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Early oral step-down to amoxicillin is safe and effective for children hospitalised with severe community-acquired pneumonia: the PediCAP trial

Late Breakers

22. Clinical trials

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Background

The WHO recommends 5 days IV antibiotics for children hospitalised with severe community-acquired pneumonia (CAP). The safety of early step-down to oral antibiotics and the optimal choice of drug and duration is unknown.

Methods

PediCAP was an open-label, parallel group, 2x5 factorial randomised trial in children 2m-6y weighing 3-30kg, hospitalised with severe CAP in Mozambique, South Africa, Uganda, Zambia, and Zimbabwe. PediCAP assessed oral step-down with dispersible tablet formulations of amoxicillin or 7:1 amoxicillin-clavulanate for five different total treatment durations (4-8 days), compared to 5-days IV-only treatment (Fig.1; 10% non-inferiority margin versus IV). Clinicians initiated step-down when children improved and were able to take oral antibiotics. The primary outcome was 28-day hospital readmission or death (intention-to-treat).

Results

Primary outcome data were available in 1055/1101 (96%) children randomised (Dec-2020 to Aug-2023). Mean total antibiotic duration was 4.4, 5.2, 6.3, 7.0, 8.1 calendar days in the 4-,5-,6-,7-,8-day arms, respectively ($p<0.001$), with 69%, 76%, 85%, 90%, 92% stepping down within the randomised duration ($p<0.001$); more children randomised to shorter treatment were not stepped-down and received only IV antibiotics.

Primary outcomes occurred in 7%, 6% and 6% of children in amoxicillin-clavulanate, amoxicillin and IV arms, respectively. Amoxicillin and amoxicillin-clavulanate oral step-down were non-inferior to fixed-duration IV antibiotics; there was no evidence of amoxicillin-clavulanate superiority to amoxicillin (Fig.2A). Primary outcomes occurred in 4%, 5%, 9%, 8% and 5% of children in the 4-8 day arms, respectively, with no evidence of overall association with duration ($p=0.34$; Fig.3), and all durations being non-inferior to 8 days (Fig.2B). Initial hospital stay was one day longer for children allocated to IV vs amoxicillin arm (95% CI: (0.1,2); $p=0.049$); in the step-down arms, there was no evidence of differences between oral antibiotics or by duration. There was no evidence of consistent differences in adverse events for either oral antibiotic or duration comparisons.

Conclusions

For children hospitalised with severe CAP, IV to oral antibiotic step-down following clinician-assessed improvement was safe, effective, and shortened hospitalisation. Amoxicillin and 4-day treatment were comparable to amoxicillin-clavulanate and longer treatment.

Figure 1. PediCAP trial schema

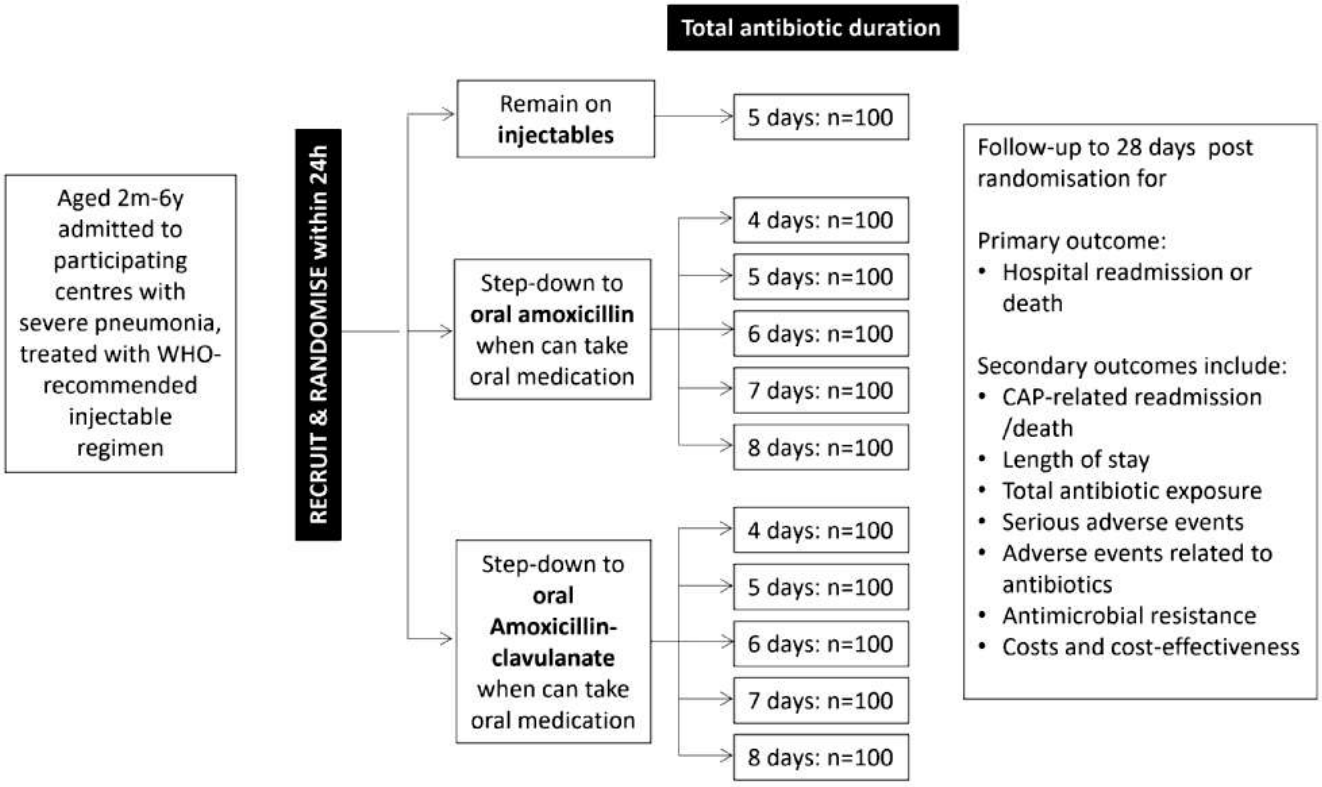
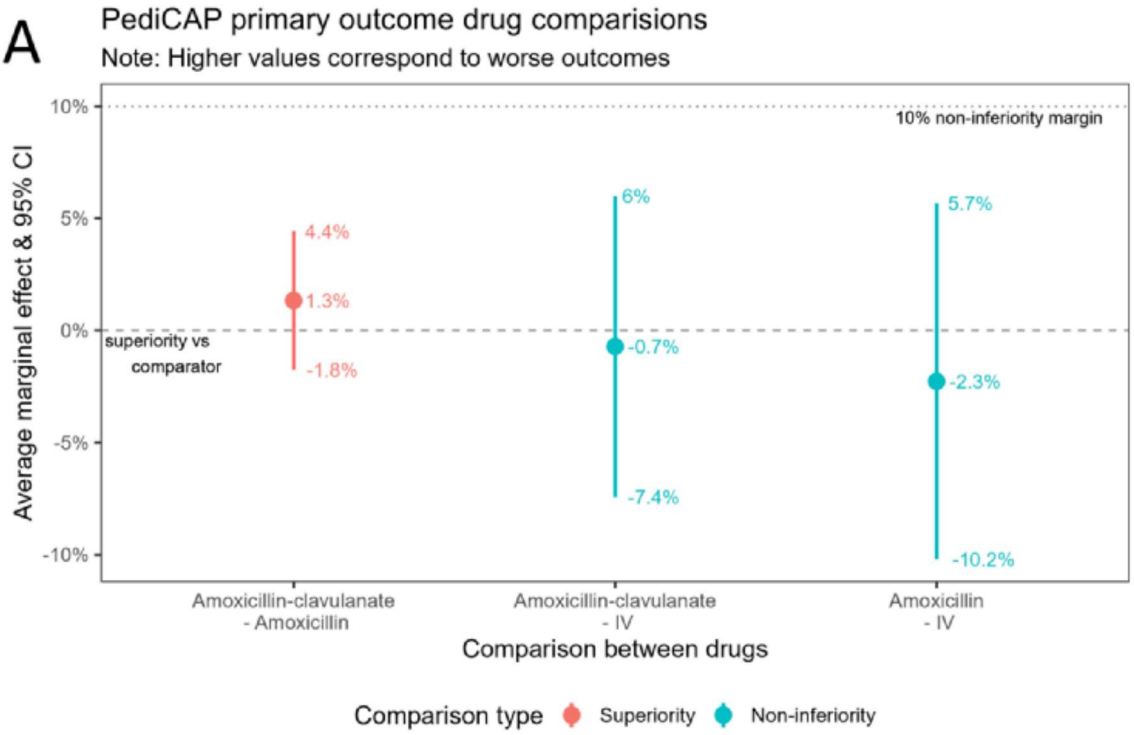


Figure 2. PediCAP drug and duration comparisons

A


PediCAP primary outcome drug comparisions
Note: Higher values correspond to worse outcomes
10% non-inferiority margin
Average marginal effect & 95% CI
10%
5%
0%
-5%
-10%
superiority vs
comparator
4.4%
1.3%
-1.8%
6%
-0.7%
-7.4%
5.7%
-2.3%
-10.2%
Amoxicillin-clavulanate
- Amoxicillin
Amoxicillin-clavulanate
- IV
Amoxicillin
- IV
Comparison between drugs
Comparison type
Superiority
Non-inferiority

B

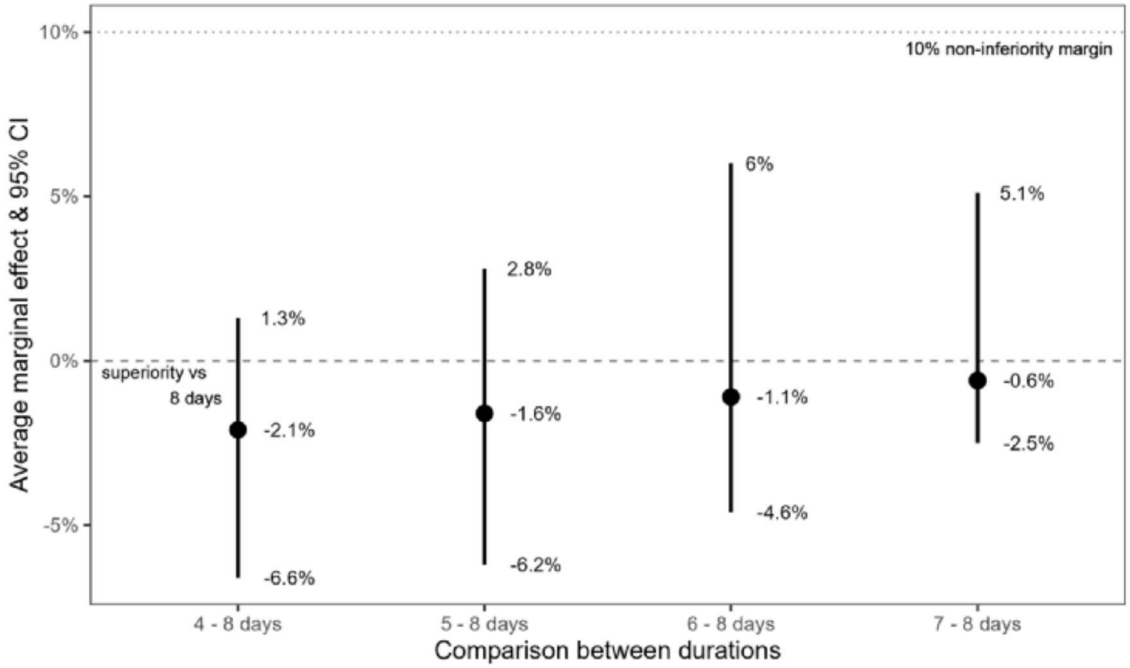

PediCAP primary outcome duration comparisions for oral-stepdown drugs
Note: Higher values correspond to worse outcomes
10% non-inferiority margin
Average marginal effect & 95% CI
10%
5%
0%
-5%
superiority vs
8 days
1.3%
-2.1%
-6.6%
2.8%
-1.6%
-6.2%
6%
-1.1%
-4.6%
5.1%
-0.6%
-2.5%
4 - 8 days
5 - 8 days
6 - 8 days
7 - 8 days
Comparison between durations

Figure 3. PediCAP fitted durations for oral step-down drugs