

Diagnosing Pneumonia by Physical Examination

Relevant or Relic?

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Background: The reliability of chest physical examination and the degree of agreement among examiners in diagnosing pneumonia based on these findings are largely unknown.

Objectives: To determine the accuracy of various physical examination maneuvers in diagnosing pneumonia and to compare the interobserver reliability of the maneuvers among 3 examiners.

Methods: Fifty-two male patients presenting to the emergency department of a university-affiliated Veterans Affairs medical center with symptoms of lower respiratory tract infection (cough and change in sputum) were prospectively examined. A comprehensive lung physical examination was performed sequentially by 3 physicians who were blind to clinical history, laboratory findings, and x-ray results. Examination findings by lung site and whether the examiner diagnosed pneumonia were recorded on a standard form. Chest x-ray films were read by a radiologist.

Results: Twenty-four patients had pneumonia confirmed by chest x-ray films. Twenty-eight patients did not have pneumonia. Abnormal lung sounds were common in both groups; the most frequently detected were rales in the upright seated position and bronchial breath sounds. Relatively high agreement among examiners ($\kappa \approx 0.5$) occurred for rales in the lateral decubitus position and for wheezes. The 3 examiners' clinical diagnosis of pneumonia had a sensitivity of 47% to 69% and specificity of 58% to 75%.

Conclusions: The degree of interobserver agreement was highly variable for different physical examination findings. The most valuable examination maneuvers in detecting pneumonia were unilateral rales and rales in the lateral decubitus position. The traditional chest physical examination is not sufficiently accurate on its own to confirm or exclude the diagnosis of pneumonia.

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INTRODUCED NEARLY 200 years ago, auscultation and percussion of the chest are considered essential in the physical examination and are taught to every medical student.^{1,2} Although chest physical examination findings can be confirmed with chest x-ray results, objective data on clinician accuracy and reproducibility of physical examination findings are limited. Surprisingly, neither the utility of the physical examination in predicting pulmonary disease nor its value in distinguishing among different pulmonary conditions has been well studied. Furthermore, teachers seldom emphasize the difficulty of eliciting chest physical signs. Increasing constraints on the time available to evaluate patients and ready access to chest radiographs have led clinicians to question the need for a detailed lung examination when lower respiratory infection is suspected. In fact, some believe that auscultation, once considered a sophisti-

cated art that helped guide diagnostic and therapeutic decisions, is "now . . . performed as a bedside ritual."³

Computerized analyses of lung sounds have confirmed distinct findings in each of 4 diseases: idiopathic pulmonary fibrosis, chronic obstructive pulmonary disease, congestive heart failure, and pneumonia.⁴ Patients with pneumonia had coarse crackles, most often pan-inspiratory, which differed from the findings in the other conditions. To our knowledge, interobserver reliability and accuracy in diagnosing pneumonia based solely on physical examination (ie, without prior knowledge of clinical history or radiologic findings) have not been previously studied. A recent review of the pulmonary clinical examination⁵ confirmed the paucity of data on the usefulness of physical examination in diagnosing community-acquired pneumonia. To assess the accuracy of specific maneuvers in diagnosing pneumonia and to compare the interob-

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METHODS

We recruited patients from 1990 through 1993 who presented for evaluation of symptoms of acute lower respiratory tract inflammation to the Veterans Affairs Puget Sound Health Care System, Seattle, Wash. Potential study cases were identified by the emergency department nurses or by a study coordinator who evaluated patients during triage on weekdays from 8 AM to 5 PM. The study was exempted from review by our Human Subjects Committee because there were no non-clinically indicated procedures or confidentiality issues involved; patients were, however, given the option to participate or to decline enrollment. Inclusion criteria were an acute cough or exacerbation of a chronic cough and an increased amount or darkening color of sputum. Presenting symptoms, other pertinent features of the medical history, and selected laboratory and microbiological data (including a complete blood cell count and sputum gram stain and culture, if performed) were recorded on an enrollment data form by the study coordinator.

Patients were assessed sequentially by at least 2 of 3 board-certified physicians. These physicians were experienced and active clinicians and included a general internist (physician A, J.E.W.), an infectious diseases subspecialist in the division of general internal medicine (physician B, B.A.L.), and a subspecialist in pulmonary medicine and infectious diseases (physician C, J.V.H.). Before enrolling patients, each physician listened to a commercially produced audiotope of lung sounds in order to enhance consistency in identifying pertinent physical findings.⁶ Each physician performed a detailed, standardized pulmonary examination on each patient. The physicians had no knowledge of the patient's history, vital signs, or radiographic findings and could not ask the patient questions. The order in which the physicians examined the patients was not prescribed. They attempted to examine the patients expeditiously but were not under a specific time constraint. The interval between the first and the third physician's examination ranged from about half an hour to 4 hours and depended on the physicians' availability.

In the sitting position, each patient was assessed for crackles, rhonchi, wheezing, tactile fremitus, whispered pectoriloquy, bronchophony, egophony, and pleural friction rub. Physical diagnostic techniques employed were auscultation, palpation, fingertip percussion, and auscultatory percussion (auscultation while percussing the patient's sternum). Patients were also examined for crackles in both the right and left lateral decubitus positions (LDPs). Each physician used his or her own standard stethoscope.

The definitions of lung findings used in this study are as follows^{3,6,7}: Rales (crackles) are discontinuous, interrupted,

explosive sounds that may occur in early or late inspiration; rales in the LDP are those detected in the dependent lung; coarse rales are low-pitched sounds; fine rales are high-pitched, "velcro-type" sounds. Rhonchi are continuous, low-pitched sounds in early inspiration that clear or decrease following cough. Wheezes are continuous, high-pitched, hissing sounds that may occur during inspiration or expiration. Vocal (or tactile) fremitus is a unilateral increase in palpable vocal vibrations transmitted through the chest wall. In this maneuver, the patient recites the word *ninety-nine* while the examiner palpates the chest wall. Bronchophony is an increase in the intensity and clarity of the patient's spoken voice as perceived transthoracically through the stethoscope. Egophony is a severe form of bronchophony, defined as a nasal or bleating quality of transmitted vocal sounds that is elicited when the patient says the letter *E* and to the examiner it sounds like the letter *A*. Whispered pectoriloquy is the unusually clear perception of the patient's whispered words (eg, *ninety-nine*) through the stethoscope. Pleural friction rub is a creaky sound traditionally described as "reminiscent of rubbing oiled leather" and may occur during any phase of the respiratory cycle. Findings were recorded on a data sheet (**Figure**) that included an assessment of the anatomical location of abnormal findings, confirmation that the examiner was truly blind to the patient's diagnosis, and identified whether the physical examination was consistent with pneumonia.

Chest radiographs (standard posterior-anterior and lateral views) were taken on all patients and interpreted by a board-certified radiologist with a special interest in chest radiography (J.T.) who was unaware of the patient's clinical findings. Pneumonia was defined as the presence of a radiographic infiltrate in the pulmonary parenchyma; the infiltrate must not have been present on any available remote chest x-ray films. A second set of chest x-ray films was obtained within the next few days when the initial radiologic interpretation was possible pneumonia. When subsequent radiographs confirmed the presence of lung consolidation, pneumonia was diagnosed. The radiographic interpretation was considered the gold standard for the presence of pneumonia. A physical finding was considered to be correct if it was present in the same general site as an infiltrate on chest x-ray film.

Statistical analyses were performed by a trained epidemiologist (E.J.B.). The reliability of pulmonary examination findings between pairs of observers was assessed using the κ statistic, a chance-corrected measure of agreement.⁸ Diagnostic likelihood ratios and 95% confidence intervals were calculated according to the method of Simel.⁹ Confidence intervals for likelihood ratios of zero could not be calculated, since we are not aware of any appropriate method.

server reliability of different clinicians examining the same patient, we prospectively examined 52 patients with suspected lower respiratory infection using a variety of chest physical examination maneuvers.

RESULTS

Fifty-two patients were enrolled in the study. Twenty-four had radiographically diagnosed pneumonia; 28 did not have pneumonia. Selected characteristics of the sub-

jects are shown in **Table 1**. Participants were all men, generally elderly, usually with a history of smoking cigarettes, and most had a history of asthma or chronic obstructive pulmonary disease. Only a minority of patients had fever, tachycardia, or leukocytosis.

Of the 24 patients who had pneumonia, 4 had chest radiographs interpreted as possible pneumonia. Most pneumonias were located in the right lung (n = 16), and they were predominantly in the right lower lobe (n = 13). The 28 patients without a pulmonary infiltrate were be-

Physical Examination of the Chest

Patient Name _____

S.S. No. _____ Date/Time Exam _____

Examiner _____

A

B

C

Maneuver	Normal	Abnormal	Site(s)
<i>Percussion</i>			
Fingertip	nL ¹	dull ²	_____
Ausc.w/percus.	nL ¹	dull ²	_____
<i>Breath Sounds</i>			
Bronch. Br. Sds.	absent ¹	present ²	_____
Rhonchi	absent ¹	present ²	_____
Rales	absent ¹	high pitched ²	_____
		low pitched ³	_____
		early inspir. ⁴	_____
		late expir. ⁵	_____
Wheezes	absent ¹	inspir. & expir. ²	_____
		late expir. ³	_____
Friction Rub	absent ¹	present ²	_____
Vocal fremitus	absent ¹	present ²	_____
Bronchophony	absent ¹	present ²	_____
Whisp. pectoriloquey	absent ¹	present ²	_____
Egophony	absent ¹	present ²	_____
Rales R lat. decubitus	absent ¹	present ²	_____
Rales L lat. decubitus	absent ¹	present ²	_____

Examiner Blinded to Exam¹

Examiner aware of infiltrate location²

Examiner aware of pneumonia status but not of X-ray findings³

DOES THE PATIENT HAVE PNEUMONIA? _____

Data sheet showing sites of chest physical examination and recorded maneuvers performed at each site. The site of any physical finding was identified by the numbers in the diagrams.

lieved to have either acute bronchitis or an exacerbation of chronic bronchitis.

The chest examination performed for this study typically took about 10 minutes. **Table 2** demonstrates the proportion of subjects with positive physical findings as detected by each physician, regardless of whether the patient had pneumonia or bronchitis. The 2 most frequent abnormal findings in all patients examined were the presence of rales in the upright seated position (22%-65%) and bronchial breath sounds (8%-43%). Some findings, including whispered pectoriloquey, vocal fremitus, and friction rub, were very uncommon.

Since each of the 3 examiners did not evaluate all of the patients, paired κ values were calculated (**Table 3**) to examine the degree of agreement among examiners for a particular physical finding. In general, κ values greater than 0.5 were considered to reflect a high level of agreement for physical examination maneuvers.⁹ Rales,

Table 1. Characteristics of Enrolled Subjects*

Characteristics	Subjects, No. (%)		
	Total (n = 52)	With Pneumonia (n = 24)	Without Pneumonia (n = 28)
Age, y†	62 (27-89)	62 (40-89)	62 (27-78)
Smoking history			
History of smoking	42 (81)	21 (88)	21 (75)
Pack-years‡	44	45	42
History of asthma and/or COPD§	35 (67)	17 (71)	18 (64)
Vital signs			
Temperature >38°C	11 (21)	8 (33)	3 (11)
Pulse >100 beats/min	17 (33)	10 (42)	7 (25)
White blood cell count, ×10 ⁹ /L†	11.4 (4.7-26.3)	12.8 (4.7-26.3)	10.2 (5.9-17.0)

*All subjects were men.

†Mean (range).

‡Mean.

§COPD indicates chronic obstructive pulmonary disease.

in any position, consistently had the highest κ values of any physical finding (κ , 0.23-0.65), followed by wheezes (κ , -0.05 to 1.00); κ values were low for bronchophony (κ , -0.14 to 0.22), egophony (κ , -0.10 to 0.18), and bronchial breath sounds (κ , -0.14 to 0.14).

The value of individual physical findings as detected by each physician in diagnosing pneumonia and the accuracy of an overall diagnosis of pneumonia by each physician are shown in **Table 4**. The sensitivity and specificity of a clinical diagnosis of pneumonia were 0.69 and 0.65, respectively, for physician A (positive predictive value [PPV], 61%); 0.47 and 0.58 for physician B (PPV, 53%); and 0.50 and 0.75 for physician C (PPV, 57%). The sensitivity and specificity of physical findings showed considerable variability among examiners as well as for a given examiner in eliciting findings between the right and left lungs. The most consistently helpful maneuvers were listening for rales with the patient in the upright position (highest sensitivity) and performing auscultatory percussion, egophony, and rales with the patient in the LDP (highest specificity). Findings of chest physical examinations were completely normal for only 2 patients. Despite detecting abnormal sounds, the examiner did not think the patient had pneumonia in many cases, attributing the findings to other respiratory disorders.

COMMENT

This study was specifically focused on the usefulness of the physical examination of the chest for diagnosing pneumonia. Examiners had no patient history other than knowing the patients had lower respiratory tract symptoms compatible with pneumonia; they also had no knowledge of the patients' vital signs but could feel their skin temperature and observe how ill they appeared. We found that for patients presenting with symptoms of lower respiratory infection, physical examination of the chest was a moderately sensitive and specific method to determine if pneumonia was present and at what site. No single maneuver

Table 2. Findings on Chest Physical Examination by Physician

Findings	No. (%) of Patients		
	Physician A (n = 46)	Physician B (n = 49)	Physician C (n = 26)
Bronchial breath sounds			
Left lung	11 (24)	13 (27)	2 (8)
Right lung	17 (37)	21 (43)	2 (8)
Bronchophony			
Left lung	11 (24)	3 (6)	2 (8)
Right lung	22 (48)	11 (22)	2 (8)
Egophony			
Left lung	8 (17)	2 (4)	2 (8)
Right lung	20 (43)	5 (10)	2 (8)
Friction rub			
Left lung	0	2 (4)	0
Right lung	1 (2)	2 (4)	0
Rales			
Left lung	16 (35)	19 (39)	7 (27)
Right lung	10 (22)	32 (65)	13 (50)
Lateral decubitus rales			
Left lung	7 (15)	5 (10)	3 (12)
Right lung	19 (41)	22 (45)	13 (50)
Percussion (auscultatory)			
Left lung	6 (13)	0	2 (8)
Right lung	8 (17)	2 (4)	6 (23)
Percussion (fingertip)			
Left lung	8 (17)	0	0
Right lung	8 (17)	4 (8)	1 (4)
Wheezes (late inspiratory)			
Left lung	11 (24)	6 (12)	5 (19)
Right lung	10 (22)	9 (18)	6 (23)
Wheezes (inspiratory/expiratory)			
Left lung	11 (24)	6 (12)	1 (4)
Right lung	10 (22)	4 (8)	2 (8)
Rhonchi			
Left lung	5 (11)	5 (10)	1 (4)
Right lung	4 (9)	5 (10)	1 (4)
Vocal fremitus			
Left lung	0	1 (2)	0
Right lung	1 (2)	2 (4)	1 (4)
Whispered pectoriloquy			
Left lung	1 (2)	0	2 (8)
Right lung	4 (9)	0	3 (12)

was uniformly highly sensitive or highly specific. Maneuvers with relatively high sensitivity or specificity for one examiner were not necessarily as useful for the other examiners. The most useful maneuvers were auscultation for rales with the patient in the upright position and LDP, but the sensitivity, specificity, and interobserver reliability of these findings were relatively low; κ values were highest for rales in the upright position (mean, 0.4; range, 0.24-0.65), fair for rales in the LDP (mean, 0.3; range, 0.23-0.47), but poor for bronchophony, egophony, and bronchial breath sounds (mean, 0.1; range, -0.14 to 0.25). A previously published study of rales in the LDP also found this finding useful in the detection of pneumonia.¹⁰ In our study, direct percussion was of limited value in detecting pneumonia, and κ values were variable. Although auscultatory percussion had high specificity, κ values were low or unmeasurable.

Our study employed a systematic approach to evaluate chest physical examination maneuvers, rigorously analyzed the findings, and examined their utility

Table 3. Physician Agreement on Findings as Reflected by κ Values

	Physician A vs Physician B	Physician B vs Physician C	Physician A vs Physician C
Bronchial breath sounds			
Left lung	0.14	-0.14	-0.14
Right lung	0.03	0.07	0.14
Bronchophony			
Left lung	-0.12	-0.06	-0.14
Right lung	0.16	0.25	0.22
Egophony			
Left lung	-0.08	0	0.18
Right lung	0.03	-0.10	0.03
Rales			
Left lung	0.35	0.64	0.51
Right lung	0.24	0.49	0.65
Lateral decubitus rales			
Left lung	0.23	0.47	0.23
Right lung	0.32	0.39	0.39
Wheezes			
Left lung	0.49	1.0	0.65
Right lung	0.17	0.65	-0.05
Rhonchi			
Left lung	0.13	0	-0.06
Right lung	0.18	-0.05	-0.05
Percussion (fingertip)			
Left lung	0	*	0
Right lung	0.40	1.0	0.28
Percussion (auscultatory)			
Left lung	0	0	0.45
Right lung	-0.04	0.28	0.10
Pneumonia diagnosis (% agreement)	0.18 (60)	0.31 (69)	0.43 (72)

* κ is not defined due to expected agreement of 1.0.

in the diagnosis of pneumonia. The results are consistent with the few previous studies on pulmonary physical examination. One other study assessed interobserver reliability in eliciting 18 physical signs.¹¹ There were 2 to 4 examiners for each finding and κ values ranged from 0.01 to 0.52. The highest levels of interobserver agreement (κ , 0.50-0.52) were for both increased and reduced percussive note, wheezes, and pleural rub; κ values were 0.41 to 0.45 for crackles, reduced breath sounds, and clubbing, and were lowest for whispered pectoriloquy, increased tactile fremitus, and tracheal displacement ($\kappa < 0.12$). A high level of agreement for crackles was consistent with the findings in our study, whereas we rarely detected whispered pectoriloquy and tactile fremitus.

Few studies have examined the value of lung sounds in diagnosing pneumonia.⁵ In a prospective study of patients with fever and respiratory complaints, the chest x-ray film was used to diagnose pneumonia.¹² In univariate analysis, the presence of rales, bronchial breath sounds, egophony, decreased breath sounds, and percussion dullness were all significantly ($P < .001$) related to the presence of radiographic pulmonary infiltrates. In multivariate analysis, however, only rales (odds ratio [OR], 3.73) and decreased breath sounds (OR, 3.58) were significantly more likely to be present

Table 4. Accuracy of Physical Findings by Physician in Diagnosis of Pneumonia*

	Physician A				Physician B			
	Sensitivity	Specificity	+LR (95% CI)	-LR (95% CI)	Sensitivity	Specificity	+LR (95% CI)	-LR (95% CI)
Bronchial								
Left lung	0.33	0.78	1.5 (0.42-5.40)	0.86 (0.48-1.56)	0.63	0.81	3.3 (1.45-7.57)	0.46 (0.18-1.14)
Right lung	0.39	0.64	1.1 (0.46-2.42)	0.95 (0.58-1.58)	0.56	0.64	1.6 (0.83-2.90)	0.69 (0.52-1.62)
Bronchophony								
Left lung	0.50	0.80	2.5 (0.91-6.88)	0.63 (0.28-1.41)	0.13	0.95	2.6 (0.28-24.29)	0.92 (0.69-1.21)
Right lung	0.69	0.61	1.8 (1.01-3.10)	0.51 (0.21-1.20)	0.25	0.79	1.2 (0.41-3.49)	0.95 (0.68-1.32)
Egophony								
Left lung	0.17	0.83	1.0 (0.15-6.66)	1.0 (0.68-1.47)	0.13	0.98	6.5 (0.40-106.22)	0.89 (0.68-1.16)
Right lung	0.54	0.61	1.4 (0.72-2.68)	0.75 (0.13-6.66)	0.19	0.94	3.2 (0.59-17.12)	0.86 (0.67-1.11)
Rales								
Left lung	0.67	0.70	2.2 (1.07-4.66)	0.47 (0.15-1.50)	0.50	0.63	1.4 (0.61-3.01)	0.79 (0.38-1.65)
Right lung	0.54	0.61	1.4 (0.72-2.68)	0.75 (0.39-1.44)	0.75	0.39	1.2 (0.83-1.82)	0.64 (0.25-1.66)
Lateral decubitus rales								
Left lung	0.33	0.88	2.8 (0.67-11.33)	0.76 (0.42-1.35)	0.25	0.93	3.6 (0.69-18.39)	0.81 (0.54-1.21)
Right lung	0.69	0.70	2.3 (1.22-4.34)	0.44 (0.19-1.03)	0.56	0.61	1.4 (0.78-2.64)	0.72 (0.39-1.34)
Percussion (auscultatory)								
Left lung	0.33	0.90	3.3 (0.76-14.37)	0.74 (0.42-1.32)	0	1.0		1.0
Right lung	0.39	0.91	4.3 (1.20-15.59)	0.67 (0.43-1.05)	0.06	0.97	2.0 (0.13-31.08)	0.97 (0.85-1.11)
Pneumonia diagnosis	0.69	0.65	2.0 (1.00-3.90)	0.48 (0.21-1.06)	0.47	0.58	1.1 (0.55-2.28)	0.91 (0.52-1.62)

*+LR indicates positive likelihood ratio; -LR, negative likelihood ratio; CI, confidence interval.

in patients with pneumonia. Other predictors of pneumonia included temperature ($>37.8^{\circ}\text{C}$; OR, 2.69), pulse (>100 beats/min; OR, 2.35), and absence of asthma (OR, 3.98). In our study, 11 (21%) of the 52 patients had temperature greater than 38.0°C , and 8 (73%) of those had the diagnosis of pneumonia confirmed on chest x-ray film. Conversely, only 3 (11%) of the 28 subjects without pneumonia confirmed on chest x-ray film had fever.

In our study, the differences in the accuracy of diagnosis among the pulmonologist and the 2 primary care internists were minimal. In diagnosing pneumonia, the least experienced internist (fewest years in practice since residency) had the highest PPV (61%) and the highest sensitivity (69%); the pulmonologist had the highest specificity (75%). After reporting their official examination findings, the examiners sometimes discussed the findings among themselves and then unofficially reexamined the patients. They observed that the findings had often changed over relatively short periods, especially in the presence of wheezing and rales. The frequency with which these findings changed was not recorded.

Our study has several limitations. First, despite the 3-year duration of the study, only 52 patients were enrolled, partly because patients were recruited only during daytime hours. Second, only 3 examiners evaluated the patients. Logistically, it would have been difficult to have more examiners and additional examinations would have created a hardship for the subjects. Third, not all examiners were able to see each patient, an inevitable consequence of the physicians' schedules. Fourth, the study population was composed exclusively of male veterans, most of whom were in late middle age and many of whom had underlying pulmonary and cardiac diseases. The re-

sults may not be generalized to younger, healthier patients or to women.

This rigorous prospective investigation adds information on the independent utility of lung examination in diagnosing pneumonia. Since older individuals and those with underlying cardiopulmonary diseases represent the bulk of adults presenting with signs of lower respiratory infection, the study results are applicable in most clinical settings. The maneuvers most valuable in detecting pneumonia are unilateral rales and rales in the LDP. Other maneuvers, which are time-consuming and somewhat awkward for the patient, were not helpful. These findings suggest that a limited chest examination, in addition to obtaining vital signs and history, should be sufficient to screen for pneumonia. However, some patients do not have abnormal lung sounds, even in the presence of pneumonia. Furthermore, lung findings during physical examination can be evanescent and may change substantially, even in a few minutes.

We conclude that physical examination alone is not sufficiently accurate to confirm or exclude a diagnosis of pneumonia. When pneumonia is suspected, chest x-ray remains the best diagnostic test. Studies of the utility of chest radiography in the emergency department support this view.¹³⁻¹⁵ The pulmonary examination has, at best, modest ability to predict the presence of pneumonia and is inconsistently interpreted, even by expert examiners.

To improve physicians' ability to correctly diagnose pneumonia, the accuracy and reliability of the pulmonary examination requires additional clinical research.

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Physician C

Sensitivity	Specificity	+LR (95% CI)	-LR (95% CI)
0	0.92	0	1.1 (0.97-1.22)
0.11	0.94	1.8 (0.13-25.81)	0.95 (0.73-1.23)
0.50	0.96	12.5 (1.13-137.9)	0.52 (0.13-2.09)
0.11	0.94	1.8 (0.13-25.81)	0.95 (0.73-1.23)
0.50	0.96	12.5 (1.13-137.90)	0.52 (0.13-2.09)
0	0.88	0	1.1 (0.95-1.35)
1.0	0.79	4.8 (2.19-10.35)	0
0.56	0.53	1.2 (0.56-2.57)	0.83 (0.35-1.97)
1.0	0.96	25.0 (3.52-177.50)	0
0.44	0.47	0.8 (0.35-1.97)	1.2 (0.55-2.57)
0.50	0.96	12.5 (1.13-137.90)	0.52 (0.13-2.09)
0.44	0.88	4.0 (0.83-16.16)	0.64 (0.35-1.17)
0.50	0.75	2.0 (0.60-6.64)	0.67 (0.31-1.43)

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