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COLOMBO SOUTH TEACHING HOSPITAL

THE UNIVERSITY OF SYDNEY

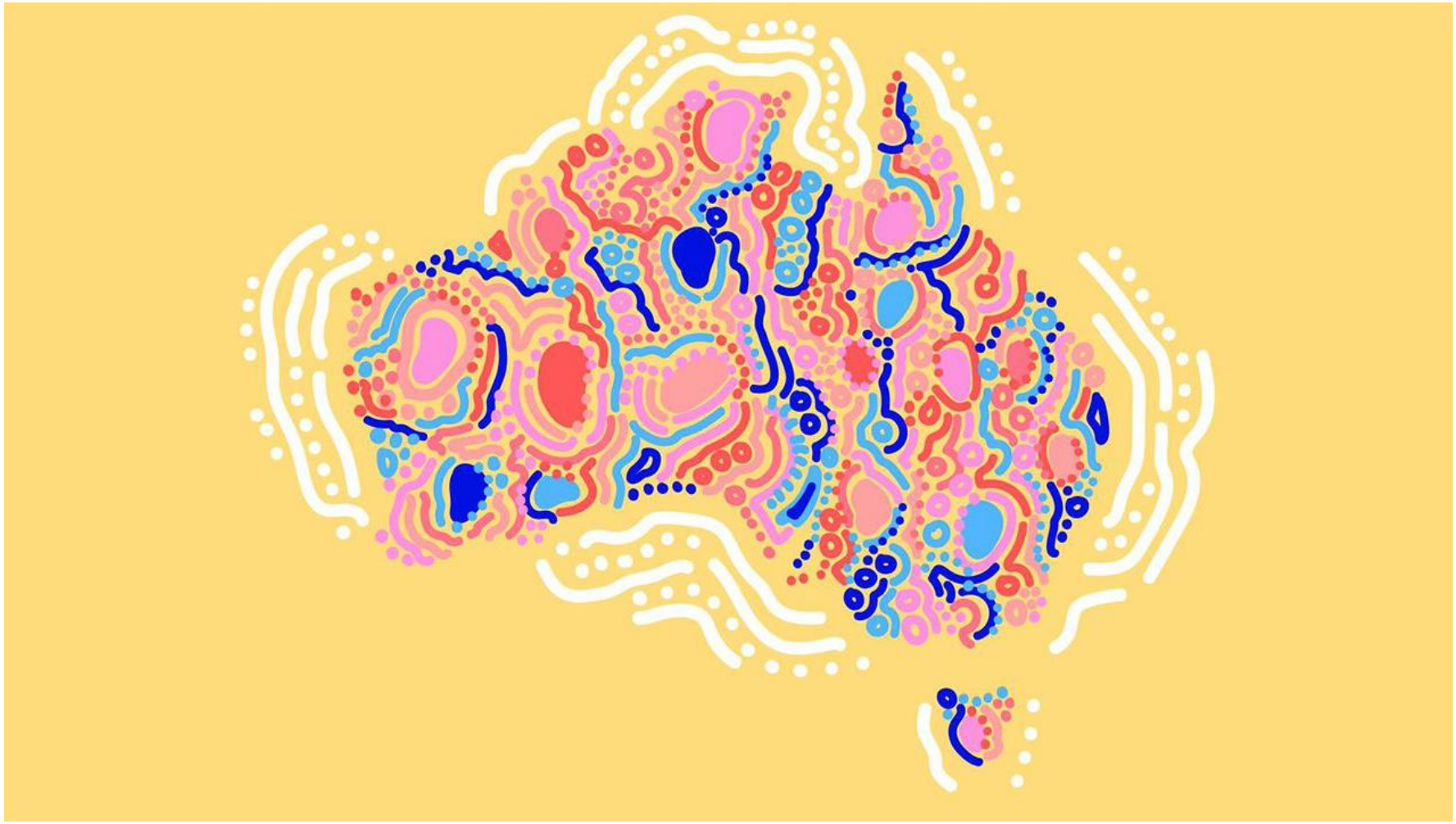
Improving the management of lower respiratory tract infections in children in Sri Lanka

Dr Gayana Gunaratna
Dr Phoebe Williams

A project supported by the International Society of Antimicrobial Chemotherapy (ISAC)

Presentation Prepared for the Alliance of Prudent Use of Antibiotics Webinar

Acknowledgement of Country



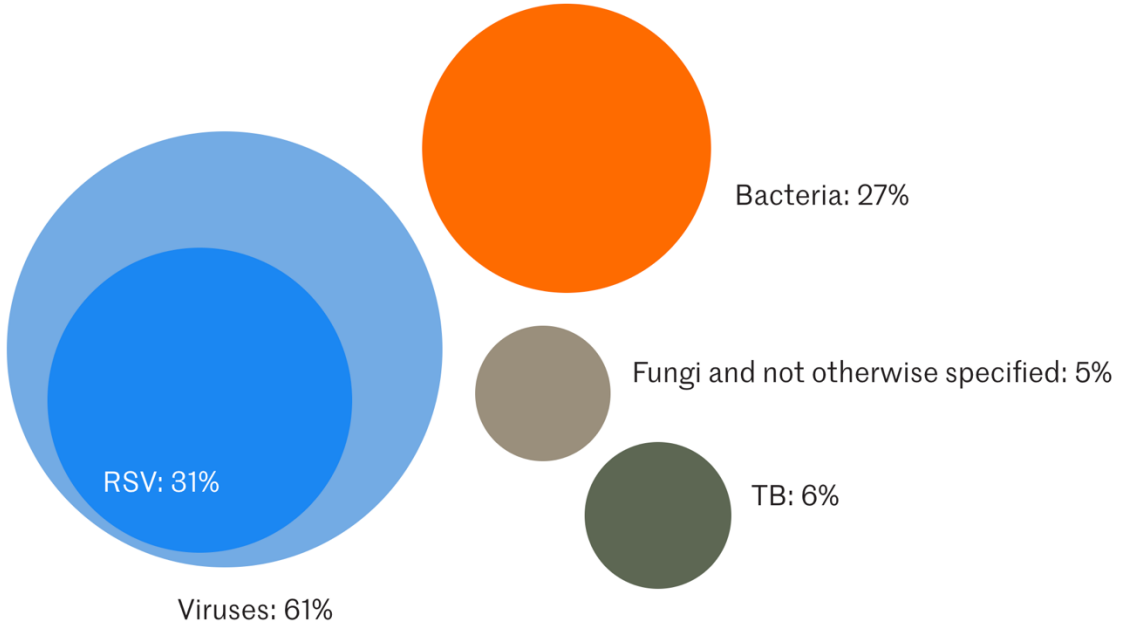
We acknowledge the tradition of custodianship and as we share our own knowledge. learning and research practices may we also pay respect to the knowledge embedded
forever within the Aboriginal Custodianship of Country.

2022 ISAC Project Grant:

The University of Sydney, Australia & Colombo South Teaching Hospital, Sri Lanka

Study Rationale:

- Lower respiratory tract infections (LRTIs) are a major cause of hospitalisation, morbidity and mortality in children, especially in those <5 years.
- Children presenting with respiratory tract symptoms are likely to be prescribed antibiotics, despite the fact that the majority of LRTIs in children are self-limiting and viral in origin.
- Excessive and irrational antibiotic use increases the risk of antimicrobial resistance (AMR)
  - However, this needs to be balanced against the risk of severe disease and death if bacterial pneumonia is not appropriately treated.
- In an era of increasing antimicrobial resistance, there is a need to improve diagnostic strategies in resource-constrained settings to prevent unnecessary antibiotic use.



2019 PERCH study (7 countries, >4,000 children): revealed viruses are responsible for 61% of hospitalised pneumonia cases in children 1mo-5yrs.

Estimates of the global, regional, and national morbidity, mortality, and aetiologies of lower respiratory infections in 195 countries, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Infect Dis* 2018; **18**: 1191–210.
O'Brien et al. Cvauses of severe pneumonia requiring hospital admission in children without HIV infection from Africa & Asia: the PERCH multicountry case-control study 2019 The Lancet. doi: 10.1016.S0140-6736
Nguyen PT, Tran HT, Fitzgerald DA, *et al.* Antibiotic use in children hospitalised with pneumonia in Central Vietnam. *Arch Dis Child* 2020; **105**: 713–9.
Basu S, Copana R, Morales RJ, *et al.* Keeping It Real: Antibiotic Use Problems and Stewardship Solutions in Low- and Middle-income Countries. *Pediatr Infect Dis J* 2022; **41**: S18–25.

Study Aim

- A major challenge in improving the management of childhood LRTIs is the need for a pragmatic, sensitive and specific algorithm to **guide clinical diagnosis and management of children with LRTIs,** particularly in resource-constrained settings where biomarker-guided decisions are limited.
- The primary aim of this study is to assess a pre-validated algorithm to reduce unnecessary hospitalisation and antibiotic use among children presenting with respiratory symptoms to a tertiary hospital in Colombo, Sri Lanka.

Clinical Infectious Diseases
MAJOR ARTICLE

Predictors of Unlikely Bacterial Pneumonia and Adverse Pneumonia Outcome in Children Admitted to a Hospital in Central Vietnam

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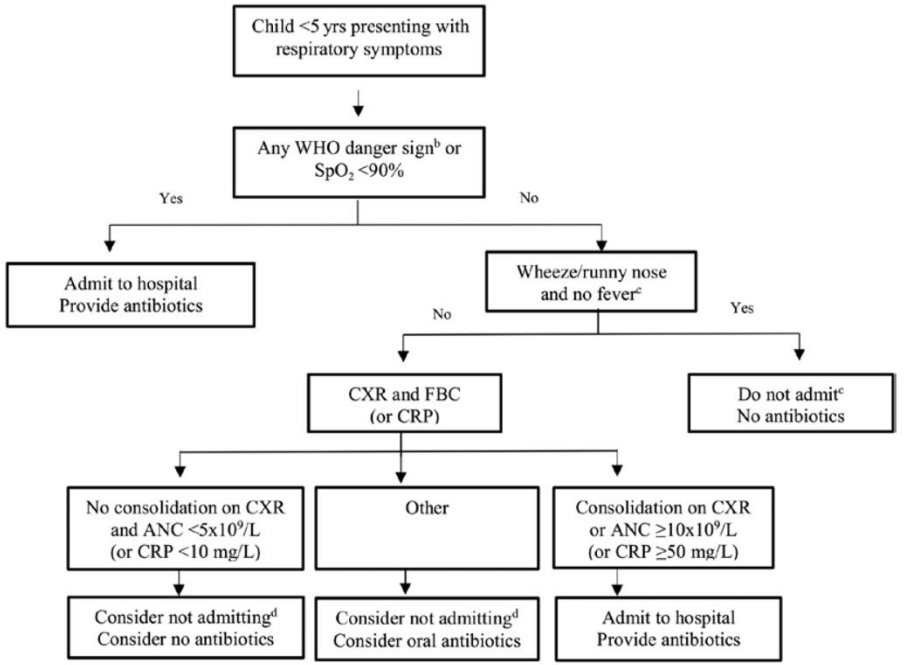


Figure 3. Proposed pragmatic algorithm[a] to guide rational antibiotic use and hospitalization in children who present to the hospital with respiratory symptoms. Abbreviations: ANC, absolute neutrophil count; CRP, C-reactive protein; CXR, chest radiograph; FBC, full blood count; SpO_2, peripheral oxygen saturation; WHO, World Health Organization. [a]Incorporating study findings, existing WHO guidance, and previous findings from Vietnam that used CRP values to guide rational antibiotic use [10]. [b]Including inability to drink or breastfeed, vomiting everything, lethargy or convulsions, respiratory distress (grunting or nasal flaring), severe malnutrition. [c]As per WHO recommendation [28]. [d]Admit and consider antibiotics if any deterioration or relevant clinical concern.

Simple algorithms can reduce antibiotic overuse and unnecessary hospitalisation in children presenting with respiratory symptoms in resource-constrained healthcare settings

Nguyen *et al. Pneumonia* (2023) 15:11
https://doi.org/10.1186/s41479-023-00113-9

Pneumonia

RESEARCH Open Access

Clinical algorithm reduces antibiotic use among children presenting with respiratory symptoms to hospital in central Vietnam

Phuong TK Nguyen[1,2*], Tam TM Nguyen[1], Lan TB Huynh[1], Stephen M Graham[3] and Ben J Marais[4,5]

Abstract

Objective To assess the safety and utility of a pragmatic clinical algorithm to guide rational antibiotic use in children presenting with respiratory infection.

Methods The effect of an algorithm to guide the management of young (< 5 years) children presenting with respiratory symptoms to the Da Nang Hospital for Women and Children, Vietnam, was evaluated in a before-after intervention analysis. The main outcome was reduction in antibiotic use, with monitoring of potential harm resulting from reduced antibiotic use. The intervention comprised a single training session of physicians in the use of an algorithm informed by local evidence; developed during a previous prospective observational study. The evaluation was performed one month after the training.

Results Of the 1290 children evaluated before the intervention, 102 (7.9%) were admitted to hospital and 556/1188 (46.8%) were sent home with antibiotics. Due to COVID-19, only 166 children were evaluated after the intervention of whom 14 (8.4%) were admitted to hospital and 54/152 (35.5%) were sent home with antibiotics. Antibiotic use was reduced (from 46.8% to 35.5%; $p = 0.009$) after clinician training, but adequate comparison was compromised. The reduction was most pronounced in children with wheeze or runny nose and no fever, or a normal chest radiograph, where antibiotic use declined from 46.7% to 28.8% ($p < 0.0001$). The frequency of repeat presentation to hospital was similar between the two study periods (141/1188; 11.9% before and 10/152; 6.6% after; $p = 0.10$). No child represented with serious disease after being sent home without antibiotics.

Conclusions We observed a reduction in antibiotic use in young children with a respiratory infection after physician training in the use of a simple evidence-based management algorithm. However, the study was severely impacted by COVID-19 restrictions, requiring further evaluation to confirm the observed effect.

Table 4 Management of children presenting to the respiratory outpatient clinic with respiratory symptoms according to algorithm classification, before and after the intervention

Classification*	Before $N = 1290$	After $N = 166$	*p*-value
Group 1[a]			
Number	22	6	-
Admitted to hospital	6 (27.3)	1 (16.7)	-
Discharged with antibiotic	13 (59.1)	4 (66.6)	0.1
Discharged without antibiotic	3 (13.6)	1 (16.7)	
Group 2[b]			
Number	355	118	-
Admitted to hospital	14 (3.9)	2 (1.7)	-
Discharged with antibiotic	166 (46.7)	34 (28.8)	< 0.0001
Discharged without antibiotic	175 (49.4)	82 (69.5)	
Group 3[c]			
Number	913	42	-
Admitted to hospital	82 (8.9)	11 (26.2)	-
Discharged with antibiotic	383 (41.9)	18 (42.9)	0.2
Discharged without antibiotic	448 (49.2)	13 (30.9)	

* Classified according to groups described in Fig. 1 from retrospective data analysis

[a] Children with any WHO danger sign or SpO2 < 90% OR consolidation on CXR or ANC ≥ 10×10^9/L (or CRP ≥ 50 mg/L). Suggested management: admit to the hospital and provide antibiotics

[b] Children with wheeze/runny nose and no fever OR No consolidation on CXR and ANC < 5×10^9/L (or CRP < 10 mg/L). Suggested management: no hospital admission and no antibiotics

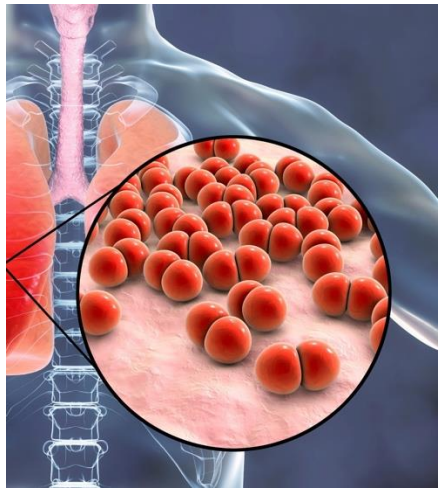
[c] Children not belonging to groups 1 or 2. Suggested management: consider not to admit and consider oral antibiotics

ANC absolute neutrophil count, *CXR* chest radiograph, *FBC* full blood count, *CRP* C reactive protein, *SpO2* peripheral oxygen saturation, *WHO* World Health Organization

Pneumococcal sub-study

- Children included in the post-intervention phase will also be consented for a **pneumococcal carriage sub-study,** to gain an understanding of the **burden of pneumococcus carriage in an unvaccinated population in Sri Lanka,** and the interplay of serotype specific species on the clinical presentation in children with respiratory tract symptoms.

- This sub-study also aims to promote the rational use of antibiotics by providing detailed analysis of local pneumococcus antibiotic susceptibilities.

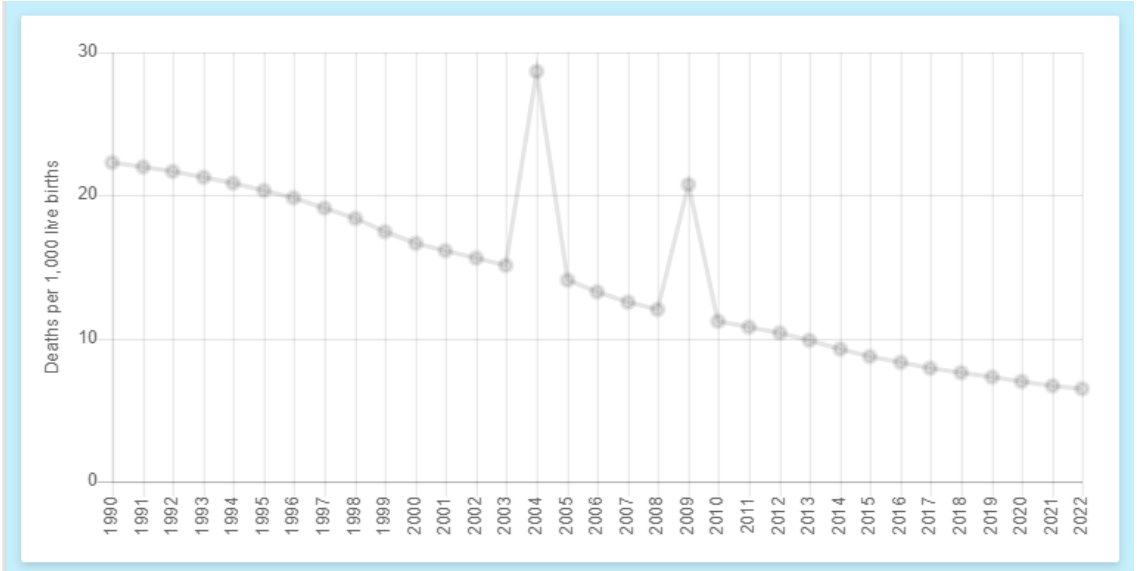


U5 Mortality in Sri Lanka

In 2016, the Sustainable Development Goals were established, with goals of:

- Reducing under 5 mortality to 25 deaths per 1,000 live births
- Reducing neonatal mortality to 12 deaths per 1,000 live births
- Ending preventable deaths of neonates and children under 5-years

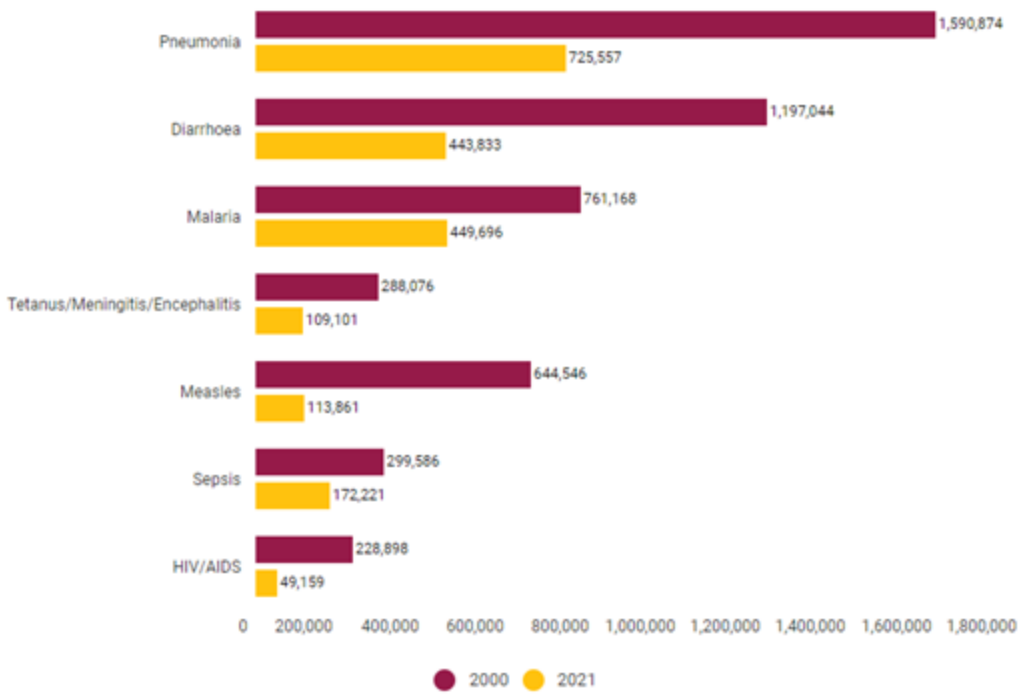
Sri Lanka has made significant gains in U5 mortality over recent decades; ranked 178th out of 241 countries, with a rate of 6.9 deaths per 1,000 live births



Spatial distribution of U5 mortality rates by districts of Sri Lanka
(Data from the 2016 Sri Lanka demographic and health survey)

https://doi.org/10.1371/journal.pone.0291246.g002

U5 Mortality in Sri Lanka, by disease (2000 vs 2021)



- Pneumonia accounts for 16% of all deaths of children under 5 years old in the world, killing nearly one million children in 2015

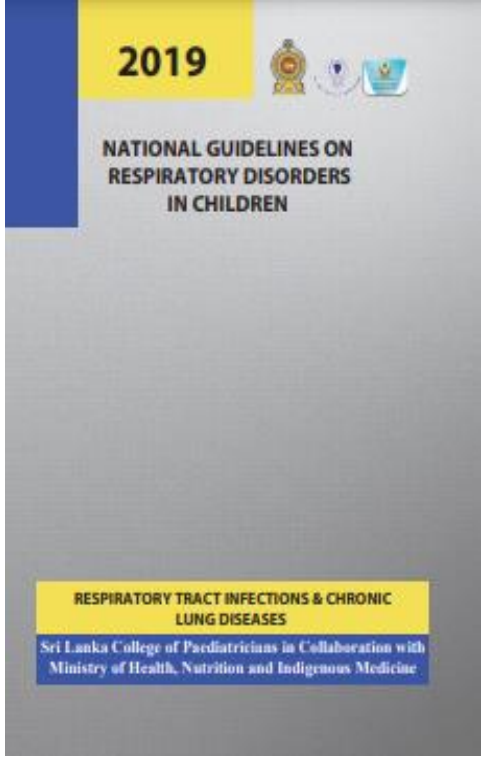
- In Sri Lanka, there were 21,000 reported cases of pneumonia in 2006, 40% were in the age group of less than 4 years

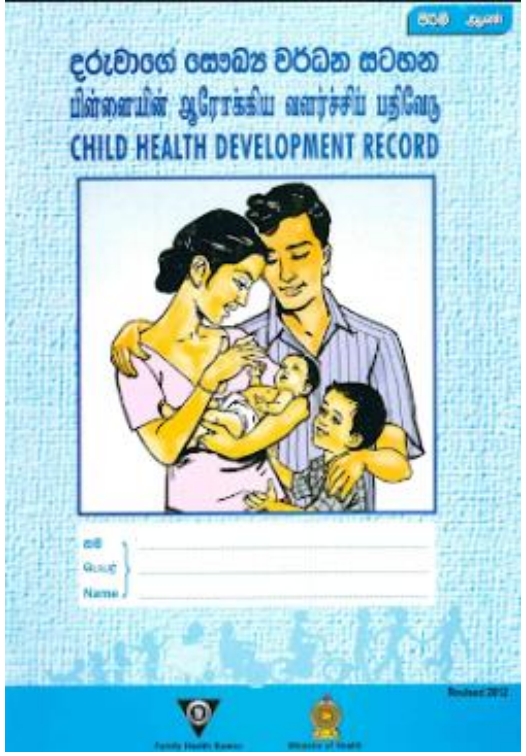
Source: UN IGME Child and Adolescent Causes of Death Estimation (CA CODE) project (2023). http://www.epid.gov.lk/web/images/pdf/wer/2016/vol_43_no_50-english.pdf. https://pneumonia.biomedcentral.com/articles/10.1186/s41479-020-00071-6#ref-CR1

The Context

- Sri Lanka is a low middle-income country, having significantly better health indices compared to many economically comparable countries
- Most of the Sri Lankan population has easy access to a health care delivery institutions with trained healthcare workers
- All the citizens are provided with free health care in government healthcare institutions
- There is a significant number of private hospitals, mainly in bigger cities
- To reduce mortality due to acute respiratory infections, Sri Lanka has:

-Free health care for all citizens
-Highly trained medical and nursing staff
-National guidelines for managing ARIs in children
-Well-implemented immunisation programs with very high coverage achieved, including against *Haemophilus influenzae* type B, though without government funding for pneumococcal conjugate vaccines
-Good access to laboratory and radiology facilities





ISAC Project Grant: Colombo South Teaching Hospital
Study Procedures: 1. Educational Intervention

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COLOMBO SOUTH TEACHING HOSPITAL

The study includes three components: an initial (pre-intervention) phase to assess existing practices, an algorithm intervention, and a post-intervention phase to evaluate the effectiveness of the algorithm in the local setting.

1. In the **Pre-intervention period** existing standard practice are observed and recorded, without any training provided.
2. **Intervention:** Doctors will then be trained in the use of a pre-tested and validated algorithm. This evaluates the patients' need for level of care, investigations, antibiotic prescription, and follow-up management. Algorithm use will be encouraged by providing individual copies of the algorithm to doctors and placing large posters in all the relevant clinical areas.
3. **Post-intervention:** In the post-intervention period, doctors' management of patients will be re-evaluated.

Human resources available at the OPD:

Consultants
3

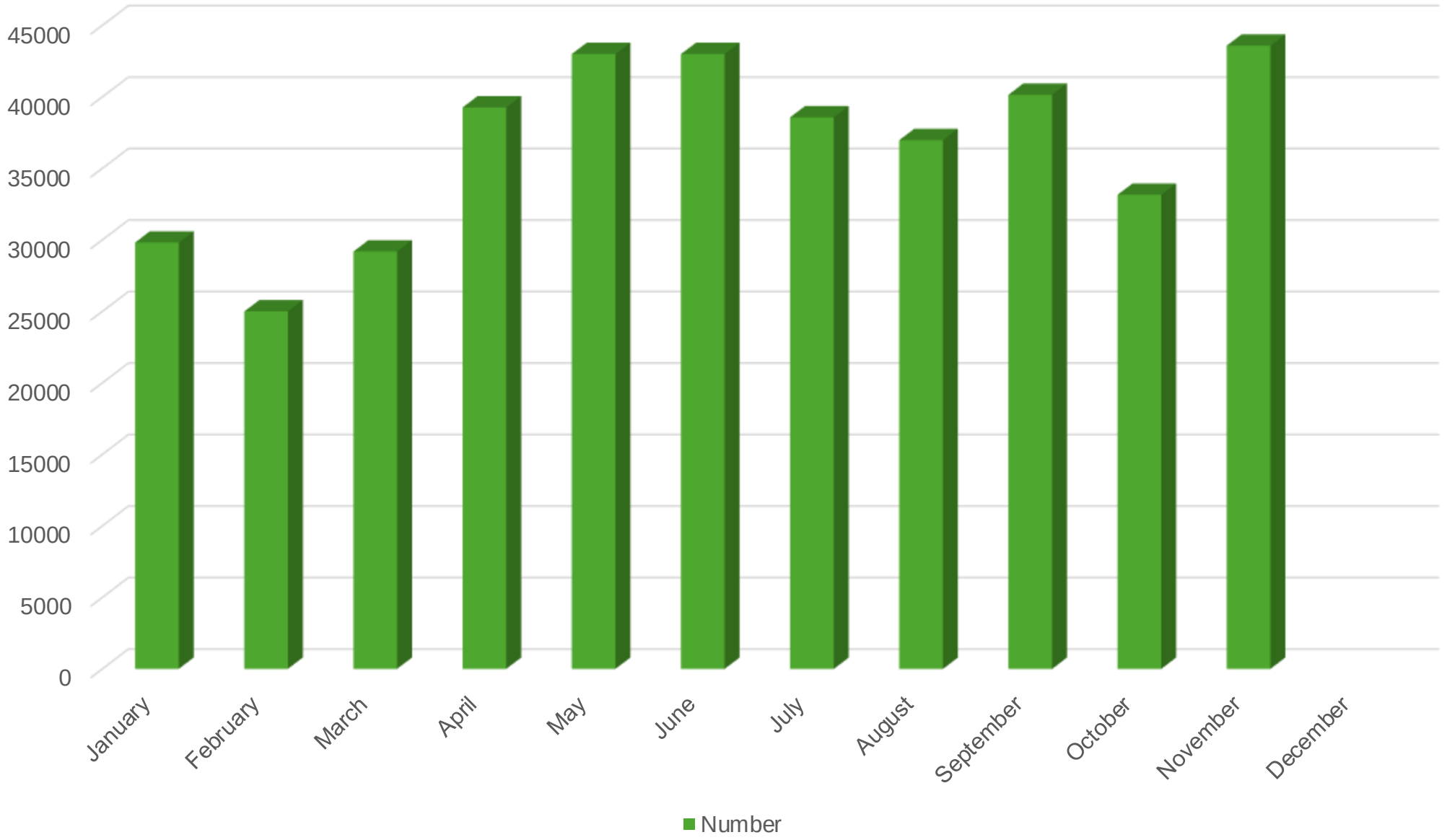
Medical Officers
42

Sister In charge
1

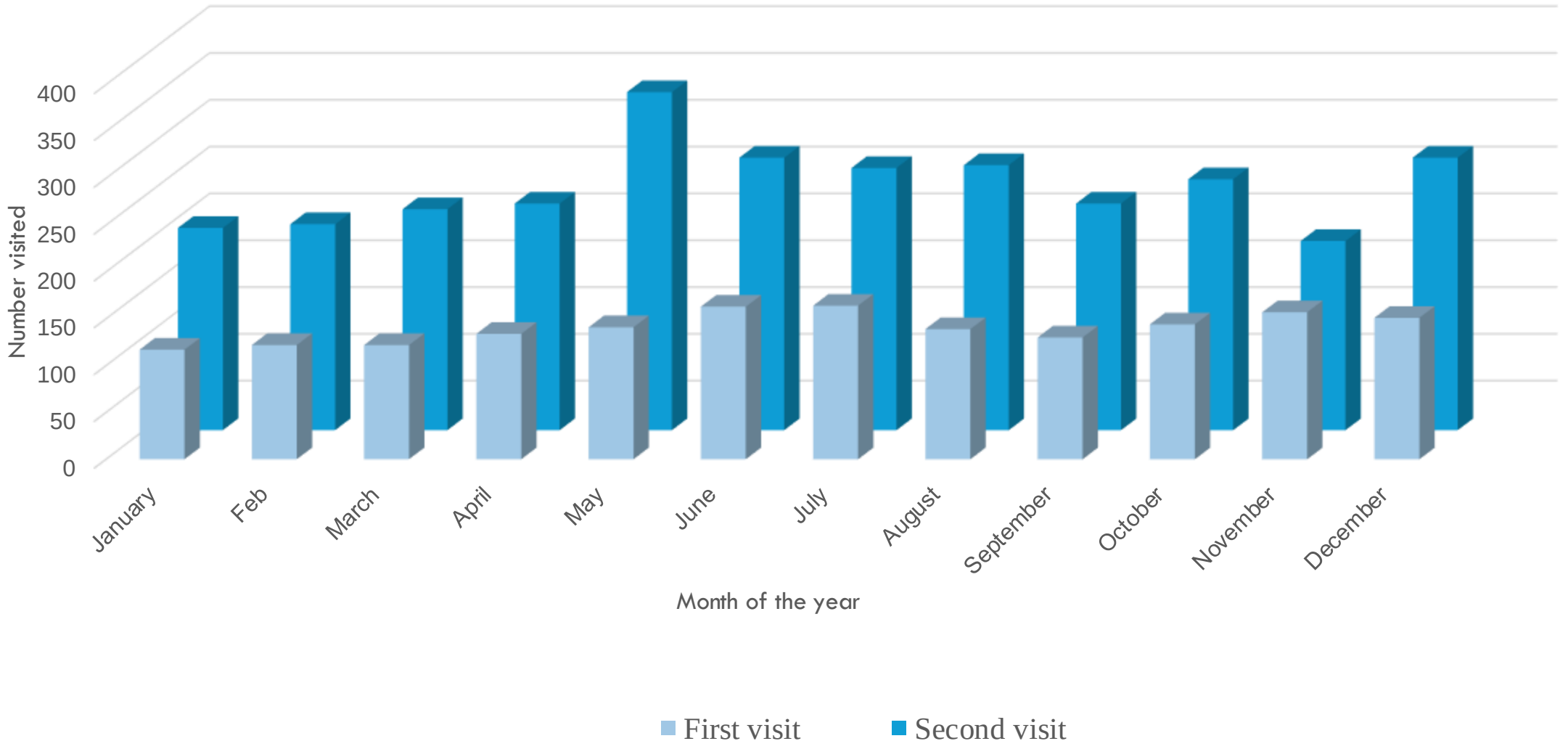
Other Healthcare Workers
29

Nursing Officers
28

Number of patients seen in the OPD; 2023



Number of children seen in the Outpatient Paediatric clinic; 2023




OPD STATISTICS
M6
2025

Results:

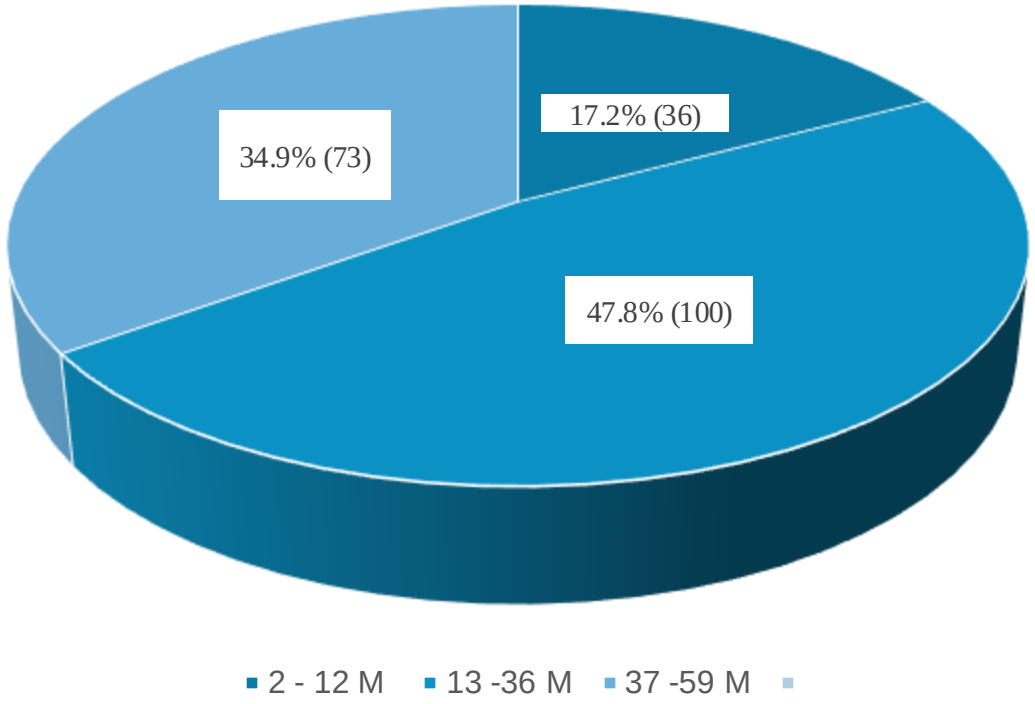
- A total of 209 children were recruited from the OPD during the pre-intervention period

  Mean age 30 months (SD 15.59, Minimum 03, Maximum 59)

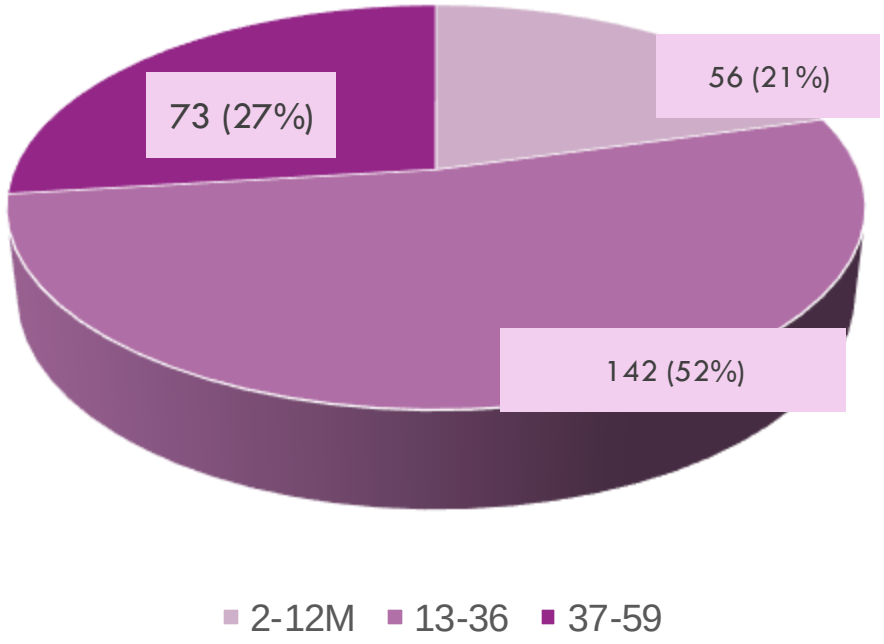
- A total of 271 children were recruited from the OPD during the Post-intervention period

  Mean age 27 months (SD 14.93, Minimum 02, Maximum 59)

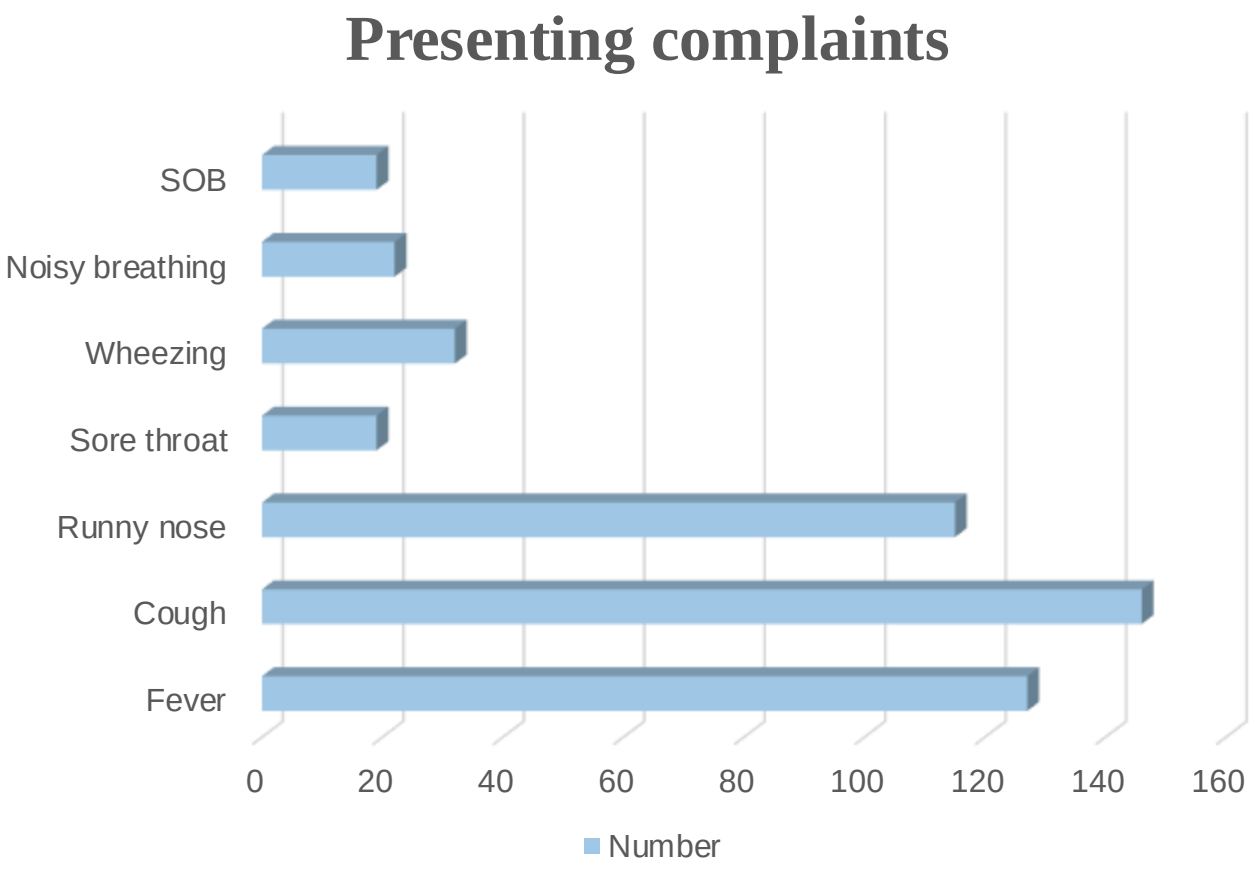
Age distribution; Pre-intervention

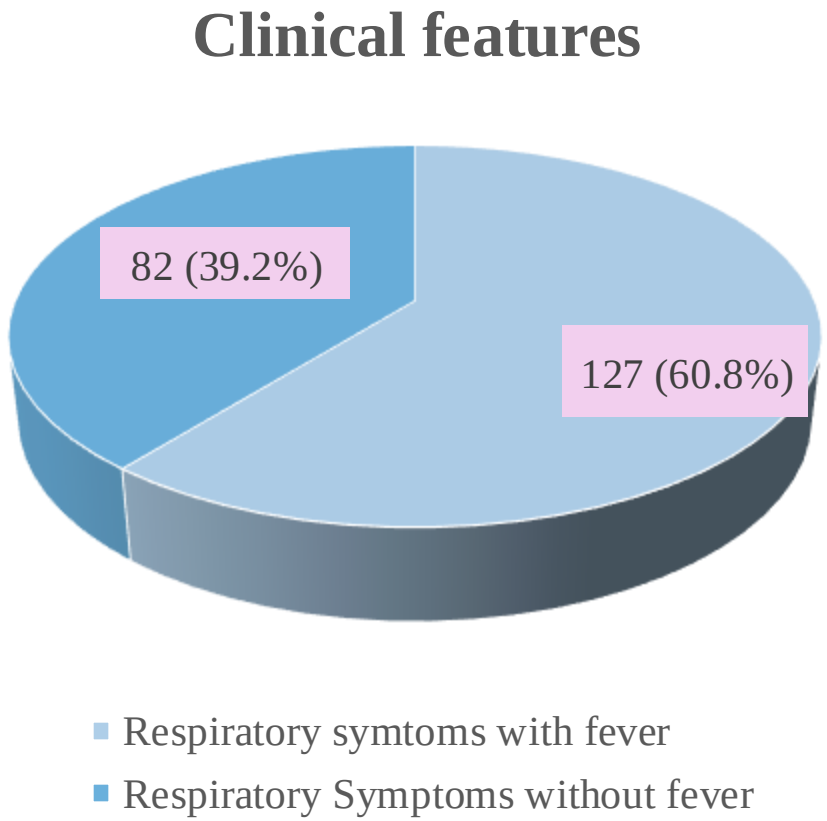


Age distribution, Post-intervention

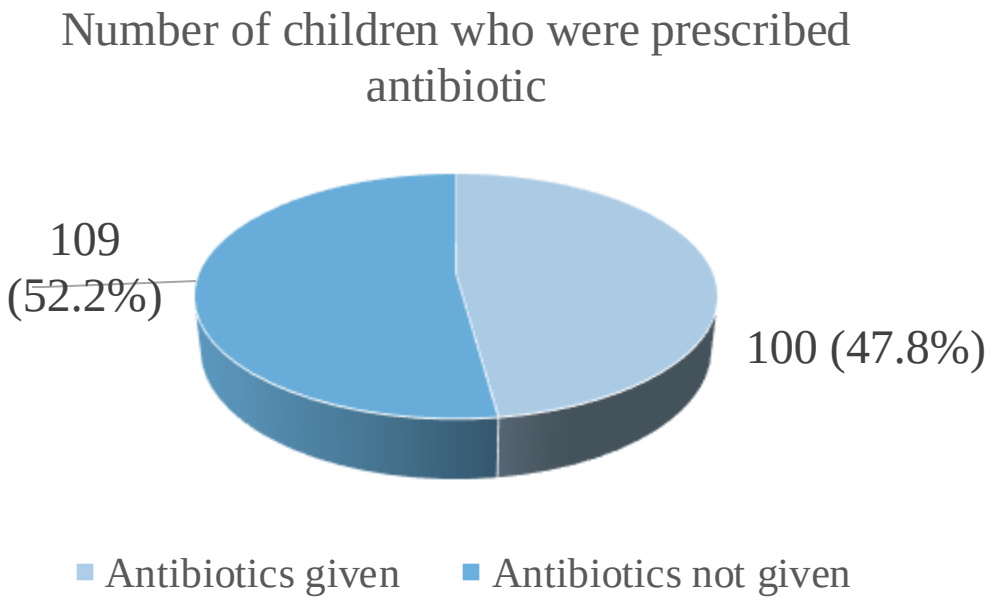


Indications to seek medical care: Pre-intervention phase





Antibiotic prescribed in the OPD settings: Pre-intervention



Reason for prescribing antibiotics	Number
Doctor's concern	73 (70%)
Comorbid conditions	7 (7.3%)
Parent expectation	5 (5.2%)
Other reasons	11 (11.4%)
Data missing	4 (4.1%)

- Of the 100 children prescribed antibiotics:

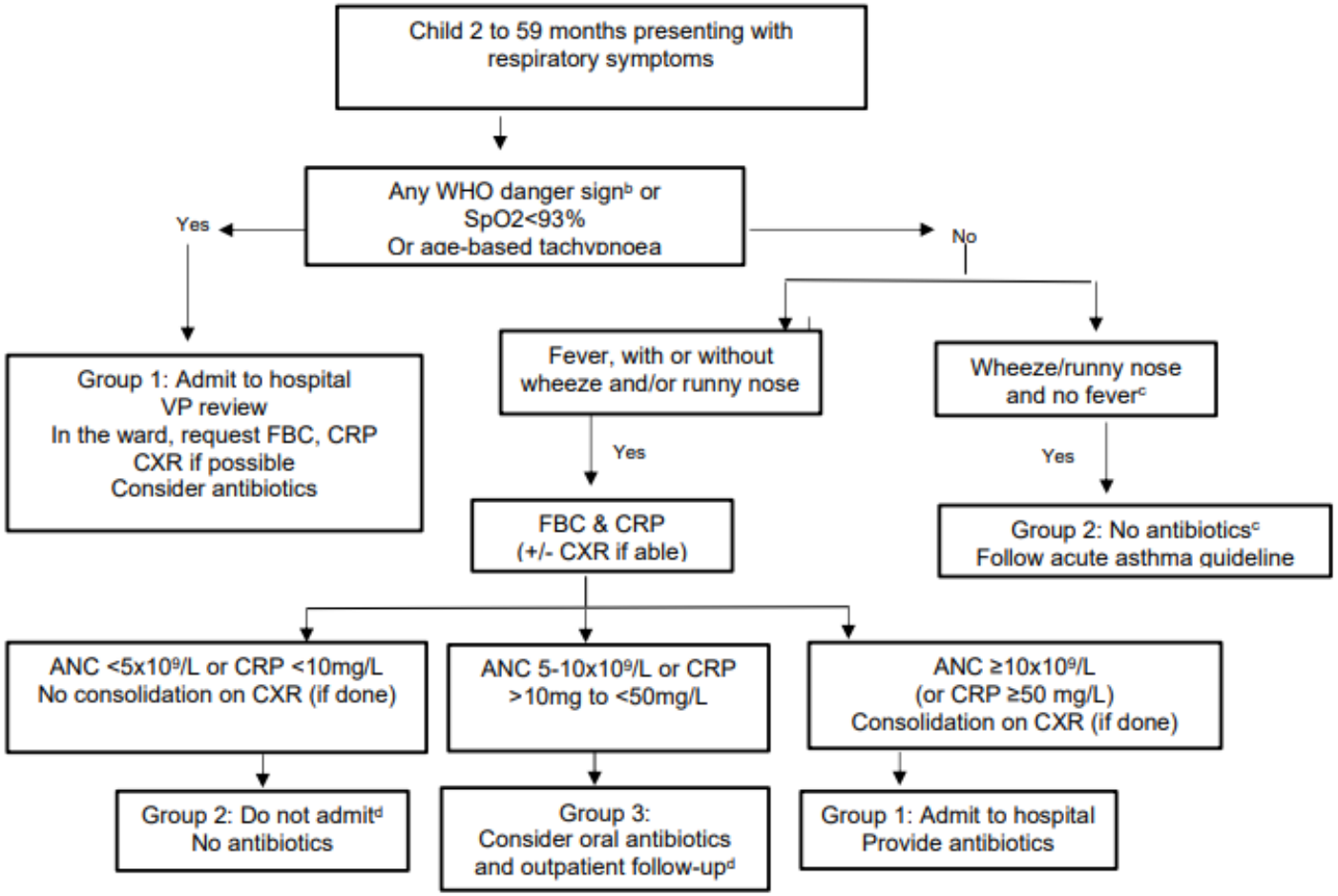
-81 received amoxicillin for 3 days

-Amoxicillin-clavulanate was given to 4 children,

-5 received oral cefuroxime

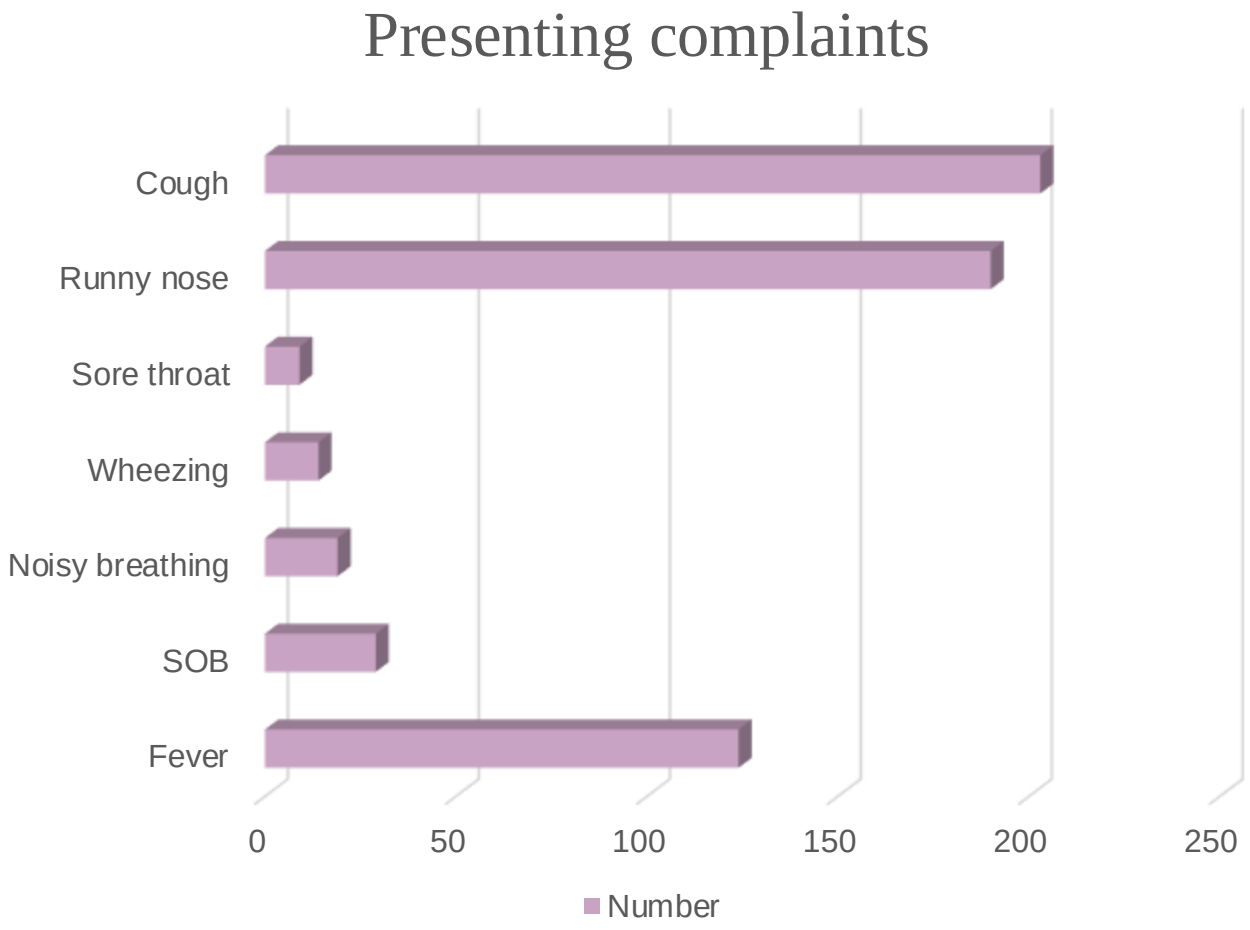
-2 received erythromycin, 5 were given azithromycin, and 4 were given clarithromycin.

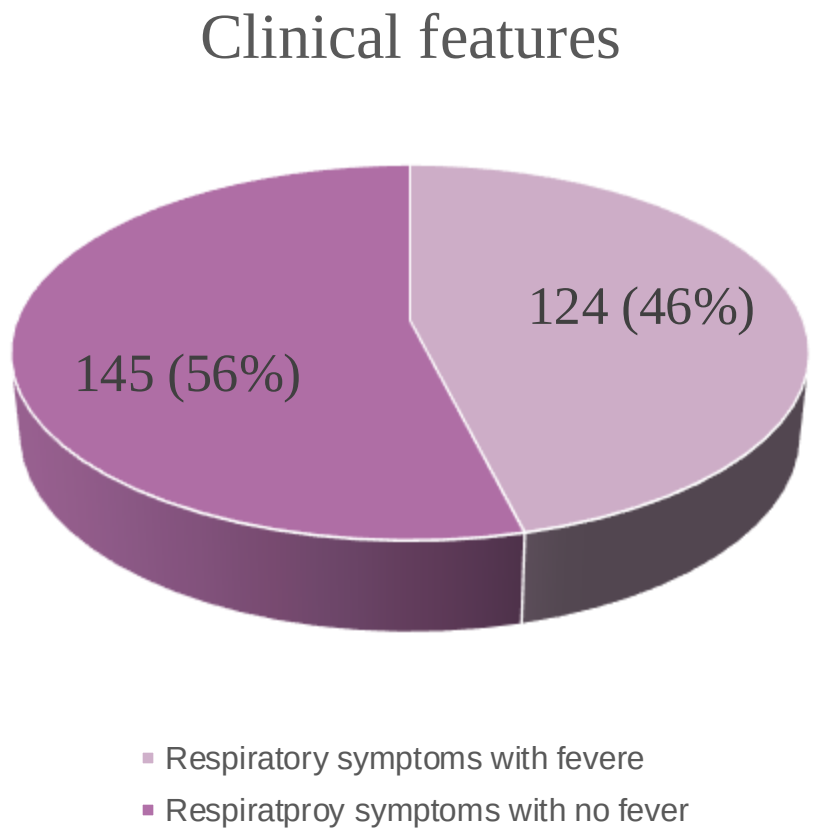
Locally-derived pragmatic clinical algorithm for the management of children presenting to hospital with acute respiratory symptoms



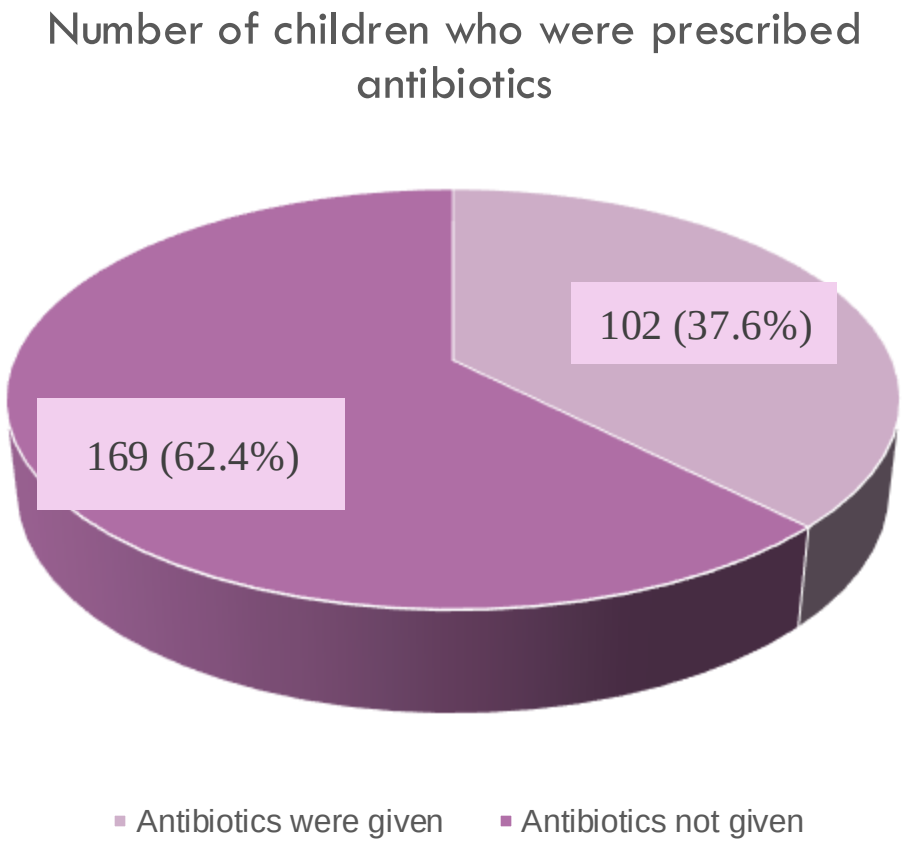
ANC – absolute neutrophil count; CXR – chest radiograph; FBC – full blood count; CRP: C reactive protein; SpO2 - peripheral oxygen saturation; WHO – World Health Organization
[a]Incorporating study findings, existing WHO guidance and previous findings from Vietnam that used CRP values to guide rational antibiotic use (17)
[b]Including inability to drink or breastfeed, vomiting everything, lethargy reduced level of consciousness, convulsions, respiratory distress (grunting or nasal flaring), severe stridor severe malnutrition
[c]As per WHO recommendation (15)
[d]Admit and consider antibiotics if any deterioration or relevant clinical concern

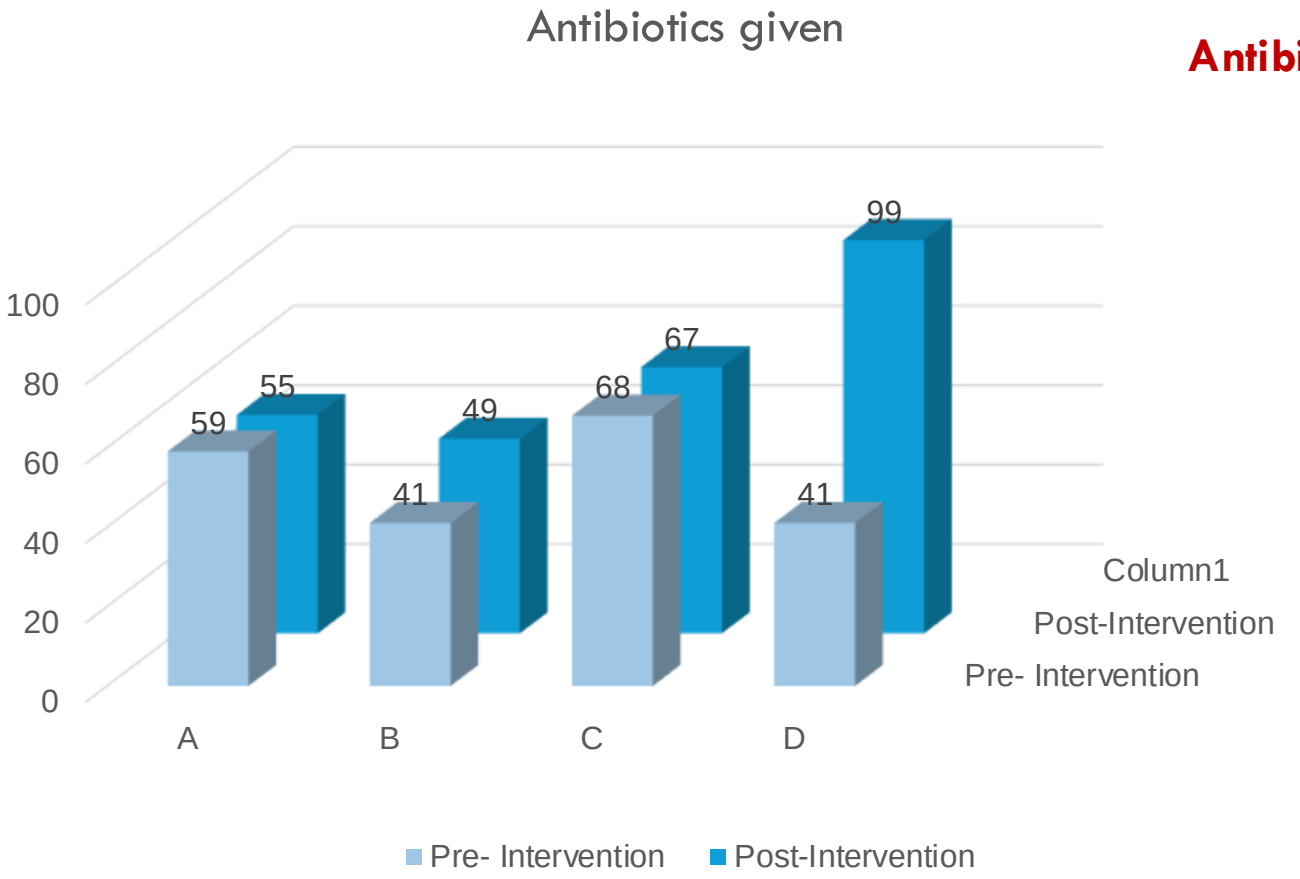
Indications to seek medical care: Post-intervention phase





Antibiotic prescribed in the OPD settings; Post-intervention





Antibiotics prescribed in the OPD settings; Post-intervention

			Fevere with and without other Respiratory Symptom		
			Fever with Other Respiratory Symptom	Fever without Other Respiratory Symptom	Total
A19_Antibiotics (yes=1, no=2)	Yes	Count	56	46	102
		% within A19_Antibiotics (yes=1, no=2)	54.9%	45.1%	100.0%
	No	Count	69	100	169
		% within A19_Antibiotics (yes=1, no=2)	40.8%	59.2%	100.0%
Total		Count	125	146	271
		% within A19_Antibiotics (yes=1, no=2)	46.1%	53.9%	100.0%

Chi-Square Tests

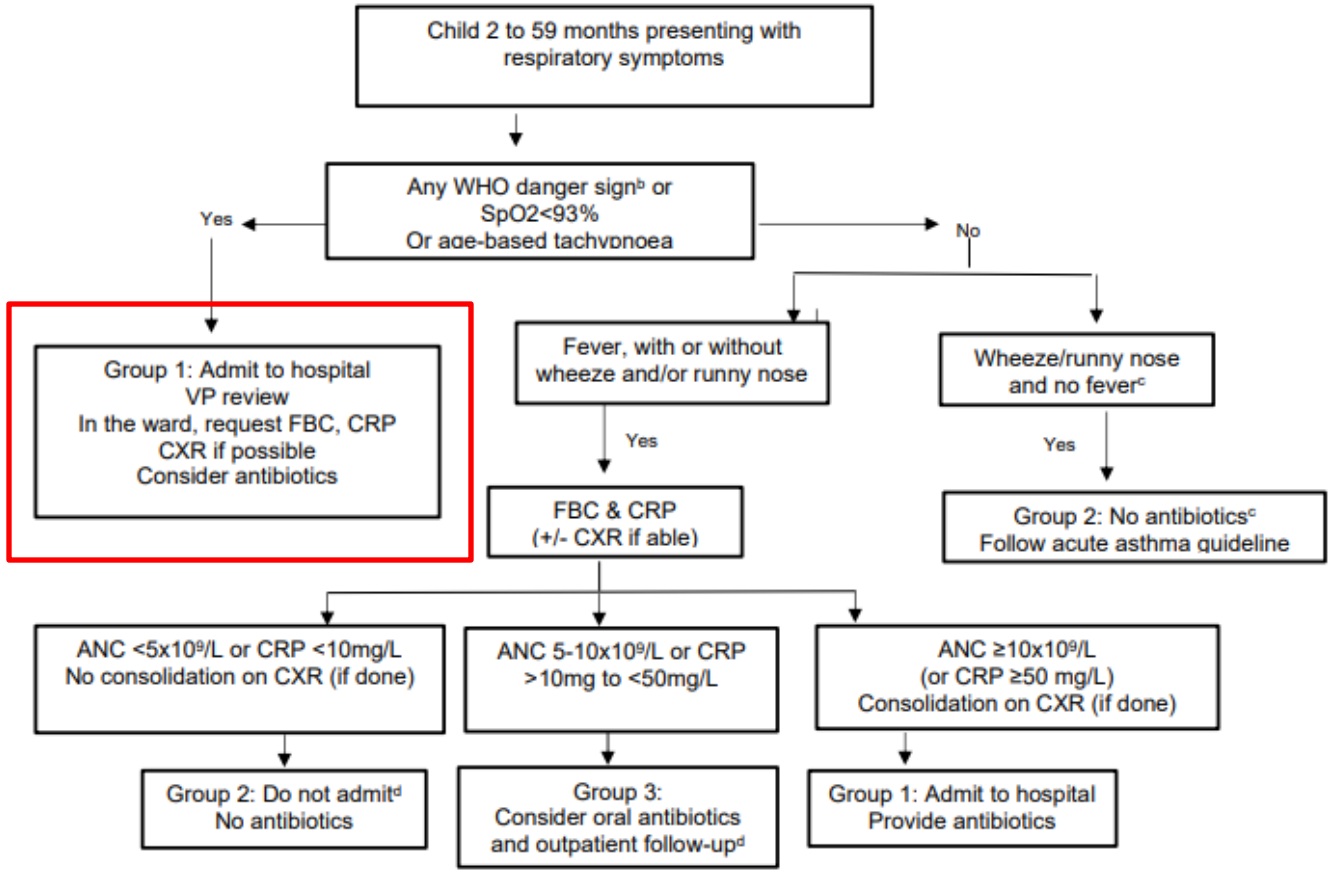
	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	5.070[b]	1	.024		
Continuity Correction[a]	4.519	1	.034		
Likelihood Ratio	5.072	1	.024		
Fisher's Exact Test				.032	.017
Linear-by-Linear Association	5.051	1	.025		
N of Valid Cases	271				

a. Computed only for a 2x2 table

b. 0 cells (.0%) have expected count less than 5. The minimum expected count is 47.05.

A	Fever (+), Antibiotics given
B	Fever (+), Antibiotics not given
C	Fever (-), Antibiotics given
D	Fever (-), Antibiotics not given

Group 1



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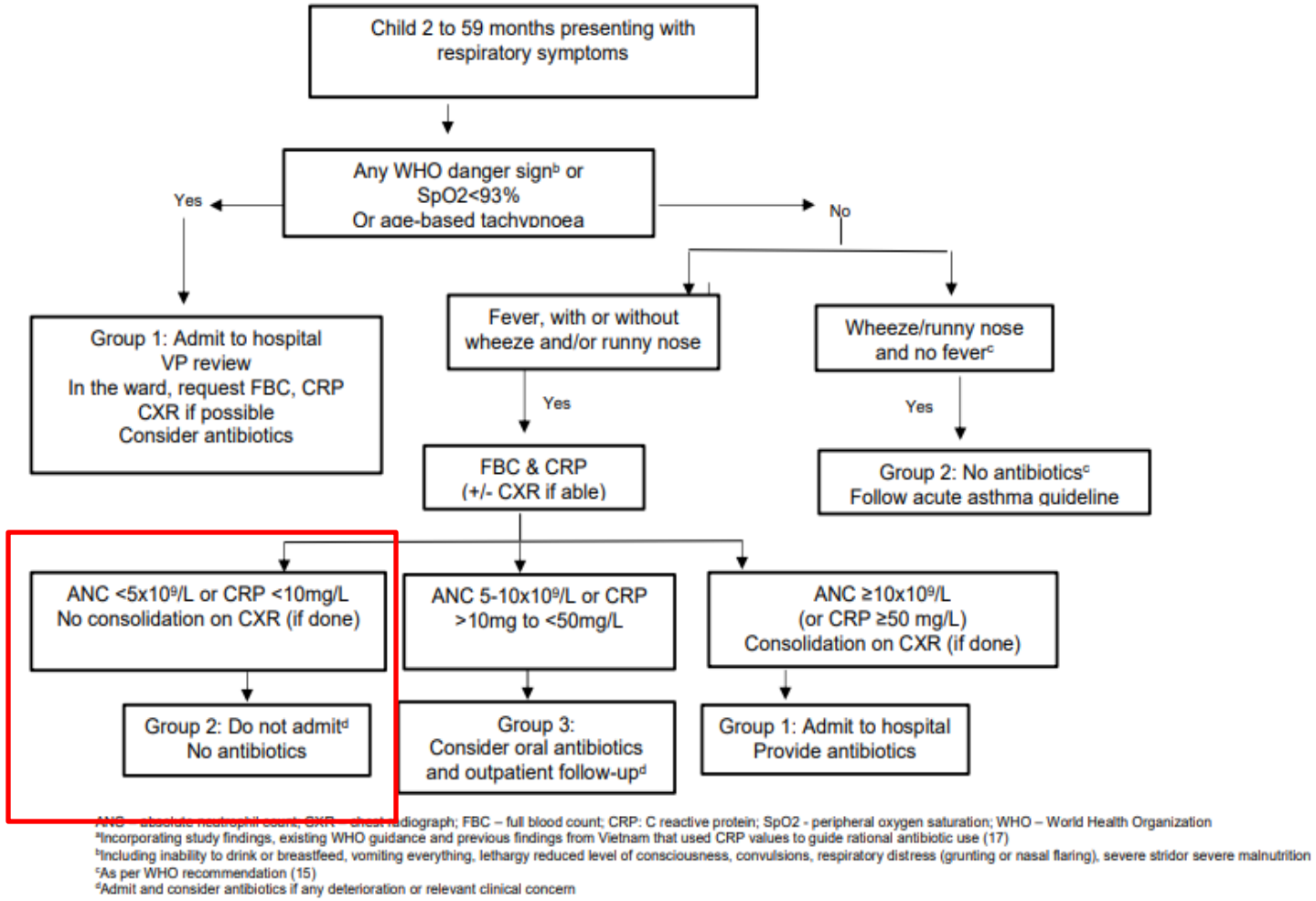
[c]As per WHO recommendation (15)
[d]Admit and consider antibiotics if any deterioration or relevant clinical concern

Two children were admitted and were managed as bronchiolitis (No antibiotics were given)

- Five children were admitted and given antibiotics -
- IV cefuroxime (1),
- IV cefotaxime (3),
- IV amoxicillin-clavulanate (1)

Group 2:



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[c]As per WHO recommendation (15)

[d]Admit and consider antibiotics if any deterioration or relevant clinical concern

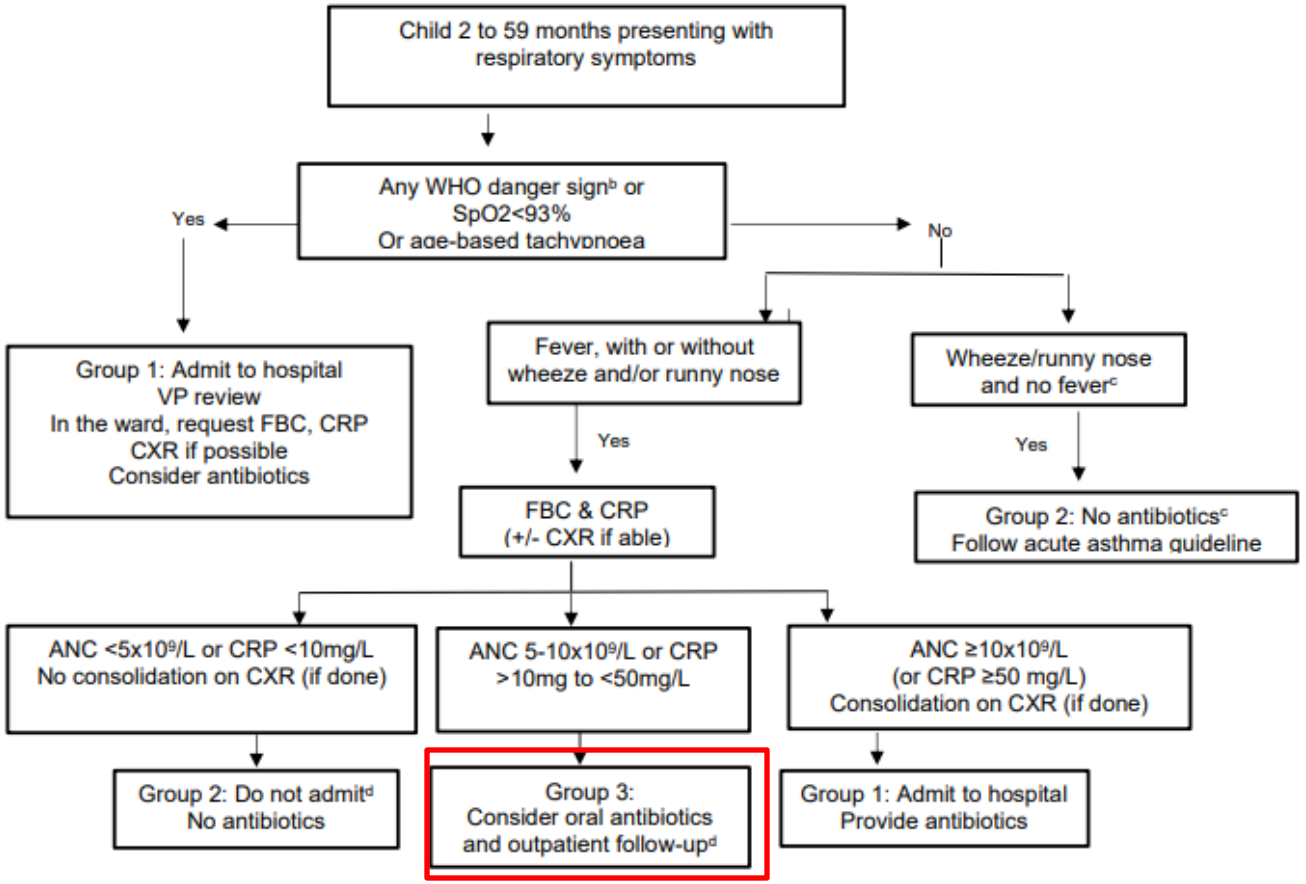
- A total of 5 children
- Three (3) children were commenced on amoxicillin
- Two (2) children were managed without antibiotics
- Three (3) children revisited the hospital for follow-up with repeat FBC

Group 2:

- Presented with wheeze and/or runny nose, No fever; No WHO danger signs, SpO2>93%, Not tachypnoeic.
- No antibiotics
- Follow acute asthma guidelines

- A total of 49 (34%) children belonging to this group were given antibiotics during the post-intervention phase

Group 3:



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[d]Admit and consider antibiotics if any deterioration or relevant clinical concern

- A total of 21 children belong to this group
- Oral antibiotics were given to 18 children
  - Amoxycillin: 15
  - Co-amoxyclv:2
  - Cefuroxime: 1
- A 12-month-old child was admitted and given IV cefuroxime
- Two (2) children were not prescribed antibiotics

Summary of Findings & Future Plans

There was no significant change in the prescribing of antibiotics for children presenting with LRTI symptoms

Possible reasons for non-adherence to clinical algorithm:

- There is already judicious use of antibiotics in this setting
- Difficulty accessing key requirements for the algorithm to be conducted – oxygen saturation machine, temperature probes etc locally
- Long-term high patient numbers, little opportunity to reinforce practice change
- No separate Paediatric Outpatient Department for walk-in patients
- Change in practice
- Limited availability of laboratory services for pathology tests required

Future Plans

- Qualitative study to explore reasons for difficulties with AMS programs in resource-constrained settings
- Repeat algorithm training sessions more regularly
- Pneumococcal colonisation sub-study to advance rationale for national PCV funding
- Further trials in other resource-constrained healthcare settings in Southeast Asia