Receipt of intravenous co-amoxiclav challenged eligibility screening for the PediCAP Trial in Johannesburg, South Africa

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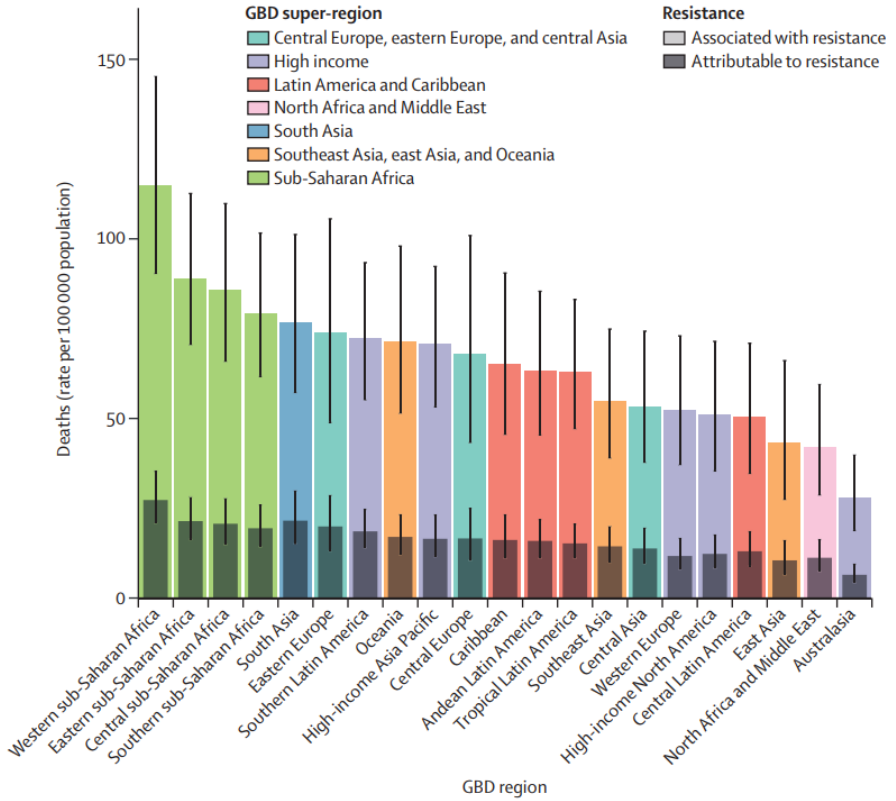
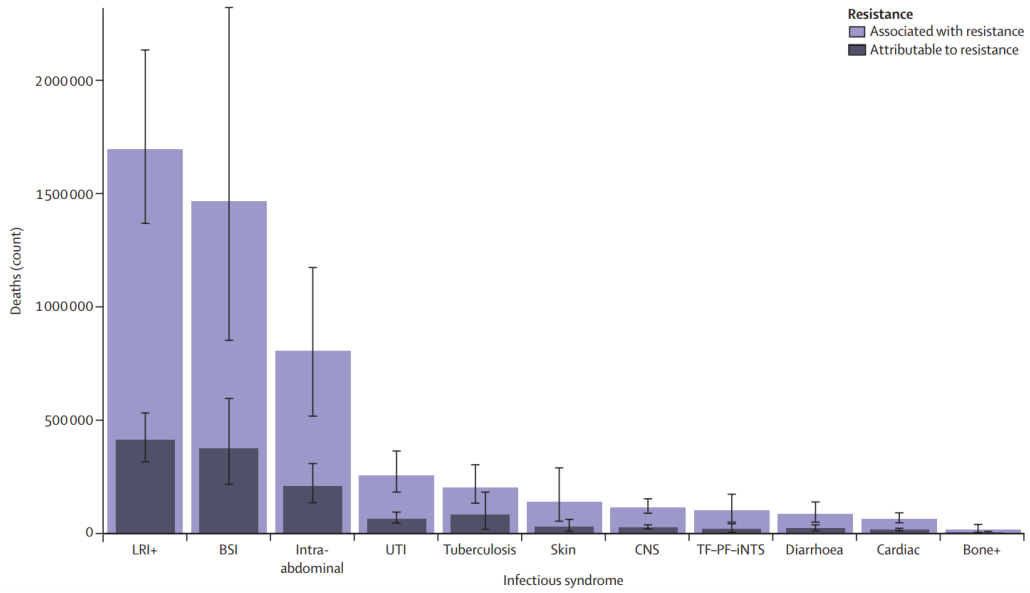
INTRODUCTION

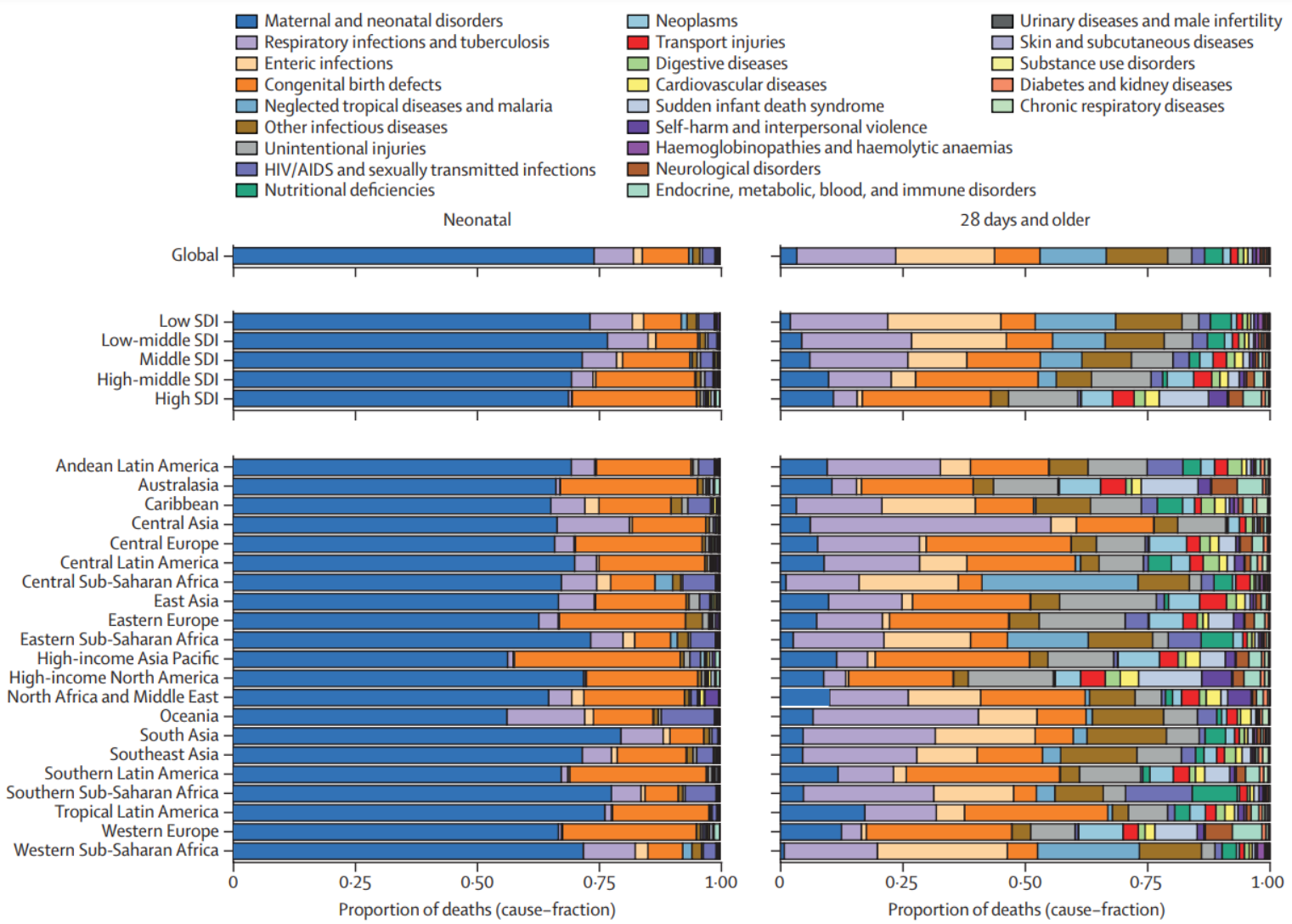
Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis

*Antimicrobial Resistance Collaborators**

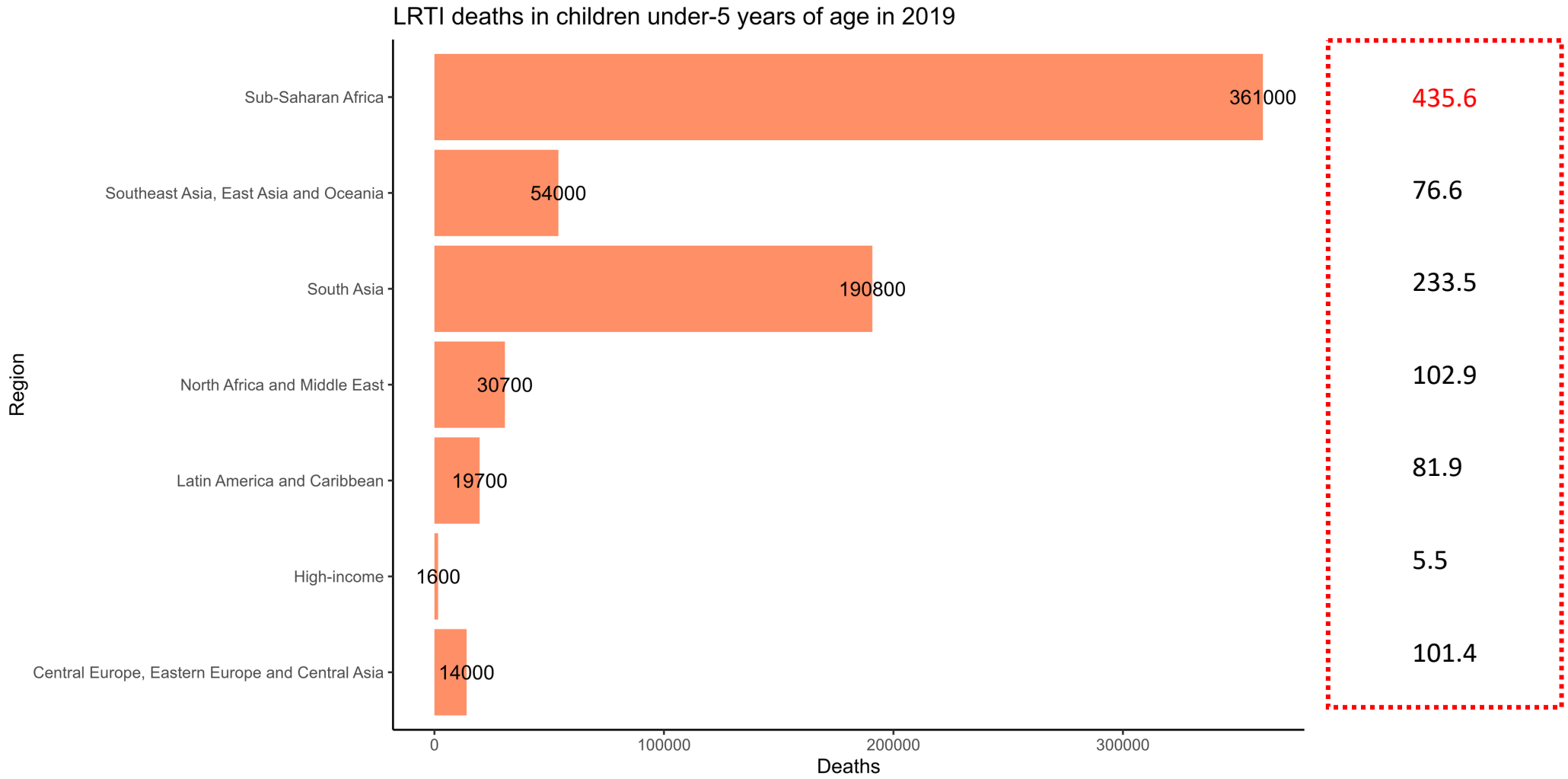




INTRODUCTION



INTRODUCTION



INTRODUCTION

GUIDELINE

Diagnosis and management of community-acquired pneumonia in children: South African Thoracic Society guidelines

H J Zar,[1,2] PhD; **D P Moore,**[3] PhD; **S Andronikou,** PhD;[1,4] **A C Argent,**[1] MD (Paediatrics); **T Avenant,**[5] FCPaed (SA); **C Cohen,**[6] PhD; **R J Green,**[5] PhD; **G Itzikowitz,**[1] MSc; **P Jeena,**[7] FCPaed (SA); **R Masekela,**[7] PhD; **M P Nicol,**[8] PhD; **A Pillay,**[7] Cert ID Paed (SA); **G Reubenson,**[9] FCPaed (SA); **S A Madhi,**[10,11] PhD

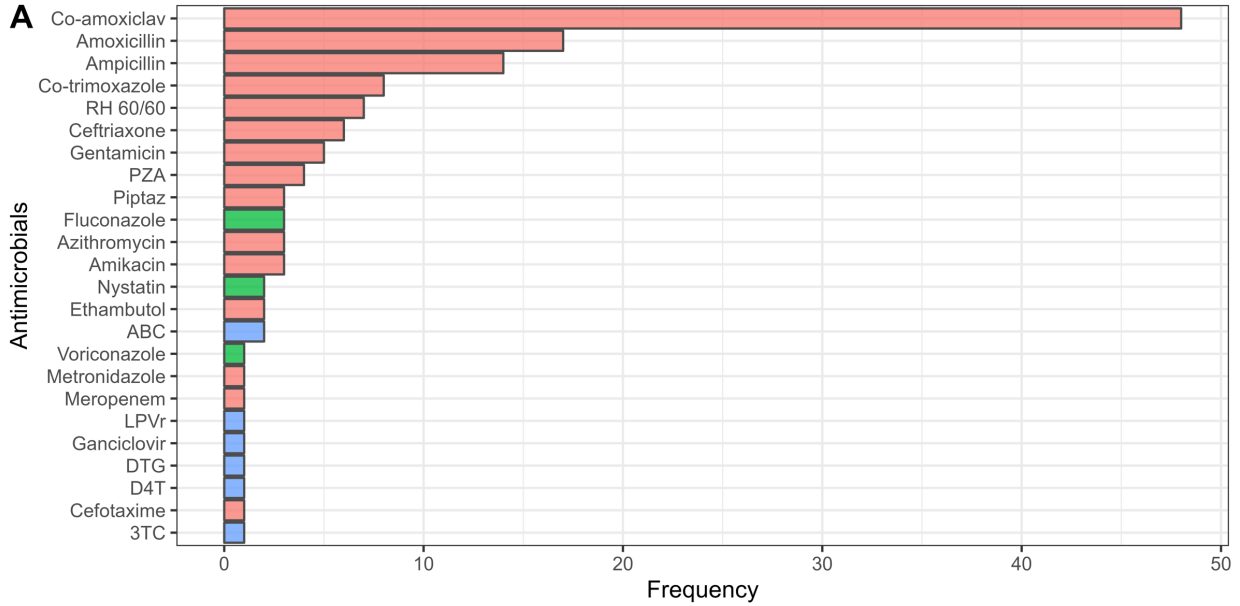
>1 month	Amoxicillin 45 mg/kg/dose 12-hourly orally × 5 d If poor response Amoxicillin-clavulanate 45 mg/kg/dose 12-hourly × 5 d **Add** Azithromycin 10 mg/kg orally daily × 5 d if *M. pneumoniae, C. pneumoniae* or *C. trachomatis* suspected (alternatives: clarithromycin 7.5 mg/kg/d orally every 12 h for 10 d or erythromycin 50 mg/kg/d for 10 - 14 d)	Amoxicillin-clavulanate 30 mg/kg/dose (of amoxicillin component) 8-hourly IV × 5 d *or* Amoxicillin-clavulanate 45 mg/kg/dose orally 12-hourly × 5 d If cultures are positive, use targeted therapy according to the organism's susceptibility pattern Step down to oral antibiotic therapy as soon as the patient is clinically stable For susceptible *S. aureus*, use Flucloxacillin 50 mg/kg orally 6-hourly × 2 - 4 weeks If poor response Ceftriaxone 50 mg/kg IV 12-hourly × 5 d *or* Cefotaxime 50 mg/kg IV 8-hourly × 5 d **Add** Vancomycin 10 - 20 mg/kg/dose 6-hourly *or* Clindamycin for suspected CA-MRSA 1 month - 16 years: 20 - 40 mg/kg IV or IM/d, in 3 - 4 equally divided doses Use higher doses for treatment of more severe infections **Add** Azithromycin 10 mg/kg orally daily × 5 d if *M. pneumoniae, C. pneumoniae* or *C. trachomatis* suspected (alternative: clarithromycin or erythromycin)

INTRODUCTION

183 children screened

85 (46.4%) enrolled

79 (89.4%) received antimicrobial Rx



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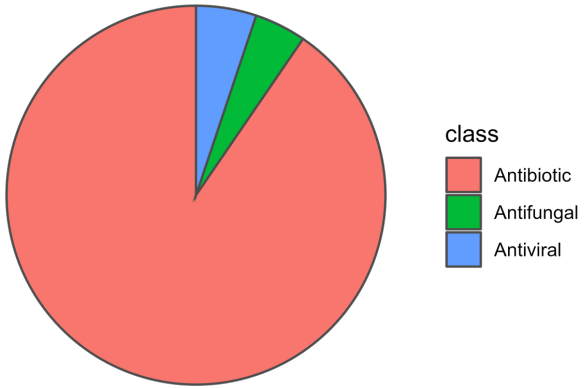

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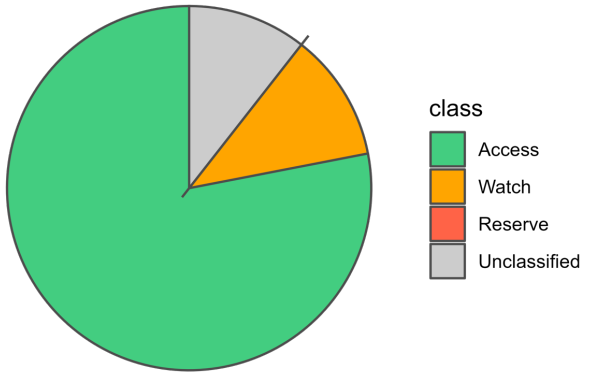


25/30 (83.3%) with bronchiolitis received antibiotics

33/37 (89.2%) with CRP <10 mg/L received antibiotics

INTRODUCTION

ANTIMICROBIAL REPORTS

The Pediatric Infectious Disease Journal • Volume 42, Number 8, August 2023

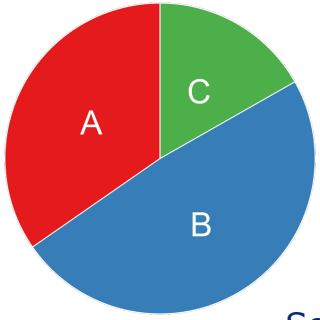
Healthcare-Associated Infections Drive Antimicrobial Prescribing in Pediatric Departments at Three Academic Hospitals in South Africa

5,200 paediatric inpatients

1,191 (22.9%) paediatric inpatients on antimicrobials

887/1,946 (45.6%) prescriptions for hospital-acquired infections

92/1,191 (7.7%) children treated for LRTI



INTRODUCTION

PediCAP

EDCTP

Penta
Child Health Research

https://projectpedicap.org/the-project/

INTRODUCTION

- Inclusion criteria in PediCAP:
  - Aged 2 months to 6 years
  - Weight ≥3 kg and <30 kg
  - Admitted to hospital with severe pneumonia requiring at least 24 hours ivi antibiotics
  - Difficulty breathing
  - About to initiate, or initiated intravenous antibiotic therapy using a World Health Organisation recommended therapy for severe pneumonia
  - Received <24 hours of intravenous therapy at the time of randomisation
  - Parent/ caregiver willing to adhere to possible randomised allocations
  - Available for follow-up for the entire study period

INTRODUCTION

- Exclusion criteria in PediCAP:
  - Point-of-care CRP <10 mg/L
  - Likely nosocomial pneumonia
  - Admitted to hospital overnight within the last 28 days
  - Known or anticipated need for invasive ventilation
  - Child <1 year of age with clinician diagnosis of "bronchiolitis alone"
  - Documented allergy to any of the trial antibiotics
  - Anticipated need for systemic treatment with an antibiotic other than the trial regimens
  - On long-term antibiotics for prophylaxis or treatment
  - Previously enrolled in PediCAP

AIM AND OBJECTIVE

- To determine how the South African guidance on severe pneumonia case management impacted on PediCAP screening and enrolment at the Johannesburg site

METHODS

- Line list of all admissions to the general paediatric wards at the Chris Hani Baragwanath Academic Hospital
- Screening of all age-eligible children with respiratory admission diagnoses
- Appraisal of the extent to which receipt of ivi co-amoxiclav impacted on participant recruitment

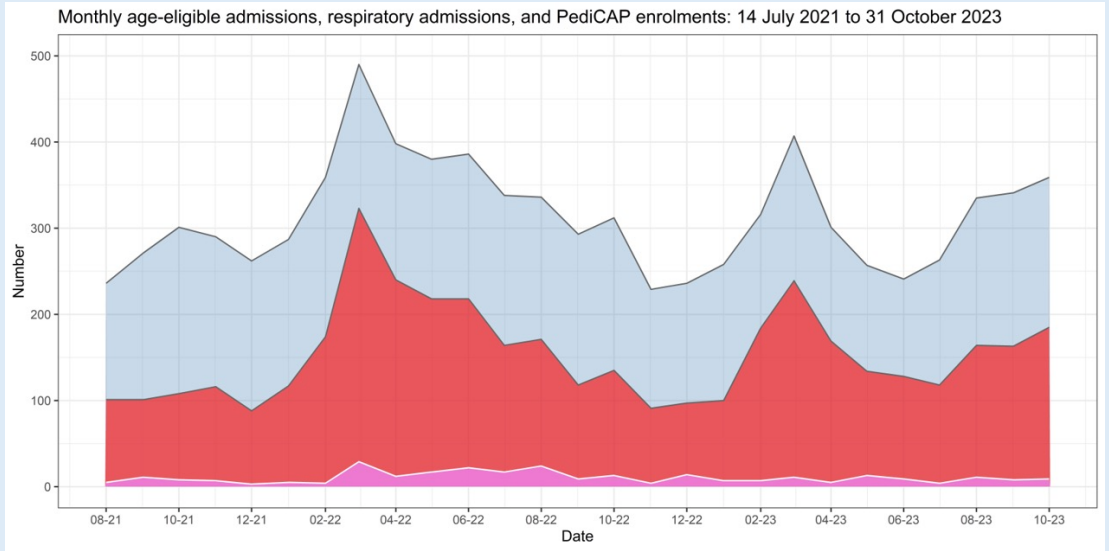
RESULTS

Study time period: 14 July 2021 to 31 October 2023:

14,949 paediatric admissions

6,346 not age-eligible

8,603 (57.5%) age-eligible



Age-eligible, on PediCAP screening days

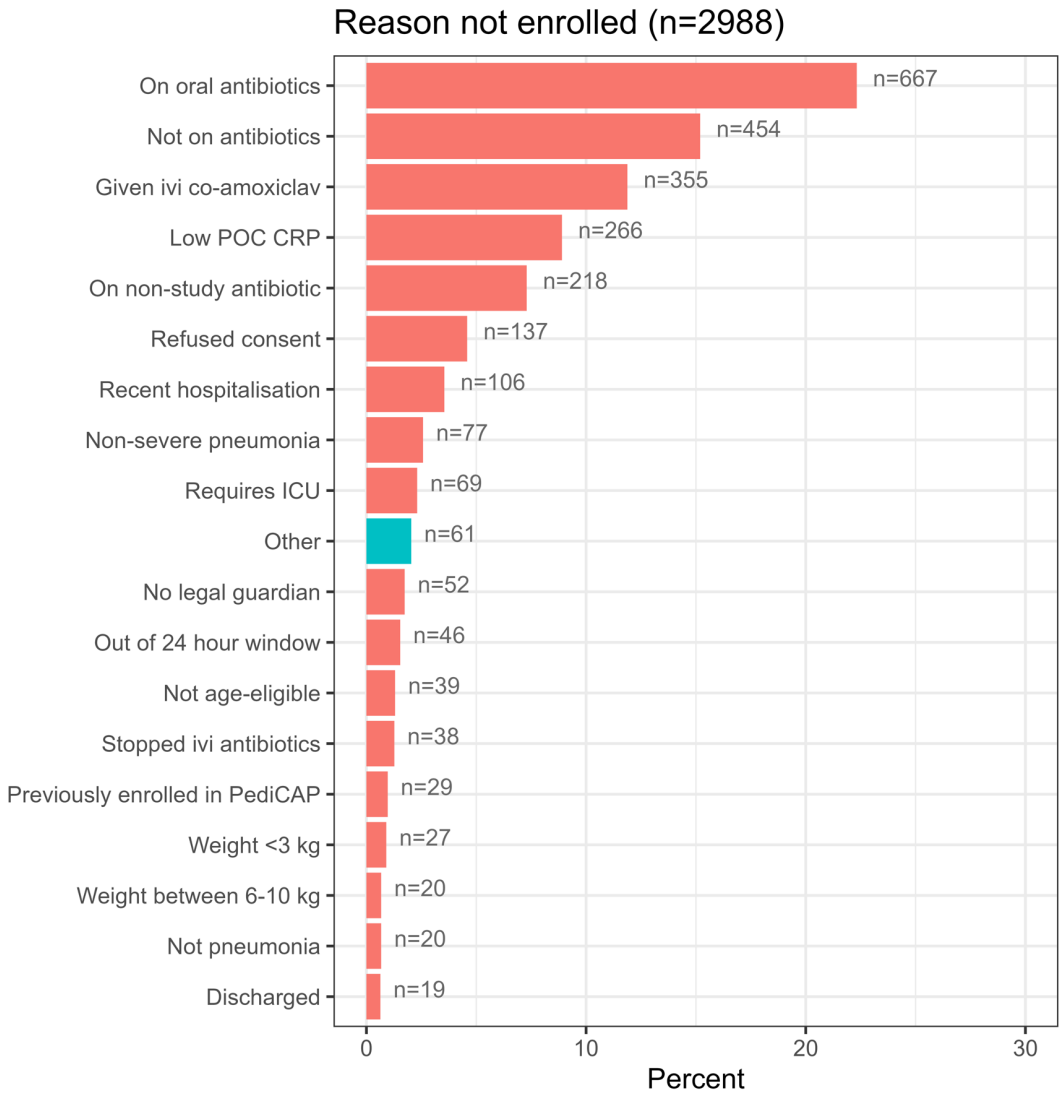
6,025 (70.0%) on PediCAP screening days

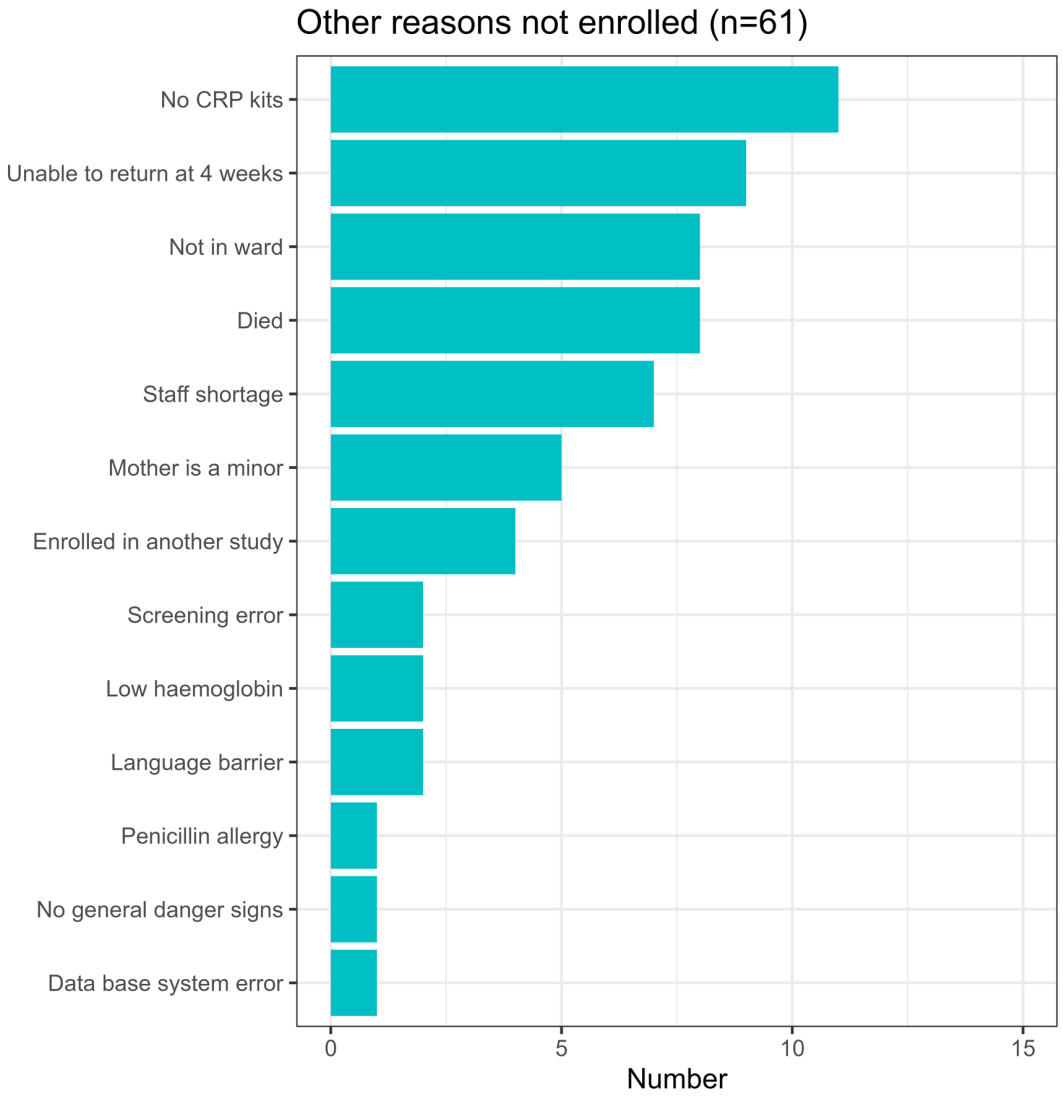
2,978 (49.4%) respiratory admissions

616 (20.7%) screened

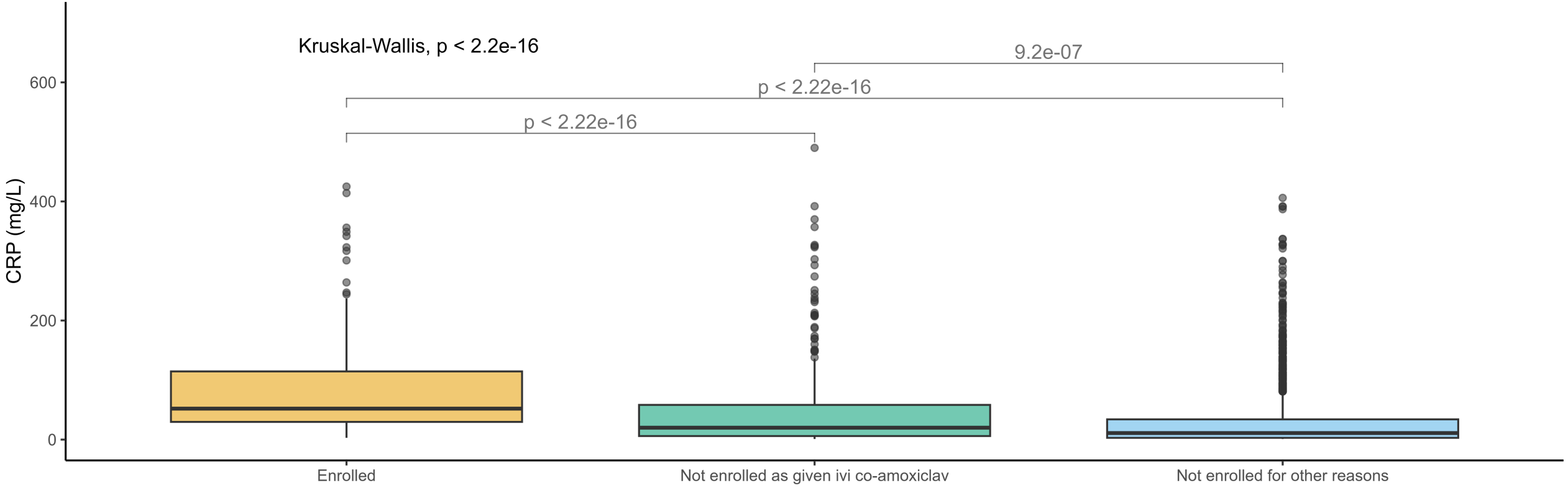
287 (46.6%) enrolled

RESULTS


Reason not enrolled (n=2988)
On oral antibiotics
Not on antibiotics
Given ivi co-amoxiclav
Low POC CRP
On non-study antibiotic
Refused consent
Recent hospitalisation
Non-severe pneumonia
Requires ICU
Other
No legal guardian
Out of 24 hour window
Not age-eligible
Stopped ivi antibiotics
Previously enrolled in PediCAP
Weight <3 kg
Weight between 6-10 kg
Not pneumonia
Discharged
n=667
n=454
n=355
n=266
n=218
n=137
n=106
n=77
n=69
n=61
n=52
n=46
n=39
n=38
n=29
n=27
n=20
n=20
n=19
0
10
20
30
Percent


Other reasons not enrolled (n=61)
No CRP kits
Unable to return at 4 weeks
Not in ward
Died
Staff shortage
Mother is a minor
Enrolled in another study
Screening error
Low haemoglobin
Language barrier
Penicillin allergy
No general danger signs
Data base system error
0
5
10
15
Number

RESULTS

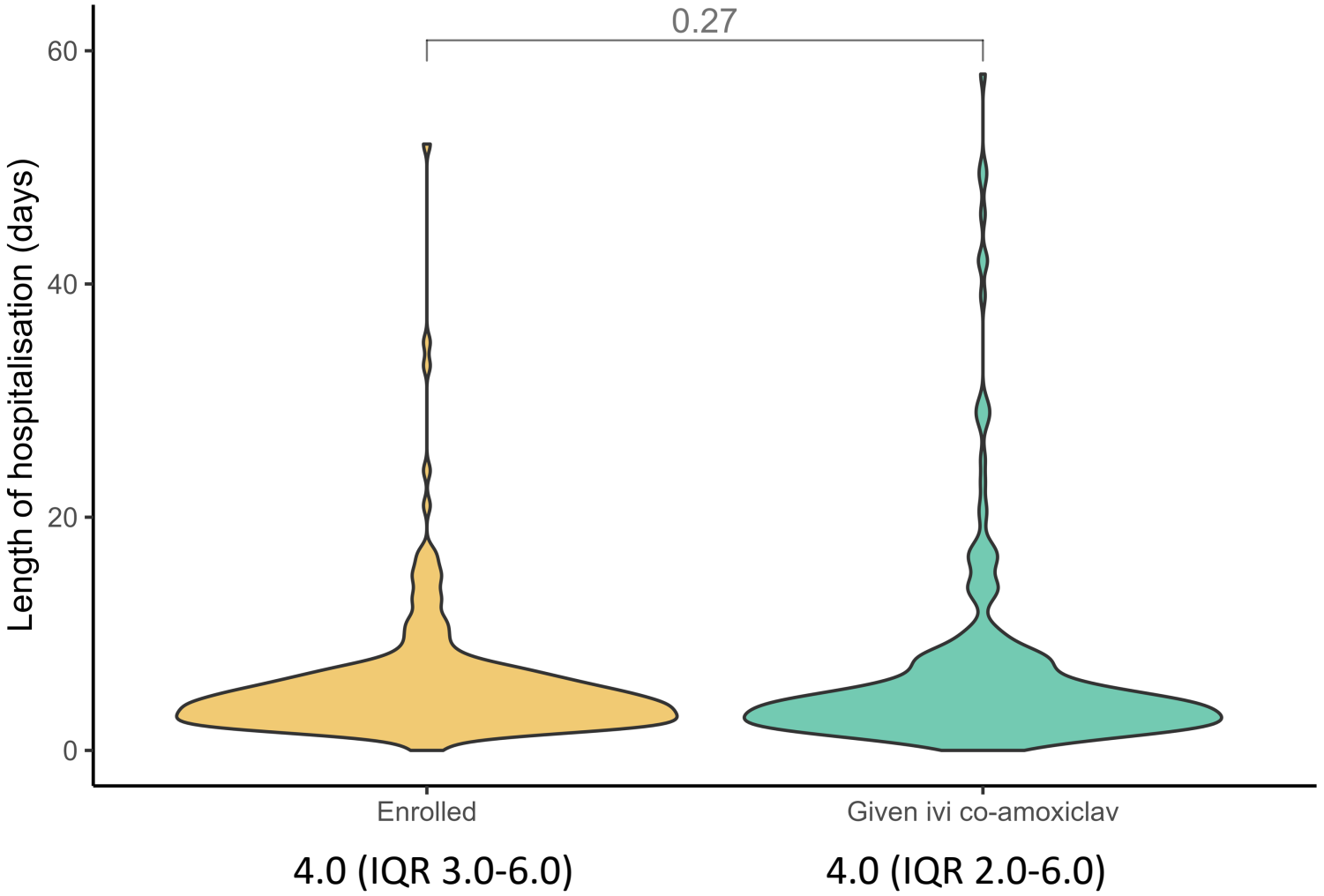


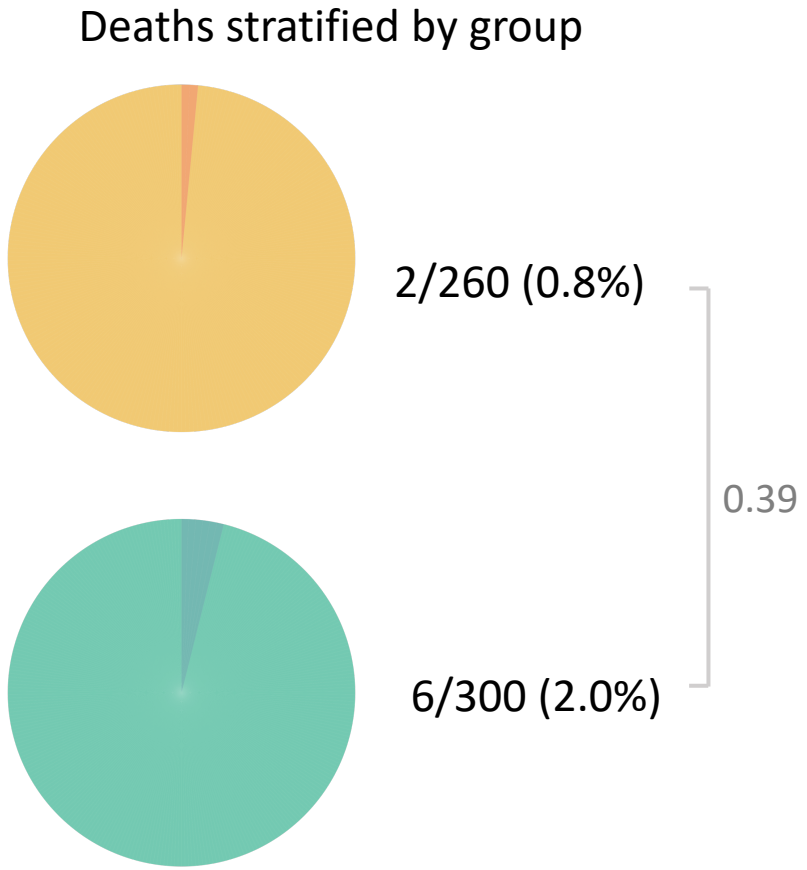
52.0 (IQR 29.8-114.5)

20.0 (IQR 6.0-58.3)

11.0 (IQR 3.0-34.0)

RESULTS


0.27
60
40
20
0
Length of hospitalisation (days)
Enrolled
Given ivi co-amoxiclav
4.0 (IQR 3.0-6.0)
4.0 (IQR 2.0-6.0)


Deaths stratified by group
2/260 (0.8%)
6/300 (2.0%)
0.39

DISCUSSION

- Children hospitalised for severe pneumonia in South Africa frequently receive empiric co-amoxiclav ivi as per local guidelines

- In PediCAP, where receipt of ivi co-amoxiclav was an exclusion criterion for participation, 12% of those screened had received ivi co-amoxiclav

DISCUSSION

- Children administered ivi co-amoxiclav had significantly lower serum CRP levels at baseline compared to those that were enrolled into the Trial

- Length-of-stay and survival outcomes were similar in children that were administered ivi co-amoxiclav empirically

DISCUSSION

- These observations open up potential new avenues for antimicrobial stewardship in our setting

- Design and set-up of multi-national studies in Africa to evaluate the impact of point-of-care biomarker tests to guide clinicians in rationalising prescribing practices may assist in transforming the current landscape of potential over-use of antibiotic therapy, and accumulation of antimicrobial resistance

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