	37 (26-45)	0 (–2 to 5)	0.59
1.6 second	Median (IQR)	29 (22-40)	30 (20-39)	0 (–3 to 4)	0.77
1.2 second	Median (IQR)	24 (14-34)	26 (15-33)	0 (–4 to 2)	0.60
Brown ADD scale: total score	Log mean	25.6	26.9	1 (0.8 to 1.1)*	0.58
Probable ADD	No (%)	16 (18)	30 (29)	0.64 (0.38 to 1.1)†	0.10
Psychiatric morbidity					
BDI-II total score	Median (IQR)	5 (2-12)	5 (1-10)	1 (–1 to 2)	0.44
Probable depression	No (%)	16 (18)	17 (16)	1.1 (0.61 to 2.1)†	0.69
State-trait anxiety inventory: total	Log mean	34.1	34.5	1 (0.9 to 1.1)*	0.74
Probable anxiety	No (%)	17 (20)	27 (26)	0.76 (0.44 to 1.3)†	0.31
Schizotypy traits questionnaire:					
Total	Median (IQR)	11 (6-15)	10 (7-15)	0 (–2 to 2)	0.78
Magical ideation	Median (IQR)	3 (1-4)	3 (1-4)	0 (–1 to 1)	0.93
Unusual perceptual experiences	Median (IQR)	1 (0-3)	2 (0-3)	0 (0 to 0)	0.97
Paranoid ideation and suspiciousness	Median (IQR)	1 (0-3)	1 (0-3)	1 (–1 to 2)	0.70
Handedness					
Laterality quotient	Median (IQR)	90 (71-100)	86 (60-100)	0 (0 to 8)	0.22
Health related quality of life					
SF-36:					
Physical functioning	Mean (SD)	86 (24)	89 (17)	–3 (–9 to 2)	0.27
Role limitation due to physical problems	Mean (SD)	78 (37)	79 (37)	–1 (–12 to 9)	0.82
Bodily pain	Mean (SD)	72 (25)	76 (21)	–4 (–11 to 2)	0.19
General health perception	Mean (SD)	74 (21)	75 (21)	–2 (–7 to 4)	0.61
Vitality	Mean (SD)	59 (19)	62 (19)	–3 (–8 to 2)	0.28
Social functioning	Mean (SD)	79 (25)	83 (23)	–3 (–10 to 3)	0.32
Role limitation due to emotional problems	Mean (SD)	72 (41)	77 (38)	–5 (–16 to 6)	0.37
Mental health	Mean (SD)	72 (18)	75 (17)	–3 (–8 to 2)	0.23
Participants reporting visual difficulty	No (%)	18 (21)	24 (23)	0.91 (0.53 to 1.6)†	0.72
Participants reporting hearing difficulties	No (%)	1 (1.2)	5 (4.8)	0.24 (0.03 to 2.0)†	0.22
Participants reporting speech difficulties	No (%)	1 (1.2)	9 (8.6)	0.13 (0.01 to 1.0)†	0.02

ADD=attention deficit disorder; BDI=Beck depression inventory; SF-36=short form 36 health survey.
*A difference between log means is a ratio and is non-significant if 95% confidence interval includes 1.
†Relative risk (95% confidence interval).

continue to use a single course of antenatal glucocorticoids for the prevention of neonatal respiratory distress syndrome.

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Contributors: SRD, AL, DMcC, AR, and JEH conceived the study. VKL collected the data. SRD, VP, and JEH did the statistical analysis. SRD, VKL, AL, DMcC, VP, AR, and JEH wrote the manuscript. SRD and JEH are guarantors.

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Competing interests: None declared.

Ethical approval: The Auckland Regional Ethics Committee approved this follow-up study.

What is already known on this topic

A single course of antenatal glucocorticoids reduces neonatal mortality and morbidity after preterm birth and is widely used for the prevention of neonatal respiratory distress syndrome

No studies have adequately looked at psychological functioning and health related quality of life in adulthood after antenatal exposure to glucocorticoids

What this study adds

Antenatal exposure to betamethasone did not alter psychological functioning or health related quality of life at 31 years of age

Obstetricians should continue to use a single course of antenatal glucocorticoids for the prevention of neonatal respiratory distress syndrome

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