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A Multicenter, Randomized, Controlled Trial of Dexamethasone for Bronchiolitis

[Original Articles]

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Abstract

Background: Bronchiolitis, the most common infection of the lower respiratory tract in infants, is a leading cause of hospitalization in childhood. Corticosteroids are commonly used to treat bronchiolitis, but evidence of their effectiveness is limited.

Methods: We conducted a double-blind, randomized trial comparing a single dose of oral dexamethasone (1 mg per kilogram of body weight) with placebo in 600 children (age range, 2 to 12 months) with a first episode of wheezing diagnosed in the emergency department as moderate-to-severe bronchiolitis (defined by a Respiratory Distress Assessment Instrument score greater/equal 6). We enrolled patients at 20 emergency departments during the months of November through April over a 3-year period. The primary outcome was hospital admission after 4 hours of emergency department observation. The secondary outcome was the Respiratory Assessment Change Score (RACS). We also evaluated later outcomes: length of hospital stay, later medical visits or admissions, and adverse events.

Results: Baseline characteristics were similar in the two groups. The admission rate was 39.7% for children assigned to dexamethasone, as compared with 41.0% for those assigned to placebo (absolute difference, -1.3%; 95% confidence interval [CI], -9.2 to 6.5). Both groups had respiratory improvement during observation; the mean 4-hour RACS was -5.3 for dexamethasone, as compared with -4.8 for placebo (absolute difference, -0.5; 95% CI, -1.3 to 0.3). Multivariate adjustment did not significantly alter the results, nor were differences detected in later outcomes.

Conclusions: In infants with acute moderate-to-severe bronchiolitis who were treated in the emergency department, a single dose of 1 mg of oral dexamethasone per kilogram did not significantly alter the rate of hospital admission, the respiratory status after 4 hours of observation, or later outcomes. (ClinicalTrials.gov number, NCT00119002.)

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Bronchiolitis is the leading cause of hospitalization for infants in the United States, [1] accounting for 100,000 admissions annually, with hospital charges alone estimated at \$700 million. [2] Hospitalization rates for infants with bronchiolitis more than doubled between 1980 and 1996, and the proportion of infant hospitalizations that were due to bronchiolitis more than tripled, from 5% to 16%. [2]

Treatment for bronchiolitis is controversial. Bronchodilators are commonly used, [3,4] but they have not been shown to have consistent benefits. [5-8] Although studies suggest that approximately a quarter of infants hospitalized with bronchiolitis receive corticosteroids, [3,4,9] the efficacy of these agents has also not been consistently demonstrated. [5,8,10] Most positive [11-15] and negative [16-19] studies of corticosteroids have been small and heterogeneous in design, but a controlled trial involving 70 infants with moderate-to-severe bronchiolitis was reported by Schuh and colleagues in 2002. [20] They found significant reductions in respiratory scores after 4 hours of observation in infants who received 1 mg of oral dexamethasone per kilogram of body weight, as compared with those who received placebo. Moreover, the admission rate was 19% in the dexamethasone group, as compared with 44% in the placebo group.

A number of experts and reviews [5,8,10,21] have called for further study of corticosteroids for bronchiolitis. The 2003 report published by the Agency for Healthcare Research and Quality (AHRQ) [5] stated that there is "no evidence that any single agent can be recommended for treatment of bronchiolitis," and it called for a "rigorously designed and adequately sized trial" of agents to include dexamethasone. The goal of our study was to determine the effectiveness of a single dose of oral dexamethasone in infants with moderate-to-severe bronchiolitis.

Methods

Patients

We conducted the study in 20 emergency departments of the Pediatric Emergency Care Applied Research Network (PECARN) [22] during bronchiolitis season (November through April) from January 2, 2004, through April 30, 2006. Planned start and end dates were the same for all centers. The institutional review boards at all sites approved the study. Written informed consent was obtained from the parent or guardian of each infant included in the study.

We included infants 2 to 12 months of age who were brought to the emergency department with a first episode of bronchiolitis, defined as wheezing (with no prior bronchiolitis, wheezing, or asthma and no bronchodilator use before the current illness), within 7 days after the onset of symptoms. In addition, the episode had to be moderate or severe as defined by a score on the Respiratory Distress Assessment Instrument (RDAI) [23] of 6 or more (on a scale of 0 to 17, with

higher scores indicating more severe respiratory symptoms) (Table 1). We excluded infants with a prior adverse reaction to dexamethasone, known heart or lung disease, premature birth (defined as birth before 36 weeks of gestation), immunosuppression or immunodeficiency, treatment with corticosteroids in the previous 14 days, active varicella or recent exposure to varicella, or inability of the parent or guardian to speak English or Spanish. Critically ill infants were also excluded.

Table 1. Wheezing and Retraction Scales for the Respiratory Distress Assessment Instrument (RDAI).^{*}

Symptom	Points					Maximum
	0	1	2	3	4	
Wheezing						
During expiration	None	End	First half	First three quarters	Throughout	4
During inspiration	None	Part	Throughout	—	—	2
No. of involved lung fields	0	1 or 2	3 or 4	—	—	2
Retractions						
Supraclavicular	None	Mild	Moderate	Marked	—	3
Intercostal	None	Mild	Moderate	Marked	—	3
Subcostal	None	Mild	Moderate	Marked	—	3
Total						17

^{*} Both wheezing and retractions were scored. The total score on the RDAI is the sum of the scores for each row, with a range of 0 to 17; higher scores indicate more severe disease.

Table 1. Wheezing and Retraction Scales for the Respiratory Distress Assessment Instrument (RDAI) .

Infants were screened for eligibility during times when a research assistant and study clinician (emergency department faculty, fellow, or nurse practitioner) were available. Each center kept a record of all screened infants, including those who arrived when study staff were available and who underwent screening but were not enrolled. Research assistants and all study clinicians received yearly training from site lead investigators in study procedures and respiratory scoring. Site monitors visited each site during and after data collection to audit all study records.

Before enrollment, study clinicians confirmed clinical bronchiolitis and determined the duration of symptoms and the RDAI score. Research assistants or clinicians obtained the medical history from parents or guardians on a standardized data-collection form, which included questions about a history of eczema in the patient, a family history of asthma in the immediate family, and the presence of smokers or pets at home. Infants with eczema or a family history of asthma were considered to have possible atopy and, as recommended in the AHRQ report, [5] were treated as a prespecified subgroup in the analysis. At enrollment and 1 hour and 4 hours after administration of the study medication, a nurse recorded clinical variables (respiratory and heart rates, temperature, and oxygen saturation while the infant was breathing ambient air). A study clinician repeated respiratory scoring 1 hour and 4 hours after the administration of the study medication and assessed each child for discharge or admission after 4 hours.

Randomization

We performed computerized randomization by telephone, using the keypad for data entry. Infants were assigned in equal numbers to the dexamethasone and placebo groups with the use of random permuted blocks stratified by center. All emergency department staff, study personnel, and parents and guardians were unaware of the group assignments. Randomization codes were secured until all data entry was complete.

Study Intervention

Using the same formulation as in prior studies, [20,24] research pharmacies prepared oral dexamethasone solutions (1 mg per milliliter of liquid) from generic dexamethasone phosphate injection solution and identical oral placebo solutions. The preparations were packaged in identical clear plastic vials labeled only with the randomization numbers. A nurse orally administered 1 ml of solution per kilogram, providing 1 mg of dexamethasone per kilogram in the dexamethasone group (maximum, 12 mg). Any episode of vomiting within 20 minutes after administration of the study medication was recorded, but the dose was not repeated.

For ethical, practical, and scientific reasons, all other bronchiolitis treatments were provided according to the clinician's preference and local standards. Any diagnostic testing, including viral testing, was also left to the clinician's discretion, and tests were performed with assays available at the participating center. Because testing for other viruses varied, only the results for respiratory syncytial virus were recorded.

After 7 to 10 days, a research assistant, who was unaware of the group assignments, reviewed the chart and conducted a brief standardized telephone interview with the parent or guardian. The interview included questions about whether hospitalization, unscheduled medical visits, or adverse reactions to the study drug (as judged by a physician or the parent or guardian) had occurred within 7 days after the initial emergency department visit.

Outcome Measures

The primary outcome was the decision to hospitalize or discharge the infant 4 hours after the administration of the study medication. Infants requiring admission to an intensive care unit before 4 hours of observation had been completed were included in the analysis of admissions. The secondary outcome was the Respiratory Assessment Change Score (RACS) at 4 hours. [23] The RACS is calculated as the sum of the change in the RDAI score and a standardized score for the change in the respiratory rate, with a reduction of 1 unit for a decrease of 5 to 15%, 2 units for a decrease of 16 to 25%, and so on. [20,23] Thus, negative RACS values signify improvement. Other investigators have interpreted a change of 2 units or more as clinically important. [20]

Adverse Events

Study clinicians and research assistants monitored the infants for adverse events during observation in the emergency department. Subsequent adverse events were determined at follow-up. A patient-safety committee, made up of people not involved with patient enrollment, tracked all adverse events.

Statistical Analysis

Assuming a 40% admission rate in the placebo group, we calculated the sample size that would be required to provide more than 80% power (with a two-sided alpha level of 0.05) to detect an absolute reduction in hospital admission rates of 12% or more in the dexamethasone group. A biostatistician participated in the study design and performed all analyses. The primary analysis was based on the intention-to-treat principle, with all patients included in their assigned group. A secondary, per-protocol analysis examined the results among infants who actually received the assigned study medication.

Hospital admission rates were compared with the use of Pearson's chi-square test. The RACS was compared in the two groups by means of a two-sample t-test. Adjusted measures and subgroup effects for admission and RACS were analyzed with the use of logistic regression and linear regression, respectively. Generalized estimating equations and linear mixed models were used to test for an interaction between treatment group and site in the admission and RACS outcomes, respectively. Changes in clinical variables after 4 hours of observation were regressed against baseline values and treatment group as predictors. Length-of-stay measures were compared by means of the two-sample Wilcoxon test. The alpha level was set at 0.05 for all analyses, 95% confidence intervals were calculated, and all comparisons were two-tailed.

Results

A total of 8686 infants were screened for study eligibility ([Figure 1](#)). Among the 7352 infants who did not meet the inclusion criteria, two thirds had either prior wheezing (41%) or an RDAI score of less than 6 (25%). Of the 600 infants who underwent randomization, 305 were assigned to the dexamethasone group and 295 to the placebo group; all were included in the intention-to-treat analysis. Two randomly assigned infants were hospitalized before administration of the study drug, leaving 598 treated infants. Five of these infants received the wrong medication because of errors in vial selection, and 1 received an insufficient dose of dexamethasone, leaving 592 patients in the per-protocol analysis. The results of this analysis did not differ qualitatively from those of the intention-to-treat analysis. A detailed subanalysis according to the results of tests for respiratory syncytial virus revealed no significant differences in any of the studied outcomes between infants with positive results and those with negative results ([Figure 2](#)).

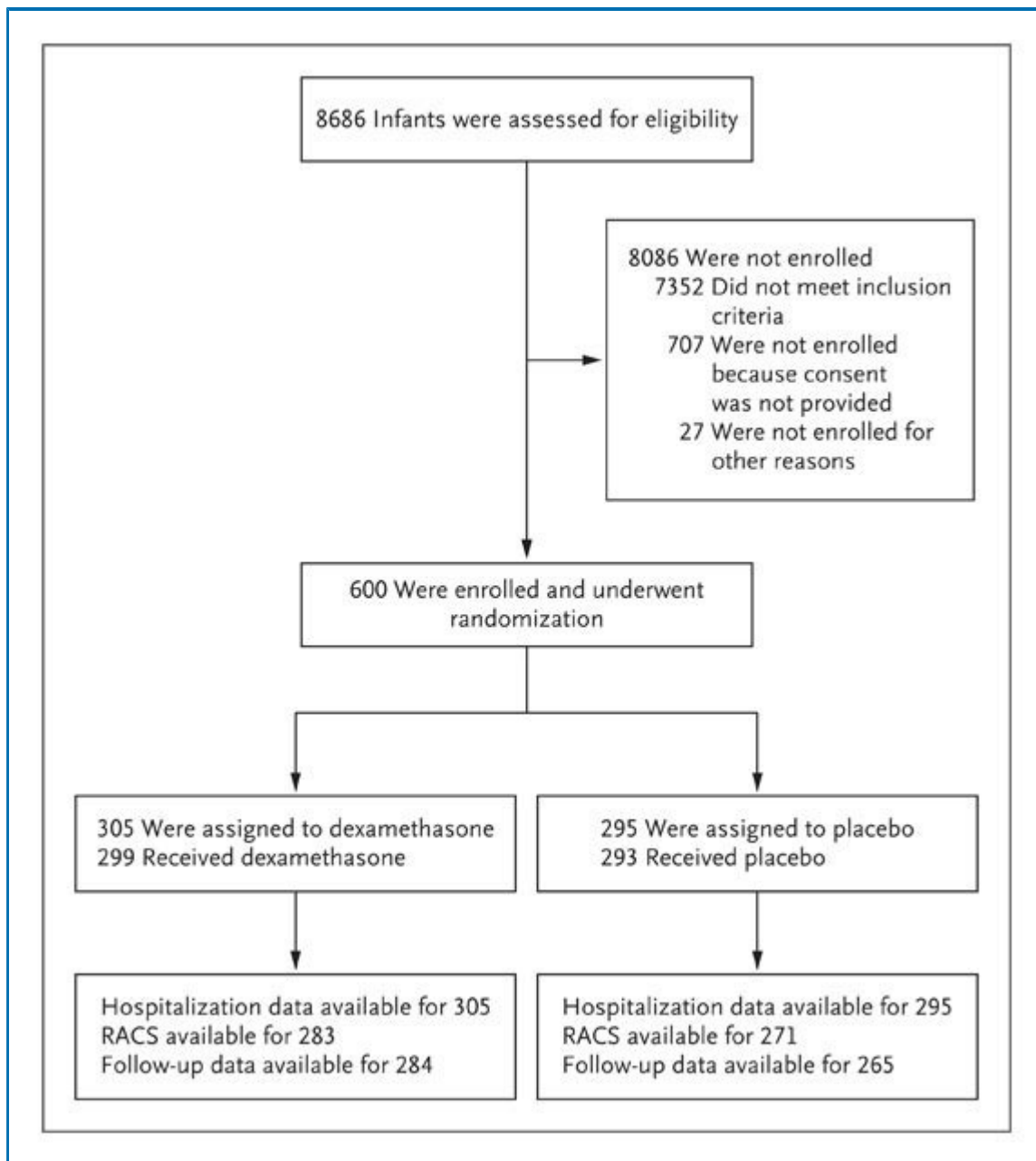


Figure 1. Eligibility, Randomization, and Follow-up. Among the 7352 infants who did not meet the criteria for inclusion in the study, two thirds had either prior wheezing or mild disease; the remainder met other exclusion criteria. For the primary outcome, hospital admission, data were available for all 600 infants in the intention-to-treat analysis. The secondary outcome, the Respiratory Assessment Change Score (RACS), included two variables, respiratory rate and Respiratory Distress Assessment Instrument (RDAI) score, that were compared at baseline and after 4 hours of observation. Follow-up involved a single telephone interview with each infant's parent or guardian .

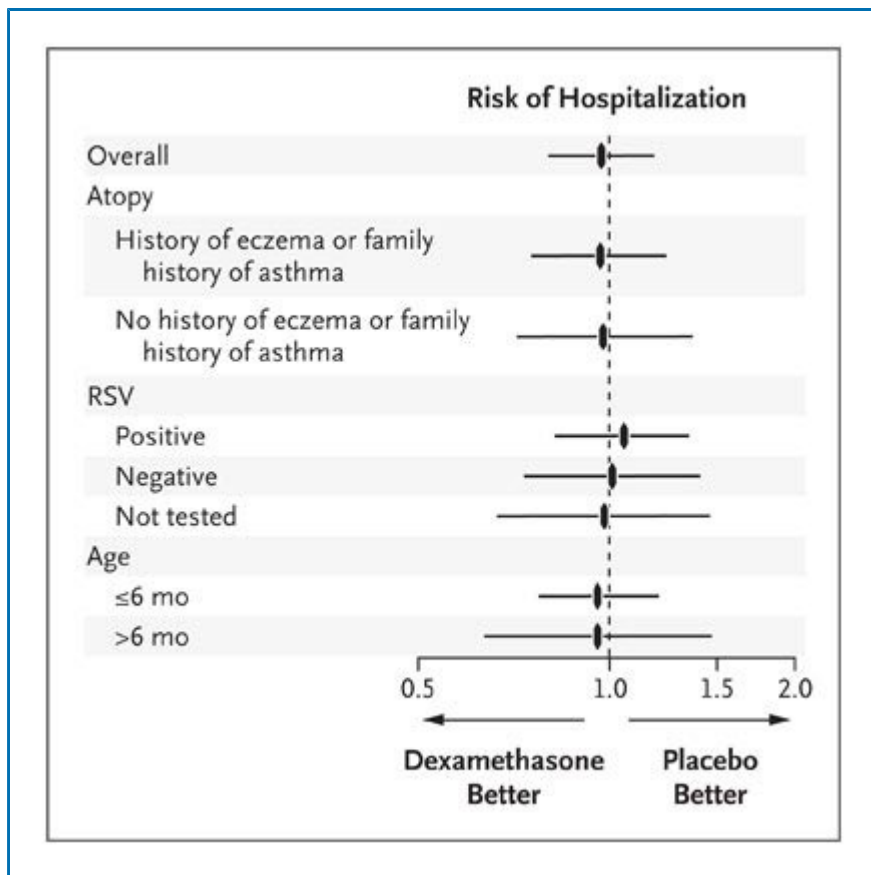


Figure 2. Risk Ratios for Hospital Admission. Estimated risk ratios (the risk of hospitalization in the dexamethasone group as compared with that in the placebo group) are shown for the overall study groups, as well as for specific subgroups evaluated in bivariate analysis. The horizontal lines represent the 95% confidence intervals. Risk ratios of less than 1.0 favor the use of dexamethasone; the value 1.0 represents equivalence between the dexamethasone group and the placebo group. Testing for the respiratory syncytial virus (RSV) was performed in 269 infants; 325 did not undergo testing, and in the case of 6 infants, it is not known whether testing was performed.

Baseline demographic and clinical characteristics were similar in the dexamethasone and placebo groups (Table 2). Similar proportions of infants received inhaled bronchodilator treatment, either with albuterol (77.0% and 80.3%, respectively) or epinephrine (15.5% and 16.7%, respectively). The number of such treatments received was also similar, with a mean of 2.0 treatments with albuterol and 1.2 treatments with epinephrine in each study group.

Table 2. Baseline Characteristics of the Infants According to the Assigned Study Group.*

Characteristic	Dexamethasone (N = 304)	Placebo (N = 294)
Male sex — no./total no. (%)	190/304 (62.5)	178/294 (60.5)
Age — mo	5.1±2.6	5.1±2.8
RDAl score	9.0±2.1	9.2±2.4
Respiratory rate — breaths/min	53±13	53±13
Heart rate — beats/min	157±20	158±21
Temperature — °C	37.6±0.8	37.7±0.8
Oxygen saturation — %	96±4	96±4
No. of days of illness	3.7±2.5	3.6±2.5
RSV-positive — no. positive/ no. tested (%)	85/127 (66.9)	81/142 (57.0)
History — no./total no. (%)		
Family history of asthma	165/295 (55.9)	170/284 (59.9)
History of eczema	76/292 (26.0)	77/281 (27.4)
Either family history of asthma or history of eczema	187/295 (63.4)	196/284 (69.0)
Smoker in home — no./total no. (%)	117/300 (39.0)	103/287 (35.9)
Pet in home — no./total no. (%)	97/299 (32.4)	90/282 (31.9)

* The data do not include two patients who were hospitalized before the administration of study medication. Plus-minus values are means ±SD. RDAl denotes Respiratory Distress Assessment Instrument, and RSV respiratory syncytial virus.

Table 2. Baseline Characteristics of the Infants According to the Assigned Study Group .

Hospital Admission

We found no significant difference between the study groups with respect to hospitalization. Of the 305 infants in the dexamethasone group, 121 (39.7%) were admitted, as compared with 121 of the 295 infants (41.0%) in the placebo group (absolute difference, -1.3%; 95% confidence interval [CI], -9.2 to 6.5; $P=0.74$). Neither was there a significant difference when admission was analyzed in the prespecified subgroup with eczema or a family history of asthma (absolute difference, -1.3%; 95% CI, -11.1 to 8.5). [Figure 2](#) shows the relative risk of admission overall and in this and other subgroups.

Respiratory Assessment Change Score

The respiratory status of both study groups improved during treatment and observation in the emergency department, but mean RACS values did not differ significantly between the groups (Table 3). Neither was there a significant difference when RACS values were analyzed in the subgroup with eczema or a family history of asthma (absolute difference, -0.4; 95% CI, -1.3 to 0.6).

Variable	Dexamethasone Group	Placebo Group	Difference between Groups (95% CI)	P Value
Hospital admission (%)	39.7	41.0	-1.3 (-9.2 to 6.5)	0.74
RACS	-5.3±4.7	-4.8±4.6	-0.5 (-1.3 to 0.3)	0.21
RDAI score	-4.4±3.1	-3.9±3.2	-0.5 (-1.0 to -0.1)	0.03
Respiratory rate (breaths/min)	-8±15	-7±14	-1.0 (-3.0 to 1.0)	0.39
Oxygen saturation (%)	0.3±3.3	0.9±3.2	-0.6 (-1.0 to -0.1)	0.02
Heart rate (beats/min)	-13±24	-5±25	-8.0 (-12.0 to -5.0)	<0.001
Temperature (°C)	-0.6±0.9	-0.2±1.0	-0.4 (-0.6 to -0.3)	<0.001

* Data for all variables except hospital admission are expressed as the change from baseline to 4 hours. RACS denotes Respiratory Assessment Change Score, and RDAI Respiratory Distress Assessment Instrument.

Table 3. Hospital Admission and Changes in Clinical Variables from Baseline to 4 Hours after Intervention .

Other Outcomes

(Table 3) also shows differences in the clinical variables between the baseline and 4-hour observations. Changes in the respiratory rate did not differ significantly between the two study groups. Although changes in the RDAI score, oxygen saturation, temperature, and heart rate did differ significantly between the groups, these differences were small.

The mean length of stay for hospitalized patients was 2.55 days in the dexamethasone group and 2.27 days in the placebo group (P=0.10). Subsequent hospital admissions in the 7 days after the intervention were reported for 12 of 284 children in the dexamethasone group (4.2%) and 10 of 265 children in the placebo group (3.8%).

The results for admission and RACS outcomes in multivariate regression models were virtually identical to those in the unadjusted models (data not shown). The site had no significant effect on treatment outcomes.

Adverse Events

There were few adverse events. Vomiting within 20 minutes after administration of the study medication occurred in 5.5% of the dexamethasone group and 4.7% of the placebo group. No infant had gastrointestinal bleeding, hypertension, or complicated varicella. Pneumonia was diagnosed in three infants; two were in the placebo group, and an empyema developed in one of these two infants.

Discussion

Our multicenter, randomized, double-blind study of 600 infants with acute, moderate-to-severe bronchiolitis in the emergency department showed no significant reduction in hospital admissions or improvement in respiratory status after 4 hours of observation when infants given a single oral dose of 1 mg of dexamethasone per kilogram were compared with infants given placebo. This was true whether or not the infants had markers of possible atopy. Furthermore, among the infants who received dexamethasone, as compared with those who received placebo, there was no reduction in the duration of hospitalization for those who were initially admitted, and there were no reductions in later, unscheduled admissions or visits to an emergency department or physician for those who were initially discharged.

Several studies have already noted the use of corticosteroids in bronchiolitis despite the absence of definitive evidence of any benefit. [3,4,9] The authors of the AHRQ report [5] thought this use of corticosteroids would persist "unless a large simple trial of the most common interventions is mounted." Following their recommendations, we designed a study with sufficient power to evaluate hospitalization rates, an "important outcome to parents, clinicians, and health systems." [5] Even at our observed limit of uncertainty (a 9.2% reduction in admissions), 11 patients would need to be treated with dexamethasone to prevent one admission.

Because the response to corticosteroids might differ in children with possible atopy, our prespecified subgroup analysis examined outcomes according to whether the infants had eczema or a family history of asthma. Because bronchiolitis is a clinical syndrome caused by several viruses, we also examined outcomes according to whether the infants were positive or negative for respiratory syncytial virus. No significant differences between the study groups were found in these analyses, which suggests that none of these factors identify a subgroup of infants who have a response to dexamethasone.

Small differences between groups (as shown in Table 3) may be statistically significant when large samples are compared. An antipyretic effect of dexamethasone may account for the small differences observed in temperature and heart rate. [21,25] Although these two variables are not typically central to the assessment of bronchiolitis, oxygen saturation is considered central to this assessment. For this variable, however, the small difference actually favored placebo. The small difference in RDAI scores between the study groups became nonsignificant when incorporated into the overall RACS.

Our findings are consistent with studies that failed to demonstrate the efficacy of corticosteroids in bronchiolitis. [8,16-19] A collective review by the Cochrane Collaboration of 13 studies of the use of corticosteroids for bronchiolitis [10] showed no significant differences between corticosteroid and placebo groups in respiratory rates, oxygen saturation, initial admission rates, length of stay, subsequent visits, or readmission rates. [10] The AHRQ report [5] analyzed five placebo-controlled studies of oral corticosteroids, including dexamethasone, and two placebo-controlled studies of parenteral dexamethasone. Only one study [20] showed a significant difference between groups. In 2006, a subcommittee of the American Academy of Pediatrics reviewed the evidence from previous studies and recommended that corticosteroids not be used routinely for bronchiolitis. [8] All of these reviews, however, note the inconclusive nature of the available evidence.

Some studies [11-14,26] have suggested a benefit of corticosteroid therapy, and the size, methods, and findings of these studies have been carefully reviewed. [5,10] A meta-analysis [27] of six trials of systemic corticosteroids in infants with bronchiolitis showed a small benefit in the corticosteroid groups, but this effect did not persist when outcomes were analyzed separately or when only studies of first-time wheezing were examined.

The results of our study differ from those of the study by Schuh et al. [20] The two studies used the same dose of dexamethasone (1 mg per kilogram), with 4 hours of observation in the emergency department and outcomes of hospitalization and RACS, but they differ in certain respects. In the study by Schuh et al., oral dexamethasone (0.6 mg per kilogram) or placebo was continued for 5 days in patients discharged home. This would not, however, affect the study's main outcomes - hospitalization and RACS after 4 hours. We studied infants in the first year of life, whereas Schuh et al. included children up to 24 months of age. By chance, the dexamethasone group in their study had a significantly higher proportion of infants with family histories of atopy than did the placebo group. Our study groups were balanced in this regard. Their study was substantially smaller and conducted at a single institution, where all infants were treated with a standardized bronchodilator regimen. Given the current wide variation in the use of bronchodilators [3,4] and uncertainty regarding their effectiveness, [5,10] we did not try to control bronchodilator use. Our study was not powered to examine possible interactions between bronchodilators and dexamethasone. We did, however, confirm that the types and numbers of bronchodilator treatments were similar in the two groups.

Our study had some limitations. For both ethical and scientific reasons, we sought to exclude children with possible early asthma, who might have benefited from dexamethasone. We therefore studied only young infants with first-time wheezing. Older children or children with recurrent wheezing might have a different response to dexamethasone.

We studied a single oral dose of dexamethasone (1 mg per kilogram). The size of the dose makes it unlikely that more medication would be effective. Oral administration and a 4-hour observation period were chosen to replicate the methods used by Schuh et al. [20] Although the biologic basis of the effect is not clear, their study and ours were predicated on extensive evidence that oral corticosteroids are effective within 4 hours in patients with asthma [28-33] and those with croup. [34-36]

It is unlikely that we missed a later benefit of dexamethasone. We collected data on later outcomes, including the length of the hospital stay among infants who were initially admitted, subsequent admissions or unscheduled medical visits, and adverse events in the two study groups. If dexamethasone had been effective after the passage of 4 hours, this result should have been apparent in one or more of these later outcomes.

In summary, in our multicenter study of 600 infants from 2 to 12 months of age who had moderate-to-severe bronchiolitis, we found that treatment with 1 mg of oral dexamethasone per kilogram did not significantly alter the rate of hospital admission or the respiratory status after 4 hours of observation. Neither did such treatment affect the length of the hospital stay among infants who were initially admitted, subsequent admissions or unscheduled medical visits, or adverse events. We recommend evaluation of other treatments and preventive strategies for

bronchiolitis.

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Appendix

In addition to the authors, the following investigators participated in the PECARN bronchiolitis study: Washington University and St. Louis Children's Hospital, St. Louis - D. Jaffe; Children's National Medical Center and George Washington University, Washington, DC - S. Teach; Devos Children's Hospital and Michigan State University, Grand Rapids - J. Hoyle, Jr.; Bellevue Hospital Center and New York University, New York - M. Tunik; University of Maryland, Baltimore - R. Lichenstein; SUNY Upstate Medical University, Syracuse, NY - J. Callahan; University of Michigan, Ann Arbor - D. Treloar; St. Barnabas Health Care System, Livingston, NJ - N. Schamban. Patient Safety Committee: N. Kuppermann, Kathleen Mahackian, M. Gorelick, W. Schalick III, R. Woods, J.P. Joad. For PECARN: Steering Committee: N. Kuppermann (chair), E. Alpern, J. Chamberlain, J.M. Dean, M. Gerardi, J. Goepp, M. Gorelick, J. Hoyle, D. Jaffe, C. Johns, N. Levick, P. Mahajan, R. Maio, K. Melville, S. Miller (deceased), D. Monroe, R. Ruddy, R. Stanley, D. Treloar, M. Tunik, A. Walker. Maternal and Child Health Bureau liaisons: D. Kavanaugh, H. Park. Central Data Management and Coordinating Center: M. Dean, R. Holubkov, S. Knight, A. Donaldson. Data Analysis and Management Subcommittee: J. Chamberlain (chair). M. Brown, H. Corneli, J. Goepp, R. Holubkov, P. Mahajan, K. Melville, E. Stremski, M. Tunik. Grants and Publications Subcommittee: M. Gorelick (chair), E. Alpern, J.M. Dean, G. Foltin, J. Joseph, S. Miller (deceased), F. Moler, R. Stanley, S. Teach. Protocol Concept Review and Development Subcommittee: D. Jaffe (chair), K. Brown, A. Cooper, J.M. Dean, C. Johns, R. Maio, N.C. Mann, D. Monroe, K. Shaw, D. Teitelbaum, D. Treloar. Quality Assurance Subcommittee: R. Stanley (chair), D. Alexander, J. Brown, M. Gerardi, M. Gregor, R. Holubkov, K. Lillis, B. Nordberg, R. Ruddy, M. Shults, A. Walker. Safety and Regulatory Affairs Subcommittee: N. Levick (chair), J. Brennan, J. Brown, J.M. Dean, J. Hoyle, R. Maio, R. Ruddy, W. Schalick, T. Singh, J. Wright.

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