

Background

- Clinicians in malaria-endemic, resource-limited settings rely on signs and symptoms to **assess cause and severity in pediatric febrile illness** using the WHO's Integrated Management of Childhood Illness (IMCI) guidelines.
- High rates of empiric antibiotic use in non-malarial fever have been shown in prior studies.
- Point-of-care (POC) biomarker tests, **C-reactive protein (CRP) and procalcitonin (PCT)**, may be used to determine those at low risk of bacterial infection.
- Utility of PCT and CRP in risk prediction for prognosis is not well described.**



Objective: To characterize the predictive ability of IMCI danger signs and POC biomarkers for poor outcomes in children with acute, non-malarial fever in a public hospital in rural Malawi.

Methods

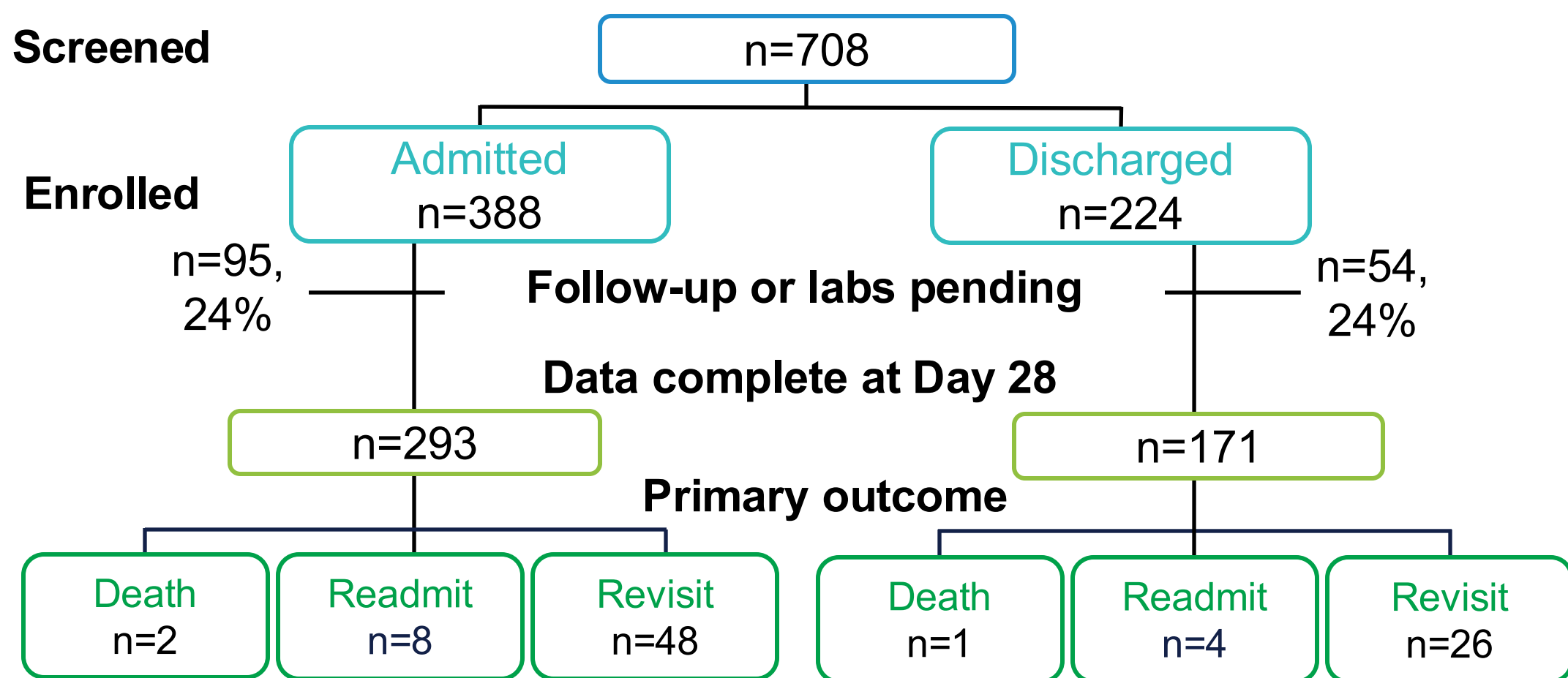
- Enrolled children <5 years, **malaria rapid test negative** in under-five Department at Thyolo District Hospital from March-November 2024 from an ongoing cohort.
- Ratio of admitted to discharged patients of 2:1** to capture severe illness.
- Clinical, socio-behavioral, and laboratory data (glucose, hemoglobin, PCT, CRP, blood culture) collected on Day 0.
- Outcomes collected on day of discharge (if admitted), and Day 28.

Primary Outcome: Composite of **death, readmission, or revisit by day 28**

- Fisher's Exact and χ^2 tests used to compare frequencies and area under the receiver operative curve (ROC) used to evaluate performance of POC tests and Danger Signs.
- Test characteristics calculated using cutoffs from literature and ROC curves for the primary outcome.

IMCI Danger Signs	Inability to drink		More info on IMCI
	Convulsions		
	Vomiting everything		IMCI Chart Booklet
	Lethargic/unconscious		

Screened

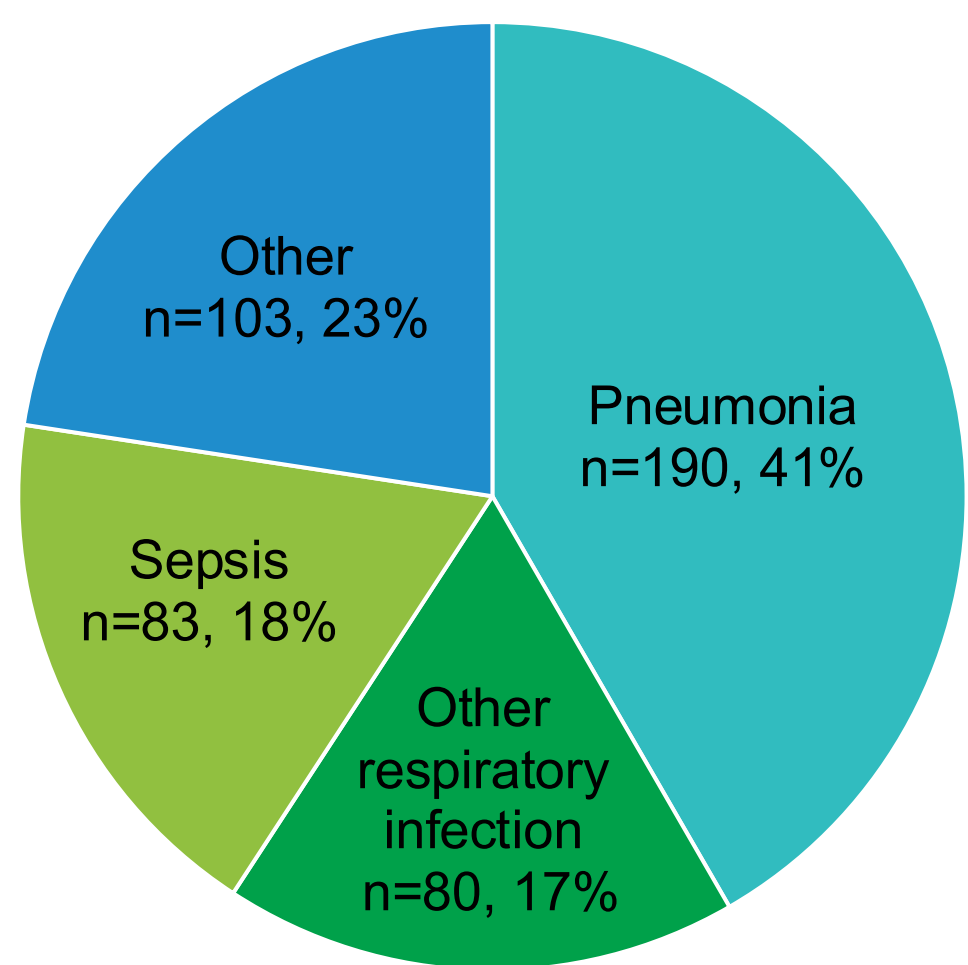


Patient risk factors by outcome

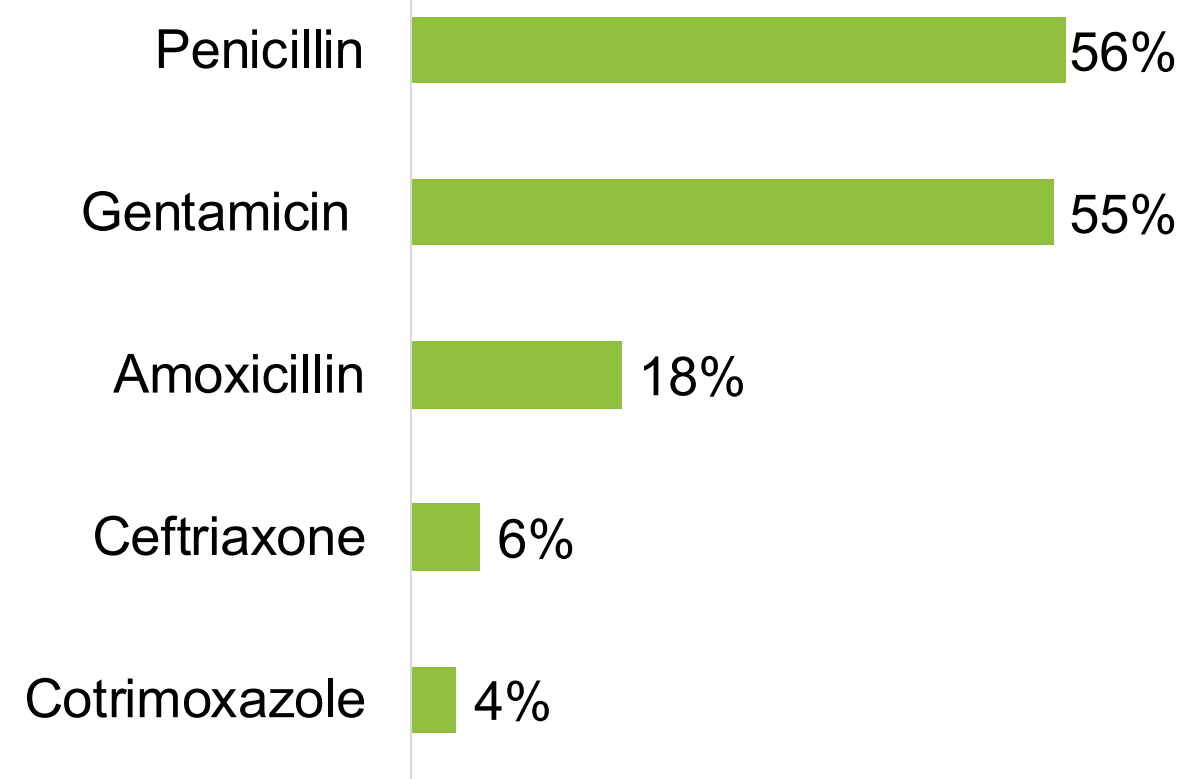
Risk Factor, n (%)	Death/Readmit/Revisit			p-value
	Overall (n=462)	No (n=382)	Yes (n=80)	
Age				0.4
<1 year	133 (29%)	115 (30%)	18 (23%)	
1-2 years	228 (60%)	51 (64%)	279 (61%)	
3-4 years	39 (10%)	11 (14%)	52 (11%)	
Sex				>0.9
Male	245 (53%)	203 (53%)	42 (53%)	
HIV status				0.6
Positive	6 (1.3%)	6 (1.6%)	0 (0%)	
Exposed	26 (5.6%)	22 (5.8%)	4 (5.0%)	
Negative	394 (85%)	322 (84%)	72 (90%)	
Indeterminate	36 (7.8%)	32 (8.4%)	4 (5.0%)	
Oxygen saturation				0.9
Mid-upper arm circumference				0.8
< 11.5 cm	2 (0.5%)	2 (0.6%)	0 (0%)	
11.5 - 12.5 cm	74 (19%)	60 (18%)	14 (20%)	
> 12.5 cm	323 (81%)	268 (81%)	55 (80%)	
PCT (ng/mL)				0.4
<0.5	279 (70%)	233 (70%)	46 (70%)	
≥0.5 to <2	59 (15%)	46 (14%)	13 (20%)	
≥2 to ≤10	46 (11%)	40 (12%)	6 (9.1%)	
≥10	17 (4.2%)	16 (4.8%)	1 (1.5%)	
Unknown	61	47	14	
CRP (mg/L)				0.074
< 10	156 (39%)	133 (40%)	23 (35%)	
10 – 49	169 (42%)	145 (43%)	24 (36%)	
50-99	43 (11%)	30 (8.9%)	13 (20%)	
> 100	34 (8.5%)	28 (8.3%)	6 (9.1%)	
Unknown	60	46	14	
Any danger sign	101 (22%)	87 (23%)	14 (18%)	0.3
Antibiotic administered	422 (91%)	347 (91%)	75 (94%)	0.4

Results

Primary diagnosis



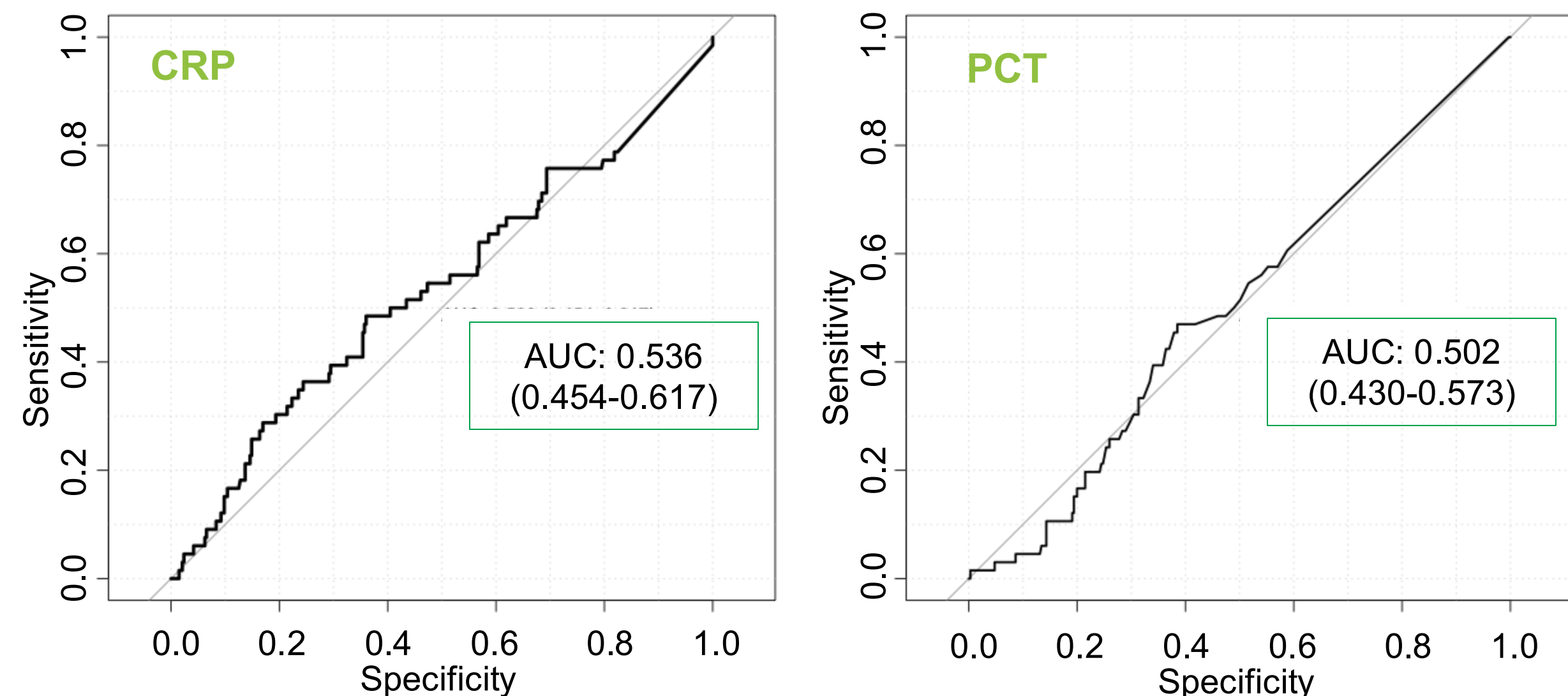
Antibiotic(s) given during visit



Test characteristics

Predictor, n (95% CI)	Sensitivity	Specificity	PPV	NPV
Any danger sign	0.17 (0.10-0.28)	0.77 (0.73-0.81)	0.19 (0.14-0.25)	0.84 (0.79-0.89)
CRP (mg/L)				
≥ 23.5	0.41 (0.30-0.53)	0.64 (0.59-0.69)	0.19 (0.14-0.26)	0.84 (0.79-0.88)
≥ 80	0.12 (0.06-0.22)	0.91 (0.88-0.94)	0.23 (0.11-0.38)	0.83 (0.79-0.87)
PCT (ng/mL)				
≥ 0.28	0.38 (0.27-0.49)	0.66 (0.61-0.71)	0.19 (0.13-0.26)	0.83 (0.79-0.87)
≥ 4.0	0.04 (0.01-0.11)	0.91 (0.88-0.94)	0.08 (0.02-0.22)	0.82 (0.78-0.85)
PCT ≥0.28, CRP ≥23.5 + any danger sign	0.62 (0.51-0.73)	0.43 (0.38-0.48)	0.19 (0.14-0.24)	0.84 (0.79-0.89)

AUROC for CRP and PCT



Conclusion

In a setting with >90% antibiotic use, point-of-care PCT and CRP were comparable to IMCI danger signs in predicting poor outcomes.

- Most patients (58%) were diagnosed with respiratory infections and treated with ampicillin and gentamicin
- Participants were healthy overall with low mortality (<1%) and reported full recovery by Day 28.
- Association of CRP level with poor outcome is trending toward significance (p=0.07)
- Future qualitative studies may help understand provider and community perspectives on antibiotic use and management of febrile illness in this context.
- Implementation/effectiveness studies are needed to determine utility of CRP and PCT as diagnostic aids within integrated clinical decision support tools to guide empiric antibiotic use.

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