

Impact of oral corticosteroids on respiratory outcomes in acute preschool wheeze: a randomised clinical trial

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ABSTRACT

Objective To determine if administration of oral prednisolone to preschool children with acute wheeze alters respiratory outcomes.

Design Double-blind, randomised, placebo-controlled equivalence trial.

Setting Three hospitals in New Zealand.

Patients 477 children aged 24–59 months with acute wheeze associated with respiratory illness.

Interventions 2 mg/kg (maximum 40 mg) oral prednisolone or similar placebo, once daily for 3 days.

Main outcome measures Primary outcome was change in Preschool Respiratory Assessment Measure (PRAM) score 24 hours after intervention. Secondary outcomes included PRAM score at 4 hours, length of emergency department and inpatient stays, admission and representation rates, time to return to normal activities and use of additional oral prednisolone or intravenous medications. Analysis was by intention-to-treat.

Results There was no difference between groups for change in PRAM score at 24 hours (difference between means -0.39 , 95% CI -0.84 to 0.06 , $p=0.09$). Absolute PRAM score was lower in the prednisolone group at 4 hours (median (IQR) 1 (0–2) vs 2 (0–3), $p=0.01$) and 24 hours (0 (0–1) vs 0 (0–1), $p=0.01$), when symptoms had resolved for most children regardless of initial treatment. Admission rate, requirement for additional oral prednisolone and use of intravenous medication were lower in the prednisolone group, although there were no differences between groups for time taken to return to normal activities or rates of representation within 7 days.

Conclusion Oral prednisolone does not alter respiratory outcomes at 24 hours or beyond in preschool children presenting with acute wheeze.

INTRODUCTION

Wheeze associated with viral respiratory illness is common in preschoolers, frequently resulting in emergency department (ED) presentation and hospital admission.^{1 2} Treatment for preschoolers presenting with acute wheeze has conventionally been similar to that of asthma in older children and adults, with administration of oral corticosteroids recommended by international guidelines.^{3–5} However, wheeze in preschoolers is a heterogeneous condition with a number of factors contributing to

What is already known on this topic?

- Wheeze associated with respiratory illness is common in preschool children and is a frequent cause for hospital presentation or admission.
- Unlike asthma in older children, the pathophysiology of wheeze in preschool children is multifactorial.
- Despite conflicting evidence, the British Thoracic Society recommends administration of a 3-day course of oral prednisolone to preschool children with moderate or severe wheeze.

What this study adds?

- Prednisolone does not alter respiratory outcomes at 24 hours or beyond.
- Prednisolone may reduce admission rate and escalation of therapy in preschool children with wheeze.
- Further studies are required to determine whether a single dose of oral prednisolone improves short-term respiratory outcomes for preschool children presenting to hospital with wheeze.

the development of a wheezy phenotype, including viral infection, atopy and allergen sensitisation, and may not be associated with subsequent asthma.^{6–8}

Although oral corticosteroids are well accepted in the management of acute asthma in adults and older children,⁹ evidence regarding the efficacy of their use in preschoolers with wheeze is contradictory.¹⁰ Efforts to clarify a unified management approach have been hampered by differences in study design, particularly regarding age and illness severity of patients included, dose and formulation of corticosteroids used, study settings and outcomes measured. For example, in a randomised placebo-controlled trial, Foster *et al* found a reduction in length of hospital stay in children aged 24–72 months presenting with virus-associated wheeze randomised to prednisolone.¹¹ By contrast, in their randomised placebo-controlled trial, Panickar found no difference in length of hospital stay, or



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other outcomes, in children aged 10–60 months treated with prednisolone.¹²

These conflicting findings have precipitated vigorous debate and variation in practice.¹⁰ A recent meta-analysis cautiously concluded that treatment with corticosteroids may be beneficial for young children with recurrent asthma or wheeze managed in hospital, but concluded further studies were needed.³ Due to the potential for outcome measures such as admission rate and length of stay to be biased by factors independent of a child's clinical state, for example, time of day, hospital occupancy and social factors, we wished to use an objective measure of respiratory status that was replicable and validated for use in children to investigate this question further. Thus, in the Wheeze and Steroids in Preschoolers (WASP) Study, we aimed to determine the effect of prednisolone on respiratory distress at 24 hours (assessed using the validated and standardised Preschool Respiratory Assessment Measure (PRAM) score,^{13 14}) and on other outcomes, in children 24–59 months of age presenting to an ED with wheeze associated with respiratory illness.

METHODS

Design

This randomised, double-blind placebo-controlled trial was undertaken in three New Zealand hospital EDs. Patients were randomised to either 3 days of oral prednisolone (2 mg/kg, maximum 40 mg), consistent with guidelines^{4 5} or placebo, once a day. Medications were dispensed in opaque bottles with placebo similar in flavour, colour and viscosity. Participants were stratified by site (block randomisation=10) using computer generated randomisation prepared by the study statistician. Participants, families/caregivers, clinicians and research staff were blinded to group allocation.

Participants

Children aged 24–59 months presenting with acute wheeze associated with any respiratory illness were eligible. Exclusion criteria were: patients presenting with non-respiratory problems and concomitant wheeze; inability for follow-up at 18–38 hours; oral corticosteroids in previous 7 days; initial PRAM score <3; chronic respiratory or cardiac disease (any condition causing persistent respiratory distress, not including asthma or recurrent wheeze); history of inhaled foreign body; current or past history of life-threatening asthma; contraindication to corticosteroids and previous study enrolment.

Study protocol

All potentially eligible children had a PRAM score assessed at triage prior to receiving salbutamol. The PRAM score, a

well-validated measure of respiratory distress in children, has five variables: wheeze, air entry, scalene retraction, suprasternal indrawing and oxygen saturation (table 1).¹³ Scores range from 0 (no disease) to 12 (severe). Once eligible, standard care for wheeze in this group was initiated; three 600 mcg treatments of inhaled salbutamol via spacer at 20 min intervals, with ongoing bronchodilator therapy as required thereafter.

During this time, parents/caregivers were approached for consent. Following written consent, randomisation ensued, with sequential WASP medication bottles dispensed. WASP medication was administered within 20 min of a dose of salbutamol, with the baseline time recorded.

Following WASP medication administration, all participants received standard treatment for wheeze with no restrictions on cointerventions. If treating clinicians considered it imperative, patients could receive corticosteroid therapy and study participation continued.

Data collection included medical and demographic data. If admitted, the PRAM score was recorded 24 hours following initial WASP medication. If discharged, nurses visited patients at home between 08:00 and 15:00 hours the following day (18–38 hours following initial WASP medication) to record a PRAM score. Prior to discharge, parents/caregivers were provided with the remainder of their WASP medication, instructions for administration of 2 further doses and a 7 day symptom diary.

A follow-up phone call made at 7 days determined further ED/primary care presentations, additional medication use and health since discharge.

Outcomes

Primary outcome was change in PRAM score from baseline to 24 hours following administration of WASP medication.

Prespecified secondary outcomes included: 4 hour PRAM score; admission rate; length of ED and inpatient stays; amount of salbutamol given by 48 hours and 7 days; treatment with additional open-label prednisolone; time to return to normal activity; and adverse events including requirement for intravenous medication, admission to intensive care, and representation to ED/primary care within 7 days with respiratory illness.

Statistical analysis

The study was designed as an equivalence trial and conservatively powered at minimal detectable difference in PRAM scores (1), below the minimal clinical difference (3), to have maximal effect on clinical practice should the null hypothesis that corticosteroids and placebo are equivalent (not different) prove correct. A pilot study (n=137) determined a SD of 2.3 for change in PRAM score at 24 hours. Allowing for 15% attrition,

Table 1 PRAM score¹¹

Signs	Score*			
	0	1	2	3
Suprasternal indrawing (tracheal tug)	Absent		Present	
Scalene retractions (neck muscles)	Absent		Present	
Wheezing	Absent	Expiratory only	Inspiratory and expiratory	Audible without stethoscope or silent chest with minimal air entry
Air entry	Normal	Decreased at bases	Wide spread decrease	Absent/minimal
Oxygen saturation in room air	>95%	92%–94%	<92%	

*Add scores from all five signs to obtain total PRAM score (maximum score: 12)
PRAM, Preschool Respiratory Assessment Measure.

400 participants were required (power=95%) to confirm equivalence ($\alpha=0.05$). During the trial, it was noted that primary outcome data were available for approximately 80%. To preserve power, recruitment was conservatively increased to ensure primary outcome data were available for 400 participants.

Analysis was by intention-to-treat (SAS V.9.4, SAS Institute, Cary, USA). Continuous data are reported as means \pm SD or medians and IQR. Differences are reported as differences between means (95% CIs) or differences between medians (95% CIs) using Hodges-Lehmann estimates.¹⁵ Dichotomised data are reported as rates, with differences reported as OR (95% CIs) and corresponding number needed to treat/harm.

A priori subgroup analysis was undertaken in participants deemed salbutamol responsive (reduction in PRAM score of ≥ 3 following three 600 mcg salbutamol doses in first hour; 80% power) and deemed at higher risk of later asthma (using Asthma Predictive Index).¹⁶ Post hoc subgroup analysis was undertaken of: change in PRAM score at 4 hours; proportion of participants with PRAM score of 0, 1–4 (mild), 5–8 (moderate) and 9–12 (severe) at 4 and 24 hours; and change in PRAM score at 24 hours for those with mild/moderate versus severe and mild versus moderate/severe PRAM scores at baseline.

RESULTS

Between August 2014 and September 2016, 3247 patients were potentially eligible. Of these, 150 patients were not approached, 2040 were excluded and 564 declined to participate, leaving 493 patients randomised to receive prednisolone ($n=246$) or placebo ($n=247$, figure 1). Eleven participants withdrew and five participants were excluded post-randomisation, leaving 477 patients (238 in the prednisolone group and 239 in the placebo group) in the intention-to-treat analysis, with primary outcome data available on 393 patients (82% overall; 195 (79%) in prednisolone group and 198 (83%) in placebo group).

Study groups were well balanced at baseline (table 2).

We found no difference between study groups for the primary outcome of change in PRAM score from baseline to 24 hours following study medication administration (difference between

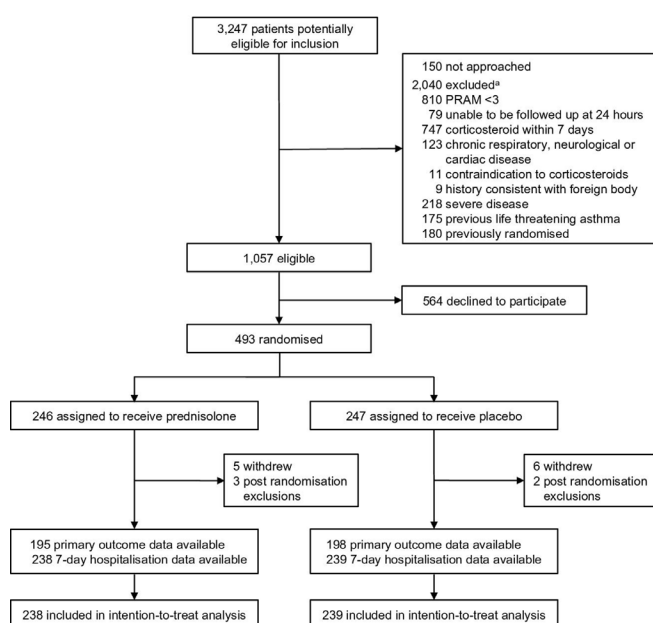


Figure 1 Consort flow diagram. *Some participants met more than one exclusion criteria.

Table 2 Baseline characteristics of prednisolone and placebo groups

	Prednisolone no. (%) (n=238)	Placebo no. (%) (n=239)
Male	147 (61.8)	137 (57.3)
Age, mean (SD), months	36.4 (10.2)	36.9 (9.9)
Ethnicity—Māori	75 (31.5)	80 (33.5)
Pacific people	67 (28.2)	59 (24.7)
Asian	9 (3.8)	12 (5.0)
European/other	87 (36.6)	88 (36.8)
Passive tobacco exposure*	100 (42.4)	95 (40.8)
Previous diagnosis of asthma	70 (29.4)	73 (30.5)
Wheeze in past—any	213 (89.5)	214 (89.5)
Wheeze in past with URTI	202 (84.9)	200 (83.7)
Wheeze in past without URTI	35 (14.7)	41 (17.2)
Previous diagnosis of eczema	102 (42.9)	102 (42.7)
Previous diagnosis of hay fever	39 (16.4)	41 (17.2)
Previous salbutamol use	184 (77.3)	187 (78.2)
Previous inhaled corticosteroid use	64 (26.6)	59 (24.7)
Salbutamol responsive†	138 (58.7)	128 (54.5)
Parental history of asthma	102 (42.9)	102 (42.7)
Positive Asthma Predictive Index	141 (59.2)	147 (61.5)
Baseline PRAM score at triage, mean (SD)	5.7 (1.8)	5.7 (1.9)
PRAM score after first hour of treatment,‡ mean (SD)	2.9 (2.1)	2.7 (2.0)

*Tobacco exposure data available for 236 patients in the prednisolone group and 233 in the placebo group.

†Defined as reduction in PRAM score of ≥ 3 recorded 20 min following three doses of 600 mcg salbutamol administered via a spacer in the first hour of treatment.

‡Recorded 20 min following three doses of 600 mcg salbutamol administered via spacer in the first hour of treatment.

PRAM, Preschool Respiratory Assessment Measure; SD, standard deviation; URTI, upper respiratory tract infection.

means, -0.39 (95% CI, -0.84 to 0.06), $p=0.09$). Similarly, on subgroup analysis, there was no difference between groups in those assessed as salbutamol responsive, for children with a positive Asthma Predictive Index, or on the basis of baseline PRAM score (table 3).

Absolute PRAM score was lower at 4 and 24 hours in the prednisolone group (table 4), with more participants in the prednisolone group having a PRAM score of 0 at 24 hours compared with the placebo group. Fewer patients in the prednisolone group received additional oral prednisolone (OR 0.22) or treatment with intravenous medication (salbutamol, hydrocortisone, magnesium sulphate or aminophylline) (OR 0.27). Decreased hospital admission and shorter ED stay if discharged in those who received prednisolone were of borderline statistical significance. There were no differences between groups for number of doses of salbutamol administered within the first 48 hours, length of stay for those admitted, representation rates to ED/primary care within 7 days or other long-term secondary outcomes (table 4).

DISCUSSION

This study found that in children aged 24–59 months presenting to hospital with acute wheeze, treatment with oral prednisolone was equivalent to placebo for respiratory outcomes at 24 hours and at 7 days after presentation. Subgroup analyses showed no evidence that treatment effect differed for children who were salbutamol responsive, had a positive Asthma Predictive Index

Table 3 Primary outcome with subgroup analyses

Outcomes	Prednisolone	N	Placebo	N	Difference (95% CI)	P value
Change in PRAM score at 24 hours,* mean (SD)	-5.12 (2.14)	198	-4.73 (2.38)	195	-0.39 (-0.84 to 0.06)	0.09
<i>Subgroup analyses</i>						
Salbutamol responsive						0.94†
Yes	-5.87 (1.97)	114	-5.53 (2.21)	103	-0.33 (-0.89 to 0.22)	
No	-4.11 (1.99)	81	-3.81 (2.25)	90	-0.30 (-0.94 to 0.34)	
Asthma Predictive Index						0.19†
Positive	-4.93 (2.16)	119	-4.78 (2.33)	119	-0.15 (-0.73 to 0.42)	
Negative	-5.41 (2.10)	79	-4.64 (2.47)	76	-0.76 (-1.49 to 0.03)	
Baseline PRAM score‡						
3 to 8 (mild/moderate)	-4.84 (1.90)	185	-4.46 (2.14)	178	-0.38 (-0.80 to 0.03)	0.13†
9 to 12 (severe)	-9.15 (0.99)	13	-7.59 (2.92)	17	-1.57 (-3.15 to 0.01)	
3 to 4 (mild)	-2.88 (1.30)	51	-2.71 (1.44)	56	-0.17 (-0.69 to 0.36)	0.65†
5 to 12 (moderate/severe)	-5.90 (1.80)	147	-5.54 (2.20)	139	-0.36 (-0.83 to 0.11)	

*PRAM score for primary outcome was measured at a mean time of 24 hours and 03 min (SD 6 hours and 33 min) in the prednisolone group and a mean time of 23 hours and 53 min (SD 7 hours and 43 min) in the placebo group (difference between means $p=0.83$).

†P value for subgroup interaction

‡Post hoc analysis

CI, confidence level; PRAM, Preschool Respiratory Assessment Measure; SD, standard deviation.

Table 4 Short-term and long-term secondary outcomes

Outcomes	Prednisolone	N	Placebo	N	Difference/OR (95% CI)	P value
<i>Short-term</i>						
PRAM score at 4 hours, median (IQR)	1 (0 to 2)	167	2 (0 to 3)	169	0 (-1 to 0)*	0.01
Change in PRAM score at 4 hours†, mean (SD)	-4.18 (2.26)	167	-3.51 (2.45)	169	-0.67 (-1.18 to -0.16)	0.01
PRAM score at 4 hours, † No. (%)						
0 (no disease)	44 (26.4%)	167	43 (25.4%)	169	-	0.003
1 to 4 (mild disease)	115 (68.9%)		97 (57.4%)			
5 to 8 (moderate disease)	8 (4.8%)		26 (15.4%)			
9 to 12 (severe disease)	0 (0%)		3 (1.8%)			
PRAM score at 24 hours, median (IQR)	1 (0 to 1)	198	0 (0 to 1)	195	0 (0 to 0)*	0.01
PRAM score at 24 hours, † No. (%)						
0 (no disease)	127 (64.1%)	198	105 (53.9%)	195	-	0.15
1 to 4 (mild disease)	67 (33.8%)		82 (42.1%)			
5 to 8 (moderate disease)	4 (2.0%)		7 (3.6%)			
9 to 12 (severe disease)	0 (0%)		1 (0.5%)			
Length of ED stay for discharged patients, median (IQR), hours	5.6 (4.2 to 7.7)	171	6.0 (4.5 to 8.9)	161	-0.57 (-1.15 to 0.02)*	0.06
Requirement for hospital admission, No. (%); OR	56 (23.5)	238	75 (31.4)	239	0.67 (0.45 to 1.01)	0.05
Length of inpatient stay, median (IQR), hours	26.3 (18.6 to 36.9)	54	29.2 (22.2 to 40.8)	70	-2.9 (-7.8 to 2.4)*	0.27
MDI doses of salbutamol in first 48 hours, median (IQR)	18 (6 to 36)	231	18 (6 to 56)	234	0 (-6 to 0)*	0.27
Treatment with additional open label oral prednisolone, No. (%); OR	3 (1.3%)	238	13 (5.4%)	239	0.22 (0.06 to 0.79)	0.01
					NNT=24 (13 to 109)	
<i>Adverse events</i>						
Admission to intensive care unit, No. (%); OR	2 (0.8%)	238	0 (0%)	239	Undefined	-
Treatment with intravenous medication, No. (%); OR	3 (1.3%)	238	11 (4.6%)	239	0.27 (0.07 to 0.96)	0.03
					NNT=30 (15 to 444)	
Representation to hospital within 7 days, No. (%); OR	2 (0.8%)	238	2 (0.8%)	239	1.00 (0.14 to 7.18)	1.00
Representation to primary care within 7 days, No. (%); OR	17 (7.1%)	238	23 (9.6%)	239	0.72 (0.38 to 1.39)	0.33
<i>Long-term</i>						
Condition improved at 7 days, No. (%); OR	195 (96.1%)	203	208 (98.1%)	212	0.47 (0.14 to 1.59)	0.22
Back to usual self at 7 days, No. (%); OR	177 (87.6%)	202	187 (87.8%)	213	0.98 (0.55 to 1.77)	0.96
MDI doses of salbutamol in first 7 days, median (IQR)	78 (36 to 126)	105	87 (42 to 135)	106	-8 (-24 to 8)*	0.33

*Medians, difference and 95% CI estimated using Hodges-Lehmann estimates, p values from Wilcoxon test.

†Post hoc analysis.

CI, confidence level; ED, emergency department; IQR, interquartile range; MDI, metered dosed inhaler; NNT, number needed to treat; OR, odds ratio; PRAM, Preschool Respiratory Assessment Measure; SD, standard deviation.

or more severe disease at presentation (higher PRAM score). However, those who received prednisolone had less respiratory distress 4 hours after medication administration and reduced requirement for hospital admission, additional corticosteroid or intravenous treatment. These findings suggest that early in-hospital administration of oral prednisolone to preschoolers with wheeze may prevent further deterioration and requirement for escalation of therapy.

Our finding of initial corticosteroid benefit is consistent with those of a recent study of 605 children aged 2–6 years with wheezy respiratory illnesses, which reports that length of stay was reduced by nearly 3 hours in patients randomised to prednisolone.¹¹ Of note, the effect of prednisolone on length of stay in that study was greater for children presenting with more severe wheeze. In contrast, in a study of 687 children aged 10–60 months presenting with wheezy respiratory illnesses, randomised to prednisolone or placebo, no differences were found for length of stay or other outcomes.¹² However, this second study included considerable numbers of very young children with a probable diagnosis of bronchiolitis, for which corticosteroids are ineffective.¹⁷

The observation that acute wheeze in preschoolers resolves in the vast majority by 24 hours with no recrudescence is novel. Median PRAM score in both groups of participants at 24 hours was 0, with only a handful of children in each group having a PRAM score >4 and no child with a score >8. These findings suggest that wheezy respiratory illnesses in preschoolers are short-lived, with the usual clinical course being rapid improvement following assessment and implementation of bronchodilator therapy. Our finding of rapid resolution of wheeze, even in the placebo participants, may help explain the inconsistent results of previous studies.¹⁰

The novel finding of rapid resolution of wheeze is discordant with the majority of international clinical practice guidelines which support treating wheezy preschoolers with a 3-day course of corticosteroids,^{4,5} as used for management of acute asthma in older children and adults. However, preschool wheeze is a heterogeneous condition with numerous factors contributing to a wheezy phenotype, often simultaneously.^{6,7} Therefore, it is perhaps inappropriate to align acute management of wheeze in preschoolers with asthma in older children. Our study is the first to suggest that corticosteroid treatment, if used at all for management of acute wheeze in preschoolers, should be of very limited duration.

Of the 1057 children eligible, 493 (47%) consented to participate, similar to rates obtained by Foster.¹¹ Our results are generalisable to the wider population of preschoolers with moderate acute wheeze, with previous diagnosis of asthma in 30% (Foster *et al* 24%¹¹; Panickar *et al* 18%¹²) and previous parental report of wheeze in 90% (Foster *et al* 69%¹¹; Panickar *et al* 66%¹²).

Study strengths include our large sample size, recruited from three hospitals, with ethnic diversity representative of the New Zealand population, and a lower age limit for participants of 24 months, ensuring that those with bronchiolitis were not included. The inclusion of children as young as 6 months in previous studies has limited the ability to draw conclusions regarding the efficacy of corticosteroids for wheezy respiratory illnesses outside of the bronchiolitis age range.^{12,18,19} A further strength was use of the PRAM score to assess respiratory status, thereby avoiding the inevitable biases inherent in outcomes such as admission rate and length of stay. This tool was developed using multivariate analysis to model respiratory signs against formal respiratory function in children aged 3–6 years presenting with wheeze and subsequently validated in controls.¹³ The

PRAM score has excellent interobserver agreement, correlates well with clinical outcomes and has been validated in infants down to 18 months old.^{14,20–22} By comparison, Foster assessed respiratory status using a pulmonary score that is not validated for children <5 years, making generalisation of findings to this younger group difficult.¹¹ However, despite the external robustness of the PRAM score, in post hoc analysis, it could not stratify at triage patients responsive to prednisolone. This suggests that preschoolers with acute wheeze declare themselves in need of admission or suitable for discharge sometime after presentation. Consistent with this, in post hoc analysis Foster *et al*¹¹ found an effect of prednisolone on length of stay only in those discharged after 4 hours.

Limitations of our study include loss to follow-up for the primary outcome and incomplete secondary outcome data. It was not possible to contact all patients following discharge. Socioeconomic deprivation is common in our population of children presenting with wheezy illnesses²³ and may have played a role in follow-up difficulties. However, the existence within New Zealand of a single healthcare identification number ensures that follow-up of subsequent presentations was complete, giving reassurance that those lost to follow-up did not have these outcomes.

This study did not include children less than 24 months of age. While most children less than 12 months of age presenting to hospital with wheeze associated with respiratory illness have bronchiolitis, a condition for which corticosteroids are ineffective,¹⁷ most wheezy children aged 12–24 months have aetiologies similar to those included in our study. Further studies are required to determine the effect of prednisolone in children aged 12–24 months presenting with wheeze. In addition, our finding of equivalent respiratory status at 24 hours with no symptom recrudescence regardless of initial treatment suggests that further doses of prednisolone are potentially unnecessary. Thus, future research is needed to investigate respiratory outcomes for children treated with a single dose of oral prednisolone in comparison to a more conventional 3-day course.

Our analysis did not adjust for multiple comparisons in secondary outcomes. A number of statistical comparisons had final p values between 0.01 and 0.05. These results would not be considered significant following most methods of adjustment for multiple comparisons.

In conclusion, administration of oral prednisolone to preschoolers presenting to hospital with wheeze does not alter respiratory outcomes at 24 hours or beyond, when most children have improved regardless of initial treatment. However, our findings of reduced requirement for hospital admission and escalation of therapy in the treatment group suggest that oral prednisolone may improve short-term respiratory outcomes for preschoolers presenting with wheeze and that subsequent doses of oral prednisolone may provide no additional therapeutic benefit. Further studies are required to investigate this hypothesis further.

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Data availability statement Data are available on reasonable request. The authors support data sharing. The WASP trial used identifiable individual patient data that are subject to restriction, including ethics, consent and privacy issues. Anonymised (deidentified) data will be available on request from the corresponding author (Professor Stuart R Dalziel s.dalziel@auckland.ac.nz), where possible within these constraints for use, following review by the trial steering committee of the protocol and statistical analysis plan.

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Correction: *Impact of oral corticosteroids on respiratory outcomes in acute preschool wheeze: a randomised clinical trial*

Wallace A, Sinclair O, Shepherd M, *et al.* Impact of oral corticosteroids on respiratory outcomes in acute preschool wheeze: a randomised clinical trial. *Arch Dis Child* 2021;106:339–44. doi: 10.1136/archdischild-2020-318971.

The trial registration number was omitted during production of this article. It is anzctr.org.au: ACTRN12614000847617.

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