The NEW ENGLAND JOURNAL of MEDICINE

Azithromycin to Reduce Childhood Mortality in Niger

A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Azithromycin to Reduce Mortality — An Adaptive Cluster-Randomized Trial by K.S. O'Brien et al. (published August 22, 2024)

In this trial, researchers evaluated the efficacy of twice-yearly azithromycin as compared with placebo in children (1 month to less than 5 years of age) and infants (1 month to less than 1 year of age) in rural communities in Niger.

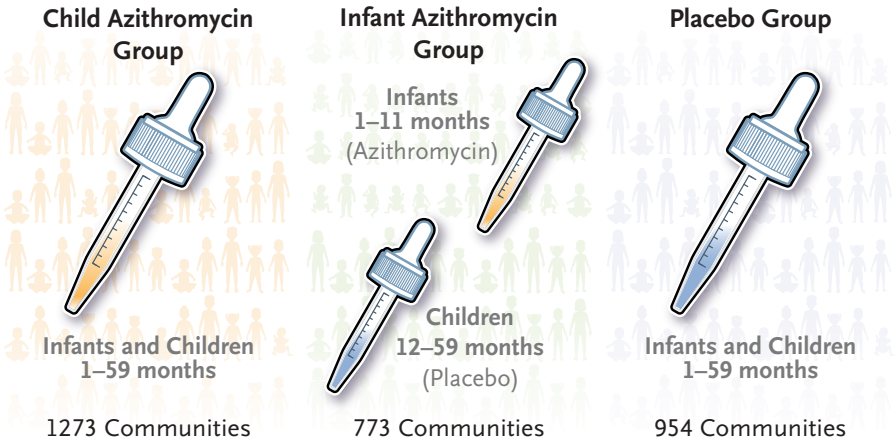
In some areas of sub-Saharan Africa, **childhood mortality** is high — nearly 10% of children do not reach their fifth birthday. The United Nations Sustainable Development Goals aim to reduce that percentage to below 2.5% by 2030.

WHY WAS THE TRIAL DONE?

Twice-yearly mass distribution of azithromycin to children 1 to 59 months of age may improve mortality outcomes. To reduce antimicrobial resistance, the World Health Organization recommended restricting distribution to infants 1 to 11 months of age, although the efficacy of treating only infants in this narrower age range was unknown.

HOW WAS THE TRIAL CONDUCTED?

Rural communities in Niger were randomly assigned to one of three groups, all with twice-yearly distribution of azithromycin or placebo: azithromycin for children 1 to 59 months of age (child azithromycin group), azithromycin for infants 1 to 11 months of age and placebo for children 12 to 59 months of age (infant azithromycin group), or placebo for children 1 to 59 months of age (placebo group). The three primary outcomes assessed community-level mortality (deaths from any cause per 1000 person-years) according to age category and group assignment. Mortality was monitored twice yearly over the course of 2 years.



PATIENTS

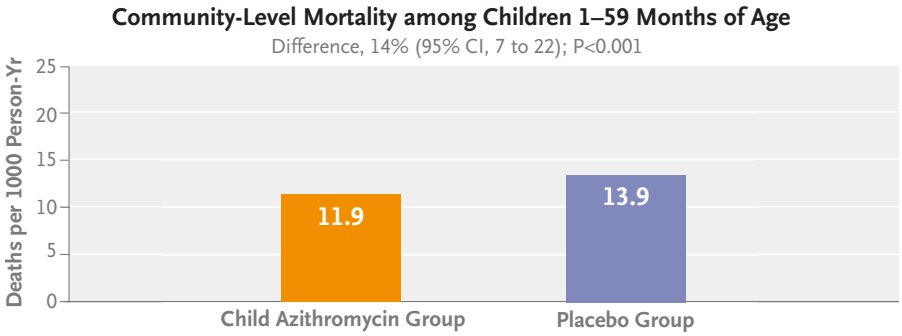
WHO	382,586 children 1 to 59 months of age Weight, at least 3 kg
CLINICAL STATUS	No known allergy to macrolide antibiotics

TRIAL DESIGN

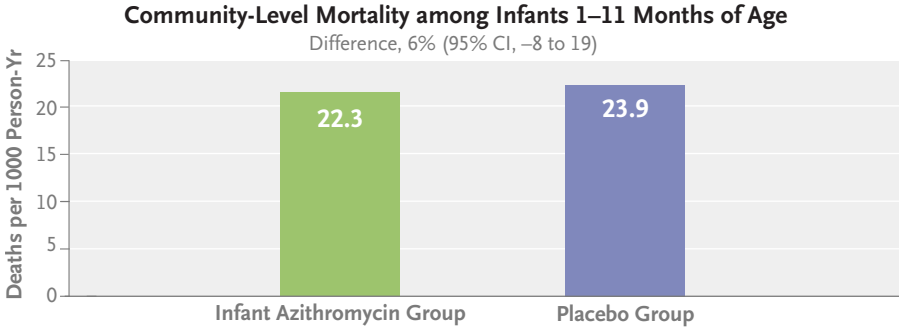
- DOUBLE-BLIND
- RESPONSE-ADAPTIVE
- CLUSTER-RANDOMIZED
- PLACEBO-CONTROLLED
- LOCATION: 3000 RURAL COMMUNITIES IN NIGER WITH POPULATIONS OF 250 TO 2499 ACCORDING TO MOST RECENT NATIONAL CENSUS

RESULTS

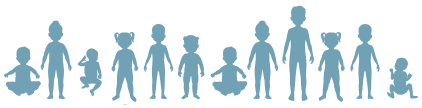
Communities in the child azithromycin group had lower mortality among children 1 to 59 months of age than communities in the placebo group.



Communities in the infant azithromycin group did not have significantly lower mortality among infants 1 to 11 months of age than communities in the placebo group. Five serious adverse events were reported, with none attributed to azithromycin.



INDIRECT BENEFIT FOR INFANTS



Infant mortality was 17% lower when older children also received azithromycin than when only infants received azithromycin.

LIMITATIONS AND REMAINING QUESTIONS

- Because of the large sample size, data collection was simplified, which limited the reporting of adverse events and secondary analyses.
- Mortality was monitored over only 2 years. Further studies are needed to assess longer-term efficacy.
- The evaluation of antimicrobial resistance in the trial is ongoing, and these data will be important to better understand the risk–benefit ratio.

CONCLUSIONS

Twice-yearly azithromycin distribution to children 1 to 59 months of age significantly reduced mortality and was more effective than treating only infants 1 to 11 months of age.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT04224987

Trial funding: The Bill and Melinda Gates Foundation

Full citation: O'Brien KS, Arzika AM, Amza A, et al. Azithromycin to reduce mortality — an adaptive cluster-randomized trial. N Engl J Med 2024;391:699-709. DOI: 10.1056/NEJMoa2312093