Giving an antibiotic to all children under 5 in Africa would save lives, researchers say

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When UC San Francisco research showed that routinely treating children in Sub-Saharan Africa with a common antibiotic could reduce deaths in children under five, the World Health Organization (WHO) moved

quickly to recommend the treatment—but only for infants between 1 and 11 months old.

Now, UCSF researchers have shown that treating babies is not enough. The antibiotic must be given to all children up to 5 years old to realize its full benefit, which is considerable: It lowers child mortality by 14% in a region where 1 in 10 children die before they turn 5.

WHO recommended limiting use of the antibiotic, azithromycin, out of concerns that broader administration would give rise to antibiotic resistance. But the research shows that the youngest and most vulnerable children—those less than a year old—gain greater protection from respiratory and other potentially lethal infections if their older siblings also are treated, so they do not transmit these infections.

"The results are very clear," said the study's first author, Kieran S. O'Brien, Ph.D., MPH, an epidemiologist and assistant professor with the Francis I. Proctor Foundation at UCSF. "By treating the older kids you can protect the younger children, who are particularly vulnerable."

The findings appear online Aug. 21 in the *New England Journal of Medicine*.

Concerns over antibiotic resistance

Azithromycin is a broad-spectrum antibiotic that works against a wide array of pathogens, including those responsible for respiratory infections, diarrhea and malaria, which are among the top causes of childhood mortality in Sub-Saharan Africa.

The initial 2018 study included nearly 200,000 children in three African countries: Niger, Malawi and Tanzania. The children were given a single dose of oral azithromycin or a placebo four times over two years.

This reduced under-five mortality by nearly 14% overall, and by 25% for babies who were less than 5 months old. And in 2020, the WHO endorsed mass administration of azithromycin to children under 1 year old. The research, however, had not demonstrated that just targeting infants would significantly reduce mortality.

In this newly published follow-up study, called AVENIR (Azithromycin pour la Vie des Enfants au Niger; Implementation and Recherche), the researchers tested the approach in different age groups to see if they could demonstrate its benefits by targeting infants alone.

The study, conducted in partnership with the Niger Ministry of Health and Centre de Recherche et Interventions en Santé Publique in Niger, repeated the same dose regimen, but was limited to just one country, Niger, which has higher child mortality rates than the other two countries in the original study.

They found that under-five mortality only went down significantly when all the children were treated.

Infants get exposed to pathogens at home

The researchers noted that most of the infants had older siblings in the household. These older children spend more time outside the household and play with other children, which increases the likelihood of infecting their younger, more vulnerable siblings.

The authors acknowledged that antibiotic resistance is a legitimate concern. But they stressed that the intervention is limited to a small subset of the population for just a few years, and the risk of resistance is outweighed by the opportunity to save lives.

Thomas M. Lietman, MD, the study's senior author and an

ophthalmologist at UCSF, hopes it will encourage the WHO to recommend the treatment for children up to 5 years old.

"We're taught in medicine to avoid using antibiotics in a nonspecific way because of the potential for antibiotic resistance; but we've found if you do that in an organized fashion, it can reduce childhood mortality," said Lietman, who was the lead author of the initial study. "How can you withhold a treatment that reduces mortality by 14% in areas where 10% of the kids aren't reaching their fifth birthday?"

More information: O'Brien et al. *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2312093.
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