

# Diagnosing suspected radiographic pneumococcal disease in children with clinical pneumonia using digitally recorded lung sounds: A PERCH (Pneumonia Etiology Research for Child Health) Substudy

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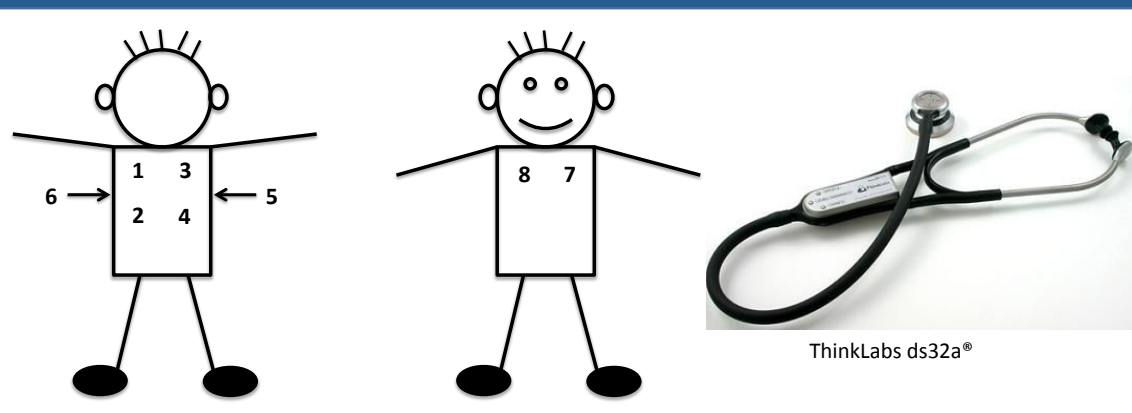
## INTRODUCTION

- Lung auscultation is not included in the diagnostic criteria of the World Health Organization (WHO) pneumonia case management algorithm (Integrated Management of Childhood Illnesses (IMCI)).
- We evaluated the performance of digitally recorded lung sounds for suspected radiographic pneumococcal disease (i.e., WHO alveolar consolidation) in children hospitalized with WHO severe or very severe pneumonia in PERCH.
- While WHO alveolar consolidation can be caused by pathogens other than pneumococcus, multiple randomized controlled trials of pneumococcal conjugate vaccine (PCV) efficacy have demonstrated a reduction in the incidence of alveolar consolidation in children receiving PCV, suggesting many children with this radiographic pattern are likely to have pneumococcal infection (*Klugman KP et al N Engl J Med 2003;349(14):1341-8*).

## METHODS

- Bangladesh, The Gambia, Kenya, South Africa, Thailand, and Zambia staff digitally recorded lung sounds from 8 chest locations (Figure) and took chest radiographs from children 1-59 months old hospitalized with WHO severe or very severe pneumonia.
- Using standardized criteria, separate physician panels blinded to patient data interpreted the lung recordings and radiographs.
- The listening panel assigned digital lung examination results of normal, crackle, wheeze, crackle and wheeze, or uninterpretable. Examinations were re-classified into 5 dichotomous categories: (1) crackle with or without wheeze, (2) crackle only (no wheeze), (3) wheeze with or without crackle, (4) wheeze only (no crackle), or (5) any crackle or any wheeze.
- We defined suspected pneumococcal pneumonia as chest radiographs with WHO alveolar consolidation (i.e. "primary endpoint pneumonia") with or without an other infiltrate.
- We assessed the association and performance of each of the 5 dichotomous lung recording categories with radiographic alveolar consolidation versus normal chest radiograph using logistic regression and descriptive statistics.

**FIGURE**  
Location and sequence of listening positions for digitally recorded lung sounds



## RESULTS

- A higher proportion of children with recorded lung sounds, compared to those without, were from Bangladesh and Thailand (26% vs 15%) and had a normal radiograph (45% vs 40%, **Table 1**). A lower proportion of digital auscultation participants, compared to non-participants, had 3 PCV doses (31% vs 37%), severe malnutrition (9% vs 12%), hypoxemia (33% vs 38%), and other infiltrate on chest radiograph (19% vs 25%, **Table 1**).
- In children with recorded lung sounds, radiographs had alveolar consolidation in 186/746 (24%) pneumonia cases (**Table 1**).
- 631/792 (79%) children with recorded lung sounds had both an interpretable recording and interpretable CXR
- In children with severe pneumonia, after controlling for age and region, crackle only had a 3.40 times greater odds consolidation on chest radiograph while wheeze only had a 3.23 times lower odds (OR 0.31, **Table 2**).
- In children with very severe pneumonia any crackle or any wheeze increased the odds of consolidation by 2.45 times (**Table 2**).
- Using chest radiograph consolidation as the reference, digital recordings with any crackle or any wheeze had the greatest sensitivity (62%), crackle only had the highest specificity (91%), positive predictive value (45%), and along with any crackle, the highest negative predictive value (76%) (**Table 3**).

**TABLE 1**  
PERCH Digital Auscultation Case Participants vs Non-participants

Characteristic	Participants	Non-participants	P value
Females, n/N (%)	343/792 (0.43)	1473/3439 (0.42)	0.807
Age in months, mean (SD)	11.3 (11.6)	11.6 (11.5)	0.451
African region, n/N (%)	580/792 (0.73)	2902/3439 (0.84)	<0.001
Asian region, n/N (%)	212/792 (0.26)	537/3439 (0.15)	<0.001
3 doses PCV, n/N (%)	159/499 (0.31)	1037/2775 (0.37)	0.018
HIV-infected or -exposed, n/N (%)	134/792 (0.16)	563/3439 (0.16)	0.707
Very severe pneumonia, n/N (%)	263/792 (0.33)	1106/3439 (0.32)	0.570
Severe malnutrition, n/N (%)	76/766 (0.09)	422/3337 (0.12)	0.037
Bacteremia, n/N (%)	24/758 (0.03)	146/3417 (0.04)	0.163
Malaria parasitemia, n/N (%)	17/464 (0.03)	75/2040 (0.03)	0.989
Hypoxemia, n/N (%)	267/789 (0.33)	1321/3432 (0.38)	0.015
Inpatient mortality, n/N (%)	61/790 (0.07)	256/3433 (0.07)	0.799
CXR: Alveolar consolidation (with or without other infiltrate), n/N (%)	186/746 (0.24)	780/3226 (0.24)	0.665
CXR: Alveolar consolidation only, n/N (%)	102/746 (0.13)	444/3226 (0.13)	0.948
CXR: Other infiltrate only, n/N (%)	146/746 (0.19)	822/3226 (0.25)	<0.001
CXR: Normal, n/N (%)	341/746 (0.45)	1311/3226 (0.40)	0.011
CXR: Uninterpretable, n/N (%)	73/746 (0.09)	313/3226 (0.09)	0.944

SD indicates standard deviation; PCV, pneumococcal conjugate vaccine; CXR, chest radiograph.



**TABLE 2**  
Association between digitally recorded lung sounds and WHO alveolar consolidation on chest radiograph

WHO severity	Digital lung examination result	WHO CXR alveolar consolidation +/- other infiltrate, n/N (%)	OR (95% CI)	P-value	aOR (95% CI)	P-value
All	Any crackle (with or without wheeze)	80/258 (0.31)	1.53 (1.05, 2.23)	0.026	1.90 (1.26, 2.84)	0.002
	Crackle only (no wheeze)	34/75 (0.45)	2.99 (1.71, 5.21)	<0.001	3.12 (1.73, 5.63)	<0.001
	Any wheeze (with or without crackle)	70/331 (0.21)	0.54 (0.36, 0.78)	0.001	0.64 (0.42, 0.94)	0.025
	Wheeze only (no crackle)	24/148 (0.16)	0.43 (0.26, 0.71)	<0.001	0.44 (0.26, 0.73)	0.001
	Any crackle or any wheeze	104/406 (0.25)	0.88 (0.59, 1.28)	0.503	1.08 (0.72, 1.62)	0.706
Severe	Any crackle (with or without wheeze)	47/189 (0.24)	1.24 (0.77, 1.99)	0.368	1.54 (0.92, 2.55)	0.095
	Crackle only (no wheeze)	20/51 (0.39)	3.25 (1.61, 6.51)	<0.001	3.40 (1.60, 7.20)	0.001
	Any wheeze (with or without crackle)	40/253 (0.15)	0.34 (0.21, 0.55)	<0.001	0.39 (0.23, 0.65)	<0.001
	Wheeze only (no crackle)	13/115 (0.11)	0.33 (0.17, 0.62)	<0.001	0.31 (0.15, 0.60)	<0.001
	Any crackle or any wheeze	60/304 (0.19)	0.55 (0.33, 0.90)	0.018	0.66 (0.38, 1.10)	0.116
Very severe	Any crackle (with or without wheeze)	33/69 (0.47)	2.99 (1.50, 5.92)	0.001	2.84 (1.40, 5.75)	0.003
	Crackle only (no wheeze)	14/24 (0.58)	2.47 (0.97, 6.28)	0.052	2.44 (0.93, 6.38)	0.068
	Any wheeze (with or without crackle)	30/78 (0.38)	1.67 (0.86, 3.21)	0.125	1.60 (0.81, 3.14)	0.170
	Wheeze only (no crackle)	11/33 (0.33)	0.89 (0.38, 2.09)	0.798	0.91 (0.37, 2.17)	0.830
	Any crackle or any wheeze	44/102 (0.43)	2.51 (1.31, 4.80)	0.004	2.45 (1.25, 4.78)	0.008

WHO indicates World Health Organization; CXR, chest radiograph; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval. Excludes uninterpretable final digital lung examination or CXR conclusions. aOR = adjusted for age (1-23 months vs 24-59 months) and region (Africa vs Asia). Reference group for OR and aOR is CXR normal.

**TABLE 3**  
Sensitivity, specificity, positive and negative predictive values, and likelihood ratios of digitally recorded lung sounds for WHO alveolar consolidation on chest radiograph

WHO severity	Digital lung examination result	Sensitivity, n/N (%) (95% CI)	Specificity, n/N (%) (95% CI)	PPV, n/N (%) (95% CI)	NPV, n/N (%) (95% CI)	LR pos	LR neg
All	Any crackle (with or without wheeze)	80/169 (0.47) (0.40, 0.55)	284/462 (0.61) (0.57, 0.66)	80/258 (0.31) (0.25, 0.37)	284/373 (0.76) (0.72, 0.79)	1.23	0.86
	Crackle only (no wheeze)	34/169 (0.20) (0.14, 0.27)	421/462 (0.91) (0.88, 0.94)	34/75 (0.45) (0.34, 0.57)	421/556 (0.76) (0.72, 0.79)	2.27	0.88
	Any wheeze (with or without crackle)	70/169 (0.41) (0.34, 0.49)	201/462 (0.44) (0.39, 0.48)	70/331 (0.21) (0.17, 0.26)	201/300 (0.67) (0.61, 0.72)	0.73	1.35
	Wheeze only (no crackle)	24/169 (0.14) (0.09, 0.20)	338/462 (0.73) (0.69, 0.77)	24/148 (0.16) (0.11, 0.23)	338/483 (0.70) (0.66, 0.74)	0.53	1.17
	Any crackle or any wheeze	104/169 (0.62) (0.54, 0.69)	160/462 (0.35) (0.30, 0.39)	104/406 (0.26) (0.21, 0.30)	160/225 (0.71) (0.65, 0.77)	0.94	1.11

WHO indicates World Health Organization; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; LR, likelihood ratio.

## CONCLUSIONS

- Digitally recorded lung crackles were associated with a significantly greater odds of consolidation on chest radiograph.
- Digitally recorded lung wheezing was associated with greatly reduced odds of radiographic consolidation.
- Lung recordings **without** crackles had a 76% probability of a normal radiographic result (i.e., negative predictive value).
- Since radiographic consolidation can be caused by pathogens other than pneumococcus we plan to evaluate associations of digital lung recordings with more specific etiologic endpoints.
- Our findings lend support to the expanded use of digitally recorded lung examinations in pediatric respiratory research in developing countries, especially when lung imaging is not feasible.
- Web-based educational tools and a hand held, automated computerized interpretation device based on PERCH digital lung recordings may aid the inclusion of lung auscultation for pneumonia diagnosis in future WHO pneumonia management algorithms.



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