

Closing gaps in access to medicine for children: how R&D and delivery efforts can be ramped up

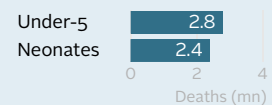
Although huge strides in reducing child mortality have been made over the years, major disparities between countries still exist and millions of children are suffering. Almost 5.2 million children under five still die every year from preventable and treatable diseases, most of whom are in low- and middle-income countries.¹ Despite the clear need to improve access to medicine for these children, the stark reality is that they are often waiting last in line. Complexities around formulations, dosage guidelines, clinical trial enrolment and regulatory requirements combined with tough market economics all limit treatment availability. Still, major opportunities exist to address this problem, and some pharmaceutical companies and organisations are now seizing the initiative to develop and deliver crucial treatments for this vulnerable population.

This analysis looks at the current actions of the pharmaceutical companies assessed in the 2021 Access to Medicine Index to develop and deploy treatments aimed specifically at children under 12. It reveals the projects in development and the newly approved treatments that have 'game-changing' potential for children in low- and middle-income countries. It also asks whether such treatments will realistically be made available for children in these countries.

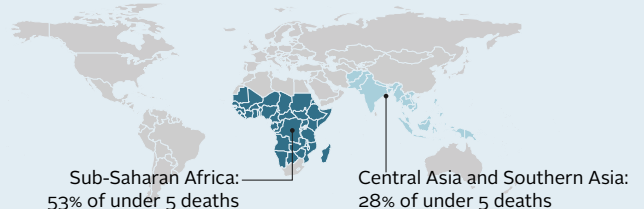
The findings cast light on the immediate opportunities available for companies to accelerate the speed at which their products become accessible to children in low- and middle-income countries. These opportunities provide an update to the Foundation's 2020 series on the urgent need for new child-friendly treatments for HIV, malaria and TB and sets out reforms for shaping policy and scaling up progress across paediatric medicine. By investing in these opportunities, the industry and their partners can help close the gap from pipeline to patient and the global inequalities in children's healthcare.

WHY ACTION IS NEEDED NOW

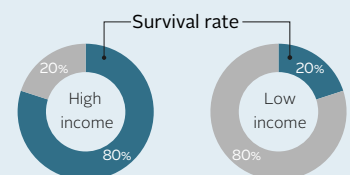
5.2 million children under 5 die each year mostly from preventable and treatable causes



Huge discrepancies in under 5 mortality rates exist between countries



The survival rate of children with cancer living in low and middle-income countries is often near 20%.³



Current challenges limiting medicines for children:

- Complex clinical trials
- Technical R&D challenges
- Regulatory costs and steps
- Financial incentives
- Product introduction and roll-out⁴



Every 39 secs, a child dies of pneumonia.

Every 3 mins, a child dies of cancer.^{2,3}

The current state of play in paediatric R&D

Of the 1,073 R&D projects assessed by the Index, less than 7% (69) target children under the age of 12, revealing major gaps in the paediatric pipeline. Eighteen of the 20 companies in scope of the Index are developing projects for children under the age of 12. Leading companies are GSK (15), Johnson & Johnson (11) and Sanofi (7).

Three diseases are the focus of most of the paediatric R&D projects: lower respiratory infections (15), followed by cancer (10) and HIV/AIDS (9). As most paediatric deaths occur in under the age of five, it is encouraging that the bulk of projects (at least 53) are designed to treat and prevent diseases in children in this age range. Yet, the number of projects for neonatal conditions like sepsis, is alarmingly low with only five projects in development. Additionally, more attention is needed for diseases that disproportionately affect children in low- and middle-income countries, such as sickle cell disease, epilepsy and various diarrhoeal diseases. The pipelines for certain diarrhoeal diseases such as *Escherichia coli* and cholera are completely empty, despite being identified as priority R&D targets by the World Health Organization (WHO) and Policy Cures Research.

While efforts are visible, there continues to be a significant lag between the approvals of treatments for adults and the child-friendly versions. Companies can accelerate paediatric trials where appropriate to close this gap by, for example, simultaneous enrolment of adults and children in clinical trials and invest in innovative technologies that may be applied to more than one dosage form type and/or route of administration.⁴

Five examples of treatments that could prove game-changers for children in low- and middle-income countries

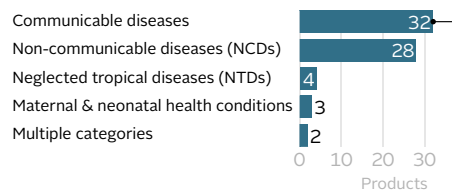
- 1 The glucagon nasal powder (Baqsimi®) for severe hypoglycaemia in children over the age of four with diabetes mellitus by **Eli Lilly** is the first nasal glucagon to enter the market.
- 2 **Bristol Myers Squibb's** dasatinib (Sprycel®) is the first oral suspension formulation for paediatric patients from the age of one with acute lymphoblastic leukaemia.
- 3 Praziquantel, a taste-masked heat stable dispersible tablet for the treatment of paediatric schistosomiasis is in Phase III clinical development by **Merck*** and **Astellas**.
- 4 Fidaxomicin (Dificid®) oral suspension by **Astellas** and **MSD**** for children over six months of age for the treatment of *Clostridioides difficile*, a common cause of diarrhoeal disease.
- 5 The dispersible tablet form of Dolutegravir (Tivicay®) by **GSK** (through ViiV Healthcare), a first-line treatment for children living with HIV weighing at least 3kg and older than four weeks of age.

Yet, these potential game changers are valuable only if they reach the children who need them.

Companies should have concrete, targeted plans in place — known as *access plans* — that help ensure new products are accessible and affordable in all the markets where they are needed. Companies with projects in the pipeline can also engage with the Global Accelerator for Paediatric Formulations (GAP-f), a collaborative network convened by WHO, which aims to provide guidance to the pharmaceutical industry and accelerate the development and availability of paediatric formulations across a range of disease areas.

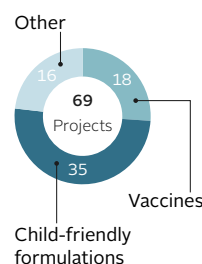
For a broader view of the full pipeline analysis, please see the 2021 Access to Medicine Index report.

Products for communicable diseases dominate the paediatric pipeline

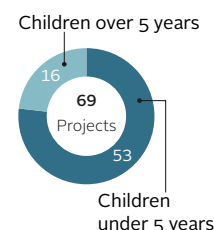


GSK and Johnson & Johnson are developing over 60% of the projects for communicable diseases.

At least 35 medicines come in a child-friendly formulation

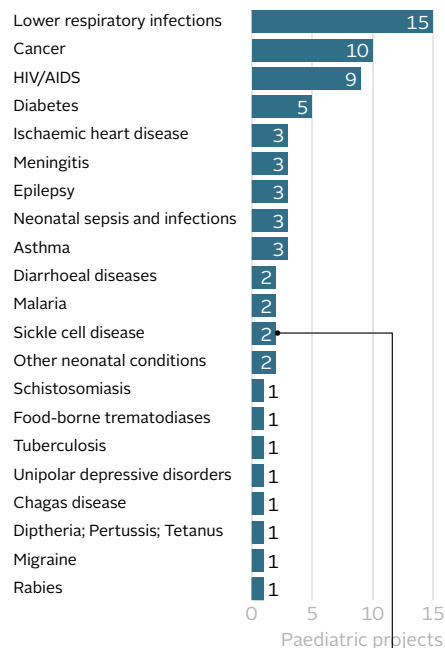


53 projects target children under the age of five



Three diseases are the focus of most of the paediatric R&D

18 companies in the Index are developing 69 paediatric projects. Lower respiratory infections, cancer and HIV/AIDS receive the most attention, while R&D for other priorities such as epilepsy and other diarrhoeal diseases such as cholera and *E. coli* are left behind.



Two projects target sickle cell disease (SCD): Novartis' crizanlizumab tested in children older than six months and AstraZeneca's ticagrelor (Brilinta®) for children over the age of two. As 90% of children in low- and middle-income countries with SCD die before the age of five, ensuring rapid access in these countries upon approval is essential.

*Merck KGaA (Darmstadt, Germany)

**Merck & Co, Inc (Kenilworth, NJ USA)

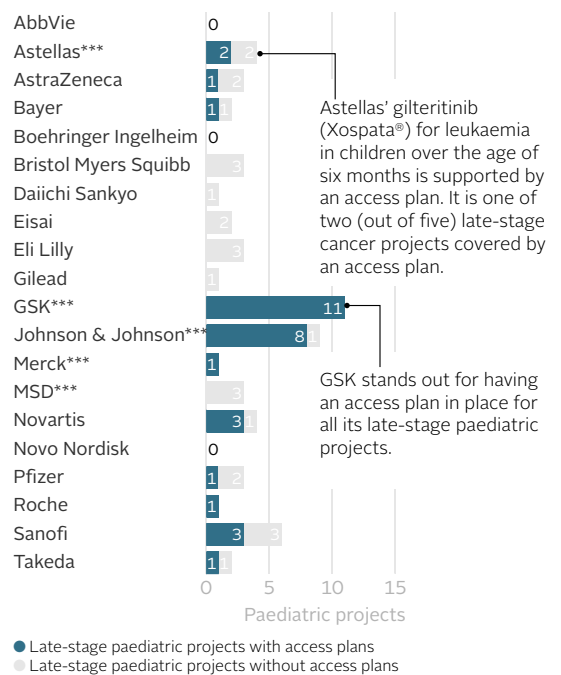
Untapped opportunities to ramp up access

Advance planning during R&D has been shown to improve the speed at which newly approved medicines are made accessible for low- and middle-income countries. Such access plans include a range of activities from prioritising countries with the highest disease burdens during registration, fairer pricing strategies, to strengthening supply chains.

Fifty-six paediatric projects are at the stage where access planning should be taking place (Phase II and onwards). This includes 13 paediatric treatments that have recently received market approval. Twenty-five of the 56 projects are not supported by any access plans, including seven newly approved treatments. Notably, access planning for paediatric non-communicable diseases (NCDs) such as ischaemic heart disease, epilepsy and diabetes mellitus are being particularly overlooked; only eight of the 22 late-stage NCD projects are supported by an access plan. This indicates that additional, more focused attention from multiple stakeholders is needed for these diseases. While new products for paediatric cancer and diabetes, amongst others, are entering the market, there are little efforts to ensure that children in low- and middle-income countries will be able to access these products rapidly. What's more, only two of the 'potential game-changing' projects mentioned previously, are supported by an access plan. By contrast, for infectious diseases, specifically neglected tropical diseases (NTDs), access plans appear to be more common — unsurprising given that these diseases are often linked to high levels of international intervention and market shaping activities. These plans often consist of applying for WHO prequalification, donation programmes and commitments to register in high-burden countries.

Twelve companies apply access plans

This chart shows the 56 late-stage projects in development by a total of 17 companies, 12 of whom show evidence of an access plan for at least one project.

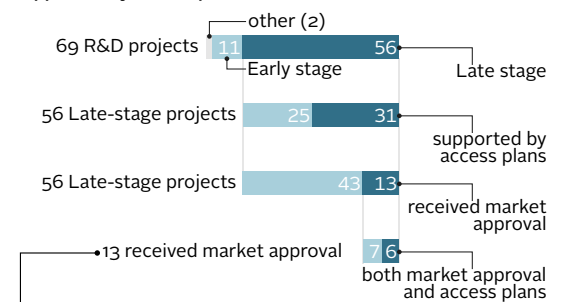


***Three projects are indicated in the pipeline of more than one company (Johnson & Johnson and GSK; Merck and Astellas; MSD and Astellas), as these projects are developed in collaboration

Two stand-out examples of early planning to boost access

- 1 **GSK** developed an access plan for its paediatric formulation of dolutegravir (Tivicay®) for the treatment of HIV/AIDS which recently received market approval. The access plan includes registration commitments, WHO prequalification, 15 non-exclusive, royalty-free voluntary licences (14 of which are in collaboration with the Medicines Patent Pool), partnership with CHAI/Unitaid and two generic medicine manufacturers.
- 2 Praziquantel, developed by **Merck** and **Astellas**, is in Phase III clinical development for the treatment of paediatric schistosomiasis, a disease which affects over 200 million people worldwide, most of whom are children. The access plan for the praziquantel paediatric formulation includes a commitment for WHO prequalification, priority registration in high-burden African countries and non-exclusive licences in agreement with the Paediatric Praziquantel Consortium partners to allow generics or local drug manufacturers to produce the treatment in endemic countries.

Nearly 45% of late-stage paediatric treatments are not supported by access plans



Of the 13 newly approved products, seven do not show any evidence of access planning - including three previously mentioned game-changers. Examples include:

- Eli Lilly's nasal glucagon (Baqsimi®);
- Bristol Myers Squibb's dasatinib (Sprycel®) (although a donation programme with the Max Foundation is in place);
- Fidaxomicin (Dificid®) oral suspension by **Astellas** and **MSD**;
- Eisai's recently approved perampanel (Fycompa®) oral suspension for paediatric epilepsy. Paediatric epilepsy is the most frequent chronic neurologic condition in children;
- Micafungin (Mycamine®) produced by **Astellas** for the treatment of neonatal candidiasis (a cause of neonatal sepsis). Neonatal sepsis kills around one million newborn babies every year.

What actions can be taken now?

For the millions of children waiting in line for medicines that are taken for granted in high-income countries, it is not enough that a few projects are in development. It is not enough that a few more mechanisms are in place to ensure some of these projects will reach children who need them. It is time to close the gaping disparities in access that persist. This clarity of purpose provides an opportunity: to invest in the significant gaps in R&D and prioritise equitable distribution for newly approved products. This is not a task for one stakeholder — improving access to medicine for children is achieved by collaboration and unity. Below are a range of tangible steps that pharmaceutical companies, product development partners, governments and the global health community can take:

- **Simplify and incentivise the paediatric R&D process** by, for example, identifying and overcoming inefficiencies in regulatory procedures, and establishing targeted economic incentives such as market entry rewards.
- **Become drivers of access through access planning** by fully integrating plans to ensure availability, supply and affordability into the late stages of the paediatric medicine development process, including for projects with limited donor involvement such as NCDs like cancer, epilepsy, sickle cell disease and diabetes mellitus.
- **Build on the advances in HIV/AIDS and malaria** by taking the fight beyond infectious diseases. Broadening activities will require coordination, collaboration and unity across governments and stakeholders who understand and specialise in meeting local needs.
- **Leverage government funding, development assistance and philanthropic finances** by shaping local paediatric markets, attract impact investors and increase the funding available for innovative approaches to expand access to paediatrics products in low- and middle-income countries.

Examples of global efforts to reduce child mortality and activate pharma engagement:

- SDG 3.2 aims to end preventable deaths of newborns and under-5 children by 2030.
- GAP-f provides guidance to the pharmaceutical industry for the development of paediatric formulations.
- Through the Rome Action Plan, pharmaceutical companies and global health stakeholders committed to accelerate the development of paediatric HIV/AIDS and TB products. Gilead, GSK (as ViiV Healthcare), Johnson & Johnson, MSD, Roche and Sanofi have signed up to the action plan.
- Specific plans for paediatric drug development are required by both the US FDA (Paediatric Study Plan) and the European Medicines Agency (Paediatric Investigation Plan).
- Government policies that prioritise paediatric access such as the United Kingdom's strategy on ending preventable deaths of mothers, newborns and children.
- Multilateral organisations supporting the development of and delivery of paediatric formulations including UNICEF and Unitaid.
- Private foundations investing in paediatric treatments such as the Bill and Melinda Gates Foundation, ELMA Group of Foundations, the Children's Investment Fund Foundation, and the UBS Optimus Foundation, among others.

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ACCESS TO MEDICINE FOUNDATION

The Access to Medicine Foundation is an independent non-profit organisation based in the Netherlands. It aims to advance access to medicine in low- and middle-income countries by stimulating and guiding the pharmaceutical industry to play a greater role in improving access.

This analysis includes relevant data from 1 June 2018 to 31 May 2020 as part of the 2021 Access to Medicine Index. It provides an update to the Foundation's 2020 series on the urgent need for new child-friendly treatments for HIV, malaria and TB.

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