GARDP
Global Antibiotic Research & Development Partnership

GLOBAL CHALLENGES

ANTIBIOTICS FOR CHILDREN

1 in 5 deaths
from antibiotic-resistant infections are in children under five

99% of which occur in LMICs

BARRIERS TO TREATMENT AND ACCESS

CHILDREN ARE NEGLECTED IN R&D
Very few clinical trials in babies and children

LIMITED INFORMATION
Limited information to guide dosage and frequency of antibiotics

REGISTRATION
Limited, especially new antibiotics in LMICs

SUPPLY
Inadequate and sometimes sparse supply, especially in LMICs

CHALLENGES FOR CHILDREN WITH ANTIBIOTIC-RESISTANT INFECTIONS

With the global antimicrobial resistance (AMR) crisis now at a critical tipping point and the number of deaths expected to rise sharply, children are one of the most at-risk groups. Despite a fall in child mortality in recent decades, children continue to remain disproportionately vulnerable to drug-resistant infections, particularly newborns. This is partly because their immature immune systems leave them more susceptible to infections, and life-threatening complications like sepsis.

Infected newborns can deteriorate so quickly that clinicians often need to treat them with antibiotics immediately, before reliable microbiology results are available. Yet, despite their greater need for protection, few antibiotics are developed for use in children or newborns. Unless this changes, treatment options for newborns will continue to be extremely limited, complex to use and often ineffective against resistant bacteria.

CHILDREN AND NEWBORNS ARE UNIQUELY VULNERABLE TO INFECTIONS

Since 2000, of the 40 or so new antibiotics approved only four have been developed with children or newborns in mind. For the other 36, there are no recommendations for how they should be used safely to treat children or infants. This means doctors must estimate the doses and the length of treatment, both of which run the risk of either insufficient treatment or overdose for the child.

Because of this, and the need to act fast, clinicians are forced to take a reactive "trial-and-error" approach to find the most suitable treatment. The standard practice is to begin with a broad-spectrum antibiotic and then watch closely, switching to a different antibiotic if the child fails to improve or worsens.

Each switch can delay effective treatment, increase toxicity risk, and add practical complexity for already stretched teams and overwhelmed families. It also can contribute to AMR by creating selective pressures that allow bacteria to adapt and survive. In many settings, a high proportion of babies do not respond to first-line regimens because pathogens are resistant.

Even when treatment appears appropriate, mortality and severe morbidity remain high, underlining the need for improved regimens and dosing strategies for infants. Currently, infections are one of the leading causes of death in newborns. The burden is especially high in sub-Saharan Africa and Asia where drug-resistant bacteria, such as *Klebsiella pneumoniae*, are common.

All this puts children and newborns disproportionately at risk from drug-resistant infections. In fact, one out of every five deaths caused by antibiotic resistance occurs in children under the age of five – 99.7% in low- and middle-income countries (LMICs). However, because of the added complexity, cost and time entailed, the development of antibiotics for children, if undertaken at all, lags behind that of adults by nearly a decade.

RETHINKING ANTIBIOTIC DEVELOPMENT FOR CHILDREN

A central part of GARDP's mission is to identify and develop new treatments for children and newborns. The aim of our Neonatal Sepsis programme is to reduce child mortality and improve outcomes for survivors of drug-resistant infections and life-threatening complications, like sepsis. To do this, GARDP has rethought how antibiotic treatments are developed for children and how treatment options can be improved and made accessible, particularly for newborns.

We are developing a range of new antibiotic treatment options for newborns and children, including the use of combination treatments. GARDP is also looking at how existing treatments can be used to protect newborns from the immediate and long-term developmental impacts of drug-resistant bacterial infections. To do this, we have had to come up with an entirely new clinical trial design.

CLINICAL TRIALS REIMAGINED

Conventional clinical trials typically compare a single experimental regimen against a single control drug. While this model works well for many therapeutic areas, it is poorly suited to the realities of treating serious infections in newborns, where clinicians often do not have the luxury of time to determine the exact pathogen before initiating treatment.

The challenge in neonatal antibiotic therapy is therefore not to identify one "perfect" regimen. Rather, it is to avoid the worst options and to identify several sufficiently effective choices that can be adapted to different infants, different pathogens and different hospital contexts.

GARDP's NeoSep1 trial was created to do precisely this, by testing multiple drug regimens simultaneously, across different patient populations and settings, and generate a ranking of options rather than a single "winner." Whatever the results, this approach guarantees success because it will ultimately better support clinicians facing high-stake decisions and improve outcomes for newborns most at risk.

NeoSep1 TRIAL

Launched in South Africa and Kenya in early 2023, the NeoSep1 trial is evaluating new combinations of existing antibiotics and comparing them to treatment regimens that are currently used to treat newborn babies with suspected sepsis. It is also looking at the appropriate dose and formulation for newborns. The innovative trial design of NeoSep1 guarantees success by generating actionable treatment data. The trial will be expanded to other countries in Africa and the Asia-Pacific region with the expected target of enrolling more than 3,000 newborns by end 2028.

The NeoSep1 trial is being conducted in collaboration with the Medical Research Council Clinical Trials Unit at University College London; City St George's, University of London; and Penta – Child Health Research. It is expected to provide robust evidence that could lead to a change in both WHO and country treatment guidelines on the recommended antibiotic treatments for neonatal sepsis.

NEONATAL SEPSIS OBSERVATIONAL STUDY

Working with partners, GARDP has conducted one of the largest-ever observational studies (NeoOBS) with over 3,200 newborns across 19 sites in 11 high-, middle- and low-income countries across four continents. The aim was to assess which antibiotics are currently being used for neonatal sepsis, and to what extent resistance makes these treatments ineffective. The study findings provided a wealth of high-quality data which has helped inform the design of the NeoSep1 trial.

LEARN MORE: WWW.GARDP.ORG

GARDP is committed to improving the global AMR response for healthier children and newborns.

€40 million

Funding needed for the period 2024–2028 to develop and make accessible effective and life-saving antibiotic treatments for neonatal sepsis.

SNIP-AFRICA

The GARDP-sponsored NeoSep1 trial also forms part of a five-year project by a consortium of partners called SNIP-AFRICA (Severe Neonatal Infection Adaptive Platform Trials in Africa), which aims to reduce mortality among newborns with sepsis in hospitals in Africa.

SNIP-AFRICA, led by Penta – Child Health Research **and supported by the Global Health EDCTP3**, is developing a clinical research platform for the implementation of adaptive trials in Sub-Saharan Africa. This includes the NeoSep1 trial as well as pharmacokinetic studies to determine the appropriate doses of antibiotics for newborns. It will also collect data on how newborns with sepsis are treated and how healthcare resources are used. For more information, visit www.snip-africa.org