Negative Chest Radiography and Risk of Pneumonia

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BACKGROUND AND OBJECTIVES: The ability of the chest radiograph (CXR) to exclude the diagnosis of pneumonia in children is unclear. We sought to determine the negative predictive value of CXR in children with suspected pneumonia.

METHODS: Children 3 months to 18 years of age undergoing CXRs for suspected pneumonia in a tertiary-care pediatric emergency department (ED) were prospectively enrolled. Children currently receiving antibiotics and those with underlying chronic medical conditions were excluded. The primary outcome was defined as a physician-ascribed diagnosis of pneumonia independent of radiographic findings. CXR results were classified as positive, equivocal, or negative according to radiologist interpretation. Children with negative CXRs and without a clinical diagnosis of pneumonia were managed for 2 weeks after the ED visit. Children subsequently diagnosed with pneumonia during the follow-up period were considered to have had false-negative CXRs at the ED visit.

RESULTS: There were **683** children enrolled during the 2-year study period, with a median age of **3.1** years (interquartile range 1.4–5.9 years). There were 457 children (72.8%) with negative CXRs; 44 of these children (8.9%) were clinically diagnosed with pneumonia, and 42 (9.3%) were given antibiotics for other bacterial syndromes. Of the 411 children with negative CXRs who were managed without antibiotics, 5 were subsequently diagnosed with pneumonia within 2 weeks (negative predictive value of CXR 98.8%; 95% confidence interval 97.0%–99.6%).

CONCLUSIONS: A negative CXR excludes pneumonia in the majority of children. Children with negative CXRs and low clinical suspicion for pneumonia can be safely observed without antibiotic therapy.





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Dr Lipsett conceptualized and designed the study, collected data, conducted the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript; Dr Monuteaux conducted the initial analyses and reviewed and revised the manuscript; Dr Bachur conceptualized and designed the study and reviewed and revised the manuscript; Mr Finn collected data and reviewed and revised the manuscript; Dr Neuman conceptualized and designed the study, designed the data collection instruments, collected data, drafted the initial manuscript; and reviewed and revised the manuscript; as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Chest

radiographs (CXRs) are often used for the evaluation of pneumonia. However, some clinicians are concerned about the accuracy of CXRs when diagnosing pneumonia in children, particularly early in disease or in children with dehydration.

WHAT THIS STUDY ADDS: The majority of children with suspected pneumonia and negative CXR results will recover without antibiotic use; thus, the CXR can be considered as a reasonable reference standard to exclude pneumonia in children.

To cite: Lipsett SC, Monuteaux MC, Bachur RG, et al. Negative Chest Radiography and Risk of Pneumonia. *Pediatrics*. 2018;142(3):e20180236 Diagnosing pneumonia in children can be challenging; a recent systematic review revealed the poor predictive value of individual signs and symptoms for the diagnosis of pneumonia.¹ Missed bacterial pneumonia can lead to significant morbidity and mortality; thus, many clinicians in the acute-care setting rely on the chest radiograph (CXR) as an additional tool to establish the diagnosis of pneumonia and determine the need for antibiotic therapy.^{2–4} However, limitations of the use of the CXR to diagnose pneumonia include variability in interpretation^{5–7} and its inability to distinguish viral from bacterial processes.⁷ Additionally, some clinicians are concerned that radiographic findings of pneumonia may be absent early in the course of the disease or in patients with dehydration,⁸ leading them to prescribe antibiotics despite a negative CXR. The ability of CXR to exclude pneumonia in children has not been determined.

Therefore, we conducted a prospective observational cohort study in children undergoing CXR for suspected pneumonia, focusing specifically on the management and outcomes of children in whom the CXR revealed no evidence of pneumonia. We sought to determine the negative predictive value (NPV) of the CXR in children with suspected pneumonia. We were particularly interested in understanding whether children with negative CXRs recover without antibiotic use. Additionally, we assessed which signs and symptoms were associated with a clinical diagnosis of pneumonia during the emergency department (ED) encounter despite a negative CXR.

METHODS

Study Setting and Participants

This prospective observational cohort study was conducted over

a 24-month period beginning May 2015 in a large, urban pediatric ED with $\sim 60\,000$ visits annually. We included children aged 3 months to 18 years who had a CXR performed to evaluate for pneumonia. The decision to perform a CXR was made at the discretion of the treating clinician. Because of the lack of reliability and sensitivity of clinical signs for the diagnosis of pneumonia,^{1,9} our ED has an established guideline recommending CXR performance for all children with suspected pneumonia, with CXRs being performed in >75% of children who are ultimately diagnosed with pneumonia. We excluded children currently receiving an antibiotic for pneumonia or another infection as well as children with complex medical conditions predisposing them to pneumonia (eg, cystic fibrosis, sickle cell disease, malignancy or immunodeficiency, risk of aspiration). Additionally, children who were deemed too ill by a treating clinician and those whose caregivers were not proficient in English were not eligible for inclusion in the study. Research coordinators identified eligible patients in real time by monitoring an electronic tracking board for CXR order placement among patients with chief complaints that were suggestive of possible pneumonia (eg, cough, fever, and difficulty breathing). Among eligible patients, informed consent was obtained from caregivers, and assent was obtained from the children when appropriate.

Data Collection

Once eligibility was confirmed and the patient and/or family consented, the patient's attending physician (board-certified pediatrician or pediatric emergency medicine physician) estimated the likelihood of radiographic findings of pneumonia (<5%, 5%–10%, 11%–20%, 21%–50%, 51%–75%, and >75%), before knowledge of radiograph results, on the basis of the physician's clinical impression. The same treating physician recorded physical examination findings (wheezing, respiratory distress, rales, and diminished breath sounds) and indicated whether the child had signs of another infection warranting antibiotic treatment (eg, streptococcal pharyngitis, otitis media, or sinusitis).

Electronic medical records from the index ED visit were reviewed to abstract demographic information, vital signs, antibiotics administered in the ED or prescribed, diagnoses ascribed, and ultimate disposition. CXR results were abstracted from the medical record by using the final reading by a board-certified pediatric radiologist. CXRs were classified according to a previously developed classification scheme¹⁰ as revealing definite evidence of pneumonia (positive), no evidence of pneumonia (negative), or equivocal findings, on the basis of the final impression by a boardcertified pediatric radiologist as part of the child's clinical care. CXRs whose reports contained descriptors such as "consolidation" or "pneumonia" were classified as positive. CXRs whose reports contained descriptors such as "no pneumonia," "peribronchial cuffing," "atelectasis," or "findings suggestive of viral bronchiolitis" were classified as negative. CXRs whose reports contained descriptors such as "atelectasis vs infiltrate," "atelectasis vs pneumonia," or "likely atelectasis but cannot rule out pneumonia" were classified as equivocal. We did not classify CXRs with equivocal findings as negative because equivocal findings may represent evolving pneumonia, and in our institutional experience, the majority of children with equivocal CXR findings are diagnosed with pneumonia.¹¹

Caregivers were contacted by phone or e-mail twice (at 4–7 days and

again at 10–14 days) after their children's ED visit regardless of whether they were discharged or admitted at the ED visit. At each contact, caregivers completed a structured questionnaire in Research Electronic Data Capture. Standardized questions were asked in order to determine the timing of symptom resolution or progression, return to school or day care, compliance with prescribed medications (if any), and revisits for additional medical care. For children who were not diagnosed with pneumonia at the ED visit, a subsequent diagnosis of pneumonia was determined by caregiver survey. Caregivers were asked, "Since leaving the ED, has your child been diagnosed with pneumonia?" Positive responses included follow-up questions about the health care setting where the diagnosis was made and the duration of time between the ED visit and the pneumonia diagnosis.

Outcome Measures

Our primary outcome was the clinical diagnosis of pneumonia, either at the ED visit or during the follow-up period. A child was considered to have a diagnosis of pneumonia at the ED visit if he or she was ascribed a discharge diagnosis of pneumonia in the ED provider's note regardless of CXR results. For patients who were not diagnosed with pneumonia at the index visit, a subsequent diagnosis of pneumonia during the follow-up period was determined by caregiver survey. For patients for whom survey responses were not received, the electronic medical record was queried for the presence of cliniciandiagnosed pneumonia during the 2-week follow-up period.

Data Analysis

Demographic and clinical characteristics are presented by using frequencies with proportions for categorical variables and

medians with interquartile ranges (IQRs) for continuous variables. Characteristics of children, stratified by CXR result and ultimate pneumonia diagnosis, were compared by using the χ^2 test for categorical variables and the Wilcoxon rank sum test for continuous variables. The NPV of the CXR was calculated as a proportion with 95% confidence intervals (CIs). We calculated the NPV in 2 ways. First, we limited our cohort to children with negative CXRs who were discharged from the ED without a diagnosis of pneumonia and without antibiotics prescribed. Among this subgroup, children with subsequent diagnoses of pneumonia during the follow-up period were considered to have had false-negative CXRs at the ED visit. We did not require the subsequent diagnosis to be based on a follow-up CXR; this allows for a more conservative estimate of the NPV of the CXR and is reflective of actual practice. We also calculated the NPV of the CXR by classifying the cohort of children who were diagnosed with pneumonia at the ED visit despite negative CXR results as having had false-negative CXRs. Data analysis was performed with Stata version 13.1 (Stata Corp, College Station, TX).

The study was approved by the Boston Children's Hospital Institutional Review Board.

RESULTS

Subjects

During the study period, 3101 children had a CXR performed for suspected pneumonia, of whom 1106 (35.7%) were eligible for inclusion. Of these, 823 (74.4%) patients and/or families were approached, and 683 (83%) were included in our study cohort (Fig 1). The median age of participants was 3.1 years (IQR 1.4–5.9 years), and 21.4% were hospitalized (Table 1). Overall, 200 patients (29.3% of the cohort) were diagnosed with pneumonia during the ED visit, 196 (98%) of whom were prescribed antibiotics. Of the 156 children with clinically diagnosed pneumonia, 78% had positive or equivocal CXRs and 44 (22%) had negative CXRs.

Radiograph Results

Overall, 16.5% of children had positive CXRs, 10.7% had equivocal CXRs, and 72.8% had negative CXRs (Table 1). Children whose CXRs were suggestive of pneumonia (both definite and equivocal) were older than children with negative CXRs; they were also more likely to have rales and respiratory distress on examination and less likely to have wheezing (Table 2). The difference in minimum oxygen saturation between the 2 groups was not clinically meaningful despite its statistical significance.

ED Management of Children by Radiograph Result

Of the 113 children with positive CXRs, 108 (96%) were diagnosed with pneumonia. Of the 73 children with equivocal CXRs, 48 (66%) were diagnosed with pneumonia (Fig 2). Children who were not diagnosed with pneumonia despite positive or equivocal results were more likely to have wheezing on examination than those who were diagnosed with pneumonia (30.0% vs 13.5%; *P* = .02). Of the 497 children with negative CXRs, 44 (8.9%) were clinically diagnosed with pneumonia at the ED visit despite the negative radiographic findings. An additional 42 children were treated with antibiotics for other reasons, the most common being otitis media. There were 411 children who were discharged from the ED without a diagnosis of pneumonia and without antibiotic treatment.

Among children with negative CXRs, the physician-estimated

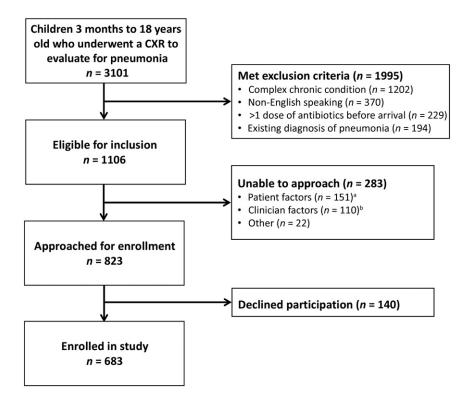


FIGURE 1

Patient screening and enrollment. ^a Deemed too sick to approach, no guardian present, or complex psychosocial issues. ^b Research coordinator or physician not available; patient discharged before approach.

TABLE 1 Patient Demographics (N = 683)

Characteristic	n (%)			
Age in y, median (IQR)	3.1 (1.4–5.9)			
Age group				
<6 mo	24 (3.5)			
6 mo to 1 y	218 (31.9)			
2—5 у	276 (40.4)			
6—11 y	116 (17.0)			
12—18 у	49 (7.2)			
Female sex	316 (46.3)			
Hospitalized	146 (21.4)			
Regular inpatient bed	128 (87.7)			
Step-up unit or ICU	18 (12.3)			
CXR results				
Definite pneumonia	113 (16.5)			
Equivocal for pneumonia	73 (10.7)			
No pneumonia	497 (72.8)			
ED diagnosis of pneumonia	200 (29.3)			
Antibiotics prescribed	244 (35.7)			
Alternative bacterial syndromes identified	56 (8.2)			
Otitis media	35			
Urinary tract infection	6			
Sinusitis	5			
Streptococcal pharyngitis	1			
Lymphadenitis	1			
Suspected pertussis	2			
Other ^a	6			

^a Other includes folliculitis, bronchitis, osteomyelitis, and leukocytosis in a child with fever.

likelihood of pneumonia before knowledge of CXR results was positively correlated with a clinical diagnosis of pneumonia (Spearman correlation coefficient 0.29; P < .001; Supplemental Fig 3). Compared with children who were not diagnosed with pneumonia, those who were diagnosed with pneumonia in the setting of a negative CXR result were more likely to have rales (50.0% vs 25.2%; *P* < .001) and respiratory distress (29.6% vs 17.0%; *P* = .04) and less likely to have wheezing (11.4% vs 26.5%; *P* = .03). Of the 111 children with a combination of fever and rales, 21 (19%) were diagnosed with pneumonia despite having a negative CXR result. There was no difference in the hospitalization rates between the 2 groups.

Outcomes of Children With Negative Results

Of the 411 children with negative CXRs who were not prescribed an antibiotic, 74 (18%) were hospitalized, and the remainder were discharged from the ED. The reason for hospitalization in most of these cases was wheezing or respiratory distress. Caregiver follow-up survey data were available for 363 children (88.3%). There were no significant differences in baseline or clinical characteristics between the groups with and without follow-up survey data available (Supplemental Table 4). At 1 week, 93.8% of children were rated as being "better" than they were at the index ED visit (versus "worse" or "about the same"), with 64.8% being rated as completely back to normal, and 86.4% of children had returned to school or day care. At 2 weeks. 81.5% of children were rated as being completely back to normal, and 96.7% had returned to school or day care.

NPV of the CXR

Of the 411 children with negative CXRs who were not prescribed an antibiotic, 5 (1.2%) were

TABLE 2 Characteristics of Children Based on Radiographic Findings

Characteristic	Definite or Equivocal Pneumonia on CXR (N = 186), n (%)	Negative for Pneumonia on CXR ($N = 497$), n (%)	P .008
Age in y, median (IQR)	3.8 (1.6–6.3)	2.9 (1.4–5.5)	
Female sex	94 (50.5)	222 (44.7)	.17
History of fever	152 (81.7)	393 (74.1)	.44
Minimum oxygen saturation in ED, median (IQR)	97 (94–98)	98 (96–99)	<.001
Physical examination findings			
Rales and/or crackles	69 (37.1)	136 (27.4)	.01
Decreased breath sounds	53 (28.5)	123 (24.8)	.32
Respiratory distress	49 (26.3)	90 (18.1)	.02
Wheezing	30 (16.1)	125 (25.2)	.01
Hospitalized	57 (30.7)	89 (17.9)	<.001
Diagnosed with pneumonia	156 (83.9)	44 (8.9)	<.001

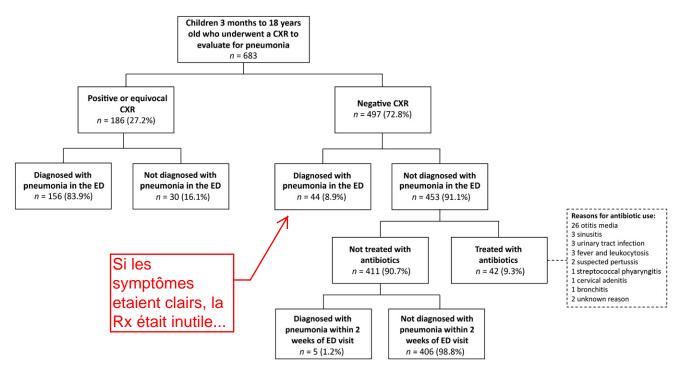


FIGURE 2

ED management based on radiographic findings.

diagnosed with pneumonia during the subsequent 2-week follow-up period (4 were identified by parent survey and 1 by medical record review), yielding an NPV of the CXR of 98.8% (95% CI 97.0%–99.6%) for the diagnosis of pneumonia in this cohort. The NPV was unchanged when the 42 children who were prescribed antibiotics for reasons other than pneumonia were included in the analysis. Characteristics of the 5 children with negative CXRs who were diagnosed with pneumonia during the follow-up period are shown in Table 3. All 5 children were <3 years of age, and the majority had fever for \leq 1 day at the time of the ED visit. None of the children received intravenous fluids for dehydration during the ED visit. Of the 5 children who were subsequently diagnosed with pneumonia during the 2-week follow-up period, only 1 had radiographic findings of pneumonia on repeat ED visit. After including the 44 children with clinically diagnosed pneumonia in the setting of negative CXRs (classified as false-negative CXRs), the NPV of the CXR was 89.2% (95% CI 85.9%–91.9%).

DISCUSSION

In this prospective observational cohort study of children undergoing radiography for suspected pneumonia, we found that among children with negative CXRs who were not treated with or prescribed antibiotics, only 1.2% were subsequently diagnosed with pneumonia within 2 weeks of the

Age, y	Duration of Fever, d	Maximum Temperature in ED, °C	Minimum Oxygen Saturation in ED	Received IV Fluids During ED Visit	Disposition From ED	Hospitalized at Follow-up	Physician Estimation of Likelihood of Pneumonia Before CXR, %	Clinical Synopsis
1.9	1	38.4	97	No	Discharged	No	<5	Patient returned 2 d after ED visit with continued fever and cough. A repeat CXR was negative for evidence of pneumonia; however, the patient was diagnosed with pneumonia and treated with amoxicillin.
0.7	2	39.0	97	No	Discharged	No	11–20	Patient returned 2 d after ED visit with worsening symptoms. Examination with new right otitis media and repeat CXR with equivocal findings (questionable densities in right-middle and left-lower lobes); diagnosed with pneumonia and treated with amoxicillin
2.3	1	39.4	95	No	Discharged	No	5–10	Diagnosed with pneumonia by primary care provider within 3 d of ED visit and treated with amoxicillin
2.9	0	37.3	98	No	Discharged	No	<5	Diagnosed with pneumonia by primary care provider within 3 d of ED visit and treated with amoxicillin
0.7	1	38.2	100	No	Discharged	No	<5	Diagnosed with pneumonia by primary care provider within 3 d of ED visit and treated with amoxicillin

TABLE 3 Characteristics of Patients With Negative CXRs Who Were Diagnosed With Pneumonia During the Follow-up Period

IV, intravenous.

ED visit. Forty-four children with negative results were nonetheless ascribed a diagnosis of pneumonia; these children were more likely to have rales or respiratory distress and less likely to have wheezing than children with negative CXRs and no pneumonia diagnosis. Our findings reveal that most children with negative results will recover fully without antibiotic use.

To our knowledge, this is the first prospective study in which researchers manage a large cohort of children with suspected pneumonia and negative CXR results and allow for the evaluation of chest radiography to exclude the diagnosis of pneumonia. Most clinicians caring for children in the outpatient setting rely on clinical signs and symptoms to determine whether to prescribe an antibiotic for the treatment of pneumonia. However, given recent literature in which the poor reliability and validity of physical examination findings are cited,^{1,12} reliance on physical examination alone may lead to the overdiagnosis of pneumonia. One recent prospective pediatric study suggested that performance of CXRs in children with suspected pneumonia may decrease unnecessary antibiotic use.¹¹ Thus, clinicians must balance the risk of antibiotic overuse against the risks and costs of chest radiography. In this investigation, we provide important new insights into the paradigm of CXR performance for the evaluation of pneumonia in children.

Despite no pediatric data to support this notion, many clinicians believe that CXRs may be falsely negative early in the course of disease.⁸ There are a few adult studies in which researchers examine the rate of initially false-negative results in patients with suspected pneumonia,^{13–15} although they are limited by their retrospective design and selection bias.^{13,14} The largest study in which researchers examine this phenomenon was a prospective cohort study of 2706 adults who were hospitalized with communityacquired pneumonia in Canada, 98% of whom underwent CXRs both on admission and within 96 hours of admission.¹⁵ One-third of the patients had negative CXRs on admission, and of these, 7% developed radiographic signs of pneumonia within 72 hours. There was no information provided about the clinical trajectory of the patients with subsequent development of radiographic findings.

Some clinicians are also concerned that typical radiographic findings of pneumonia may be absent in children with dehydration,⁸ driven by the theory that dehydration causes a lower hydrostatic pressure and elevated oncotic pressure in the lungs, leading to a net reduction in the fluid in the pulmonary capillaries.¹⁶ In the only experimental study on the subject, 2 groups of dogs (4 normally hydrated and 4 moderately dehydrated) received intrabronchial instillation of *Streptococcus pneumoniae*.¹⁶ All dogs had abnormal findings on CXR 5 hours after instillation. with no difference observed in the extent of pneumonia or time to radiographic appearance of pneumonia between the dogs that were well hydrated and those that were dehydrated. Human data on dehydration are limited to adults, with mixed findings observed. A small retrospective review of 125 adults who were hospitalized with pneumonia in a community teaching hospital revealed higher serum urea nitrogen levels and mean fluid intake in patients who had progressive radiographic findings within 96 hours compared with those with unchanged or improving radiograph findings.¹⁷ However, these findings have not been replicated in other studies.^{13,15} In our study, none of the 5 children who were subsequently diagnosed with pneumonia required intravenous fluid administration at the ED visit, making it unlikely that any of them were significantly dehydrated at the time of the initial radiograph.

In our cohort, 44 children were clinically diagnosed with pneumonia at the ED visit despite negative CXRs. This practice highlights the challenging nature of pneumonia diagnosis, which can be based on clinical findings, radiographic findings, or a combination of both. Within the confines of our study methods, it is impossible to know if repeat radiographs would have revealed the evolution of radiographic signs that are consistent with pneumonia or whether these children would have recovered without antibiotic treatment. These children may have appeared clinically ill, although the hospitalization rate was not higher in this group. It is also possible that anchoring bias played a role; previous work has demonstrated that clinicians who are strongly suspicious of pneumonia in their patients before CXR performance

may be more likely to minimize the significance of negative radiographic findings.¹¹ Regardless, there was something different about these children that led clinicians to diagnose pneumonia in the setting of a negative CXR. Our finding that respiratory distress and rales were more common in these children suggests that clinicians rely on these characteristics to aid in decisionmaking for diagnosing pneumonia. In contrast, patients who presented with wheezing were less likely to be diagnosed with pneumonia than those without wheezing regardless of CXR results. This may reflect a belief that wheezing is more suggestive of a viral pathogen or may suggest that these children's physical examination findings improved after bronchodilator therapy, leading clinicians to be less suspicious of pneumonia as the cause of their symptoms. When these 44 children were included in our NPV calculation as having falsenegative CXRs, the NPV decreased but remained high at 89.2%.

Our study has several notable limitations. First, the primary outcome of pneumonia was based on the clinical diagnosis by an attending physician. Clinicians diagnose pneumonia on the basis of a combination of signs and symptoms, often in conjunction with radiographic findings because there is no universally accepted gold standard for the diagnosis of pneumonia in children. This is an important limitation of pneumonia research. Second, the decision to perform a CXR and prescribe an antibiotic was left to the discretion of the treating clinician, and follow-up radiographs were not obtained systematically on all patients. Thus, it is possible that some of the children with negative CXRs who recovered without antibiotic therapy may have had positive radiographic findings if repeat radiographs were obtained.

We are also unable to know if the 3 children who were subsequently diagnosed with pneumonia by their primary care providers truly had pneumonia that was missed on the original radiograph or if their continued symptoms were from another cause, such as a viral respiratory tract infection. On a related note, we relied on self-report to determine whether a patient was diagnosed with pneumonia during follow-up. We were unable to verify the manner in which pneumonia was diagnosed or whether a CXR was obtained. Third, we acknowledge that radiographic pneumonia is not synonymous with bacterial pneumonia^{18–20}; however, for the purposes of our study, we were most interested in understanding whether children with negative CXR results recover fully without antibiotics, and thus, the distinction between bacterial versus viral is less relevant. Fourth, radiograph classifications were based on final impressions by nonblinded pediatric radiologists as part of the children's clinical care. Knowledge of the clinical information prompting the radiograph may have led to bias in interpretation. Previous studies have also revealed varying interrater reliability when interpreting pediatric CXRs,^{5,6} although agreement is higher when evaluating for the presence of airspace disease.^{6,21} Finally, we were unable to enroll 100% of eligible patients for a variety of reasons, including complex psychosocial issues, critical illness, and a lack of research coordinator availability at certain times. Additionally, we were not able to acquire follow-up data on the entire sample, and in our medical record review, we may have missed medical care that occurred outside of our provider network. However, no significant differences in baseline clinical or demographic characteristics were noted between those patients who did and did not respond to the follow-up assessments (Supplemental Table 4), so it is

unlikely that the attrition introduced bias into our results.

We have found that the CXR has a high NPV for the diagnosis of pneumonia in children presenting to the ED with signs and symptoms of acute lower respiratory tract infection. We recognize that the diagnosis of pneumonia often relies on a combination of clinical and radiographic features. However, our findings reveal that the majority of children with suspected pneumonia and negative CXRs, especially those in whom the clinical suspicion of pneumonia is low, can be safely managed without antibiotic therapy.

ABBREVIATIONS

CI: confidence interval CXR: chest radiograph ED: emergency department IQR: interquartile range NPV: negative predictive value

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Negative Chest Radiography and Risk of Pneumonia

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