



FILLING THE GLOBAL HEALTH GAPS – HOW COULD EU R&I FUNDING CONTRIBUTE?

DSW
Deutsche Stiftung
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Poverty-related and neglected disease (PRNDs) R&I is anchored in Horizon Europe:

‘Infectious diseases, including poverty-related and neglected diseases’ are one of the health cluster’s intervention areas, and one line of activity therein details ‘specific challenges in low- and middle-income countries (LMICs), such as AIDS, tuberculosis (TB), and neglected tropical diseases, including malaria’¹. The first strategic plan includes ‘combat[ing] infectious diseases, including antimicrobial resistance (AMR) and emerging epidemics and pandemics’ as one of the expected impacts².

Progress made on PRNDs is under threat

The ongoing COVID-19 pandemic has revealed chronic underinvestment in health research; exposing gaps in the global capacity to tackle infectious disease outbreaks and disrupting research efforts and elimination programmes that are crucial in the fight against PRNDs. Measures to curb the spread of the virus, together with reallocation of resources resulted in reduced testing, increased barriers to treatment, and soaring infection rates. There was an estimated 11 percent decline in the number of people reached with HIV prevention programmes in 2020, compared with 2019, and around one million fewer people with TB were treated in the same time frame.³ These statistics highlight that improved tools to tackle PRNDs are needed more than ever. While investments in, and lessons learned from PRND R&I contributed to a faster, more coordinated response to COVID-19, highlighting its key contribution to pandemic preparedness and response, there is an urgent need to build on the COVID-19 experience to catalyse research and product development for PRNDs.⁴

Horizon Europe work programmes should therefore contribute to filling research gaps for PRNDs



PREVENTIVE METHODS AND TOOLS NEEDED TO REDUCE THE BURDEN OF DISEASES

For many Poverty-Related and Neglected Tropical Diseases (NTDs), although interventions exist to help reduce the disease burden, **there is a significant gap in prevention technologies**. These tools are urgently needed if we are to drastically alter the trajectory of these diseases. In malaria, some interventions that have helped to significantly prevent the disease burden, such as insecticide-treated bed-nets and indoor residual spraying in malaria control, **risk losing their effectiveness with vectors’ increasing insecticide resistance**⁵. This risk needs to be addressed.

The following tools would be key to improving prevention and vector control:

Seasonal malaria chemoprevention (SMC) and intermittent preventive treatment for malaria in pregnancy (IPTp) need to be constantly improved. Bettered antimalarials are also needed to prevent relapse in *Plasmodium vivax* malaria.

Dual insecticide-treated bed nets with novel active ingredients and new modes of action, to address the growing threat of insecticide (pyrethroid) resistance.

New tools to address the growing threat of outdoor biting, such as Attractive Targeted Sugar Baits (ATSBs).

Extra long-lasting next-generation Indoor Residual Spray (up to 12 months) which could be sprayed at any time of the year and proactively rotated sub-nationally.



NO LICENSED VACCINE AVAILABLE FOR THE MAJORITY OF PRNDs

Vaccines are the most powerful public health tool in the fight against communicable diseases. Vaccines prevent disease, are more cost-effective and more sustainable than treatment, help decrease the risk of future drug resistance, and contribute to improved educational and economic outcomes.

Highest burden NTDs have no licensed vaccine

Among the 20 (groups of) NTDs⁶, vaccines are only available for the rabies and dengue viruses⁷. **Safe, effective, and low-cost vaccines** against the most common neglected diseases need to be developed and should be **heat-stable and easy-to-administer** to allow use by frontline health workers in low-resource health settings. There is also a need to look into other infectious diseases that are clearly poverty-related and that disproportionately affect marginalised populations in LMICs, such as **diarrheal diseases including Shigella**⁸, and Group A Streptococcus (rheumatic heart disease), against which there are no approved vaccines⁹.

The urgent need for new TB vaccines

The TB vaccine field has recently seen exciting scientific breakthroughs, with candidates generating positive results in clinical trials¹⁰. **Across the pipeline, there are six novel TB vaccine candidates** in late-stage trials and other promising candidates in clinical and preclinical stages. It is, therefore, **necessary to invest in all phases of TB vaccine research and development**¹¹ as new, more effective vaccines that protect against all forms of TB in all age groups and populations are urgently needed. Without them, we will not be able to meet WHO's END TB Strategy¹² of eliminating TB as a global health problem by 2030.

HIV vaccines need further support

Experts agree that an effective HIV vaccine could help save millions of lives and billions in healthcare costs, and is an important part of the comprehensive prevention toolkit that is needed to ultimately end the pandemic. With no vaccines in late-stage trials but several candidates in development, **further investment is needed to accelerate the testing of vaccine candidates, including identifying more neutralising antibodies** with the potential to help fight HIV infection.

Second-generation malaria vaccines are needed

The world's first malaria vaccine is now recommended by the WHO for deployment in African infants¹³, and at least one other first-generation vaccine is in late-stage testing. While RTS,S/AS01 is an important additional tool to help reduce illness and death among young children, **investments in vaccine development, as well as studies on multiple interventions and non-falciparum malaria, are still needed** if we are to move from malaria control through to elimination and eradication.





ESSENTIAL DIAGNOSTICS ARE MISSING

Access to appropriate diagnostic tools is critical to identify causes of disease, interrupt transmission, prevent the development of disabilities, monitor and evaluate treatment outcomes, and protect against the potential development of drug resistance. Diagnostics are essential for the control, elimination, and eradication of PRNDs in LMICs, as well as for epidemic surveillance and outbreak responses.

Due to the resource-poor, climatically challenging, and often remote rural environments in which PRNDs mostly occur, **point-of-care, easy-to-use, reliable, and low-cost diagnostic tools** that can be used at the primary healthcare level are needed. This means investment in:

Tests that detect multiple infections and target multiple pathogens in the same specimen
(e.g. soil-transmitted helminthiases and *Schistosoma mansoni* in stool specimens)

Tests to guide antibiotic prescription to fight growing antimicrobial resistance
(e.g. to differentiate bacterial vs. non-bacterial infections)

Tests for non-specific symptoms that require a 'syndromic approach'
(e.g. for fever or diarrhoea)

Tests that can be used outside of the clinic, including rapid tests
(e.g. self-tests for HIV and hepatitis C)

Non-invasive tests
(e.g. for Leishmania, cryptococcal meningitis, TB, and other diseases)

Tests that are appropriate for children
(e.g. for TB diagnostics)



¹ Council Decision (EU) 2021/764 of 10 May 2021 establishing the Specific Programme implementing Horizon Europe – the Framework Programme for Research and Innovation, available at: <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32021D0764>

² Cf. European Commission: Horizon Europe Strategic Plan (2021 – 2024), available at: https://ec.europa.eu/info/sites/default/files/research_and_innovation/funding/documents/ec_rtd_horizon-europe-strategic-plan-2021-24.pdf

³ Global Fund: Results Report, 2021, available at: https://www.theglobalfund.org/media/11304/corporate_2021resultsreport_report_en.pdf

⁴ Cf. DSW: EU-Africa Cooperation on Epidemic Preparedness and Health Security: Success Stories and Lessons Learned from COVID-19 (2021), available at: https://www.dsw.org/en/wp-content/uploads/2021/06/DSW_2-Page_EP_v4-3.pdf

⁵ WHO. Global report on insecticide resistance in malaria vectors 2010-2016, (2018) available at: <https://apps.who.int/iris/bitstream/handle/10665/272533/9789241514057-eng.pdf>

⁶ For more information please refer to the WHO website on NTDs, available at: https://www.who.int/neglected_diseases/diseases/en/

⁷ Controversies around Dengvaxia, the only licensed Dengue virus vaccine persist, and FDA approval was granted only for individuals with a laboratory-documented prior infection.

⁸ Cf. Thomas F Wierzbza: The search for an efficacious shigella vaccine, *The Lancet* (November 2020), available at: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(20\)30588-0/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(20)30588-0/fulltext)



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Significant gaps remain for TB tests

TB is the world's biggest infectious disease killer¹⁴ but appropriate diagnostic tools for both latent and active TB infection are missing or not available at the point of care. To prevent TB (re)activation in people at increased risk, **a diagnostic test that reliably predicts the occurrence of TB disease** needs to be developed. Despite the recent progress made by the implementation of molecular technologies for the diagnosis of active TB, there is still a gap and a need for a **rapid, easy-to-perform, point-of-care, non-sputum-based diagnostic test for active TB**.

Better diagnostics for childhood pneumonia

Pneumonia is the single biggest killer of children under five worldwide, despite being largely preventable and treatable. Research to identify and evaluate new **diagnostic tools for improved classification and diagnosis of pneumonia at the community level** (i.e., automated respiration counter, child's jacket with digital monitors, an automated integrated device to monitor vital signs, the possibility of pulse oximetry, etc.) and to understand the contribution of Haemophilus influenzae type b (Hib), non-typeable H. influenzae (NTHi) and Mycobacterium tuberculosis to the burden of pneumonia would be invaluable.

Urgent need for diagnostics for leprosy

Leprosy is one of the oldest-known diseases but still lacks **a sufficiently sensitive and field-friendly diagnostic test for disease and infection**. Research into diagnostic tests, including at community and point-of-care level is considered of key importance in the new WHO Global Leprosy Strategy¹⁵.

⁹ Cf. WHA, A Global resolution on Rheumatic Fever and Rheumatic Heart Disease (2018), available at: https://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_25-en.pdf

¹⁰ Cf. Lewis K Schragger, MD, et al.: The status of tuberculosis vaccine development, The Lancet (January 2020), available at: [https://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(19\)30625-5/fulltext](https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30625-5/fulltext)

¹¹ Cf. EDCTP and AIGHD, Global roadmap for research and development of tuberculosis vaccines (2021), available at: <http://www.edctp.org/web/app/uploads/2021/04/EDCTP-TB-vaccine-roadmap-full-version-final.pdf>

¹² Cf., WHO End TB Strategy, 2014, available at: <https://www.who.int/westernpacific/activities/implementing-the-end-tb-strategy#:~:text=WHO%20developed%20the%20End%20TB,global%20TB%20epidemic%E2%80%9D%20by%202035>.

¹³ Cf. WHO: WHO recommends groundbreaking malaria vaccine for children at risk (October 2021), available at: <https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk>

¹⁴ TB claimed 1.3 million TB deaths among HIV-negative people according to the WHO Global Tuberculosis Report (2021), available at: <https://www.who.int/publications/i/item/9789240037021>

¹⁵ Cf. WHO Towards zero leprosy. Global leprosy (Hansen's Disease) strategy 2021–2030: <https://www.who.int/publications/i/item/9789290228509>



APPROPRIATE TREATMENT OPTIONS ARE LACKING

Many drugs to treat PRNDs have suboptimal efficacy, toxicity, and protocol complexity, and are prohibitively expensive, difficult to administer, or require hospitalisation. This harms patients, hinders treatment adherence, may introduce resistant strains in endemic populations, and hampers moving from control to elimination programmes. Although NTDs¹⁶ account for 11 percent of the global disease burden only 4 percent of new therapeutic products approved between 2000 and 2011 were indicated for neglected diseases¹⁷. Additionally, in some cases, like HIV & AIDS, advancing research towards a cure would accelerate progress towards ending the pandemic by helping overcome challenges posed by treatment drop-out, stigma and discrimination, and uncertainties related to the financial sustainability of programmes.

New, improved treatment options or combinations of existing drugs need to be developed and tested in clinical trials, including:

Chagas: a shorter, safer, and more effective treatment with existing drugs, and a new drug for chronic disease that works in both stages of the disease.

Cryptosporidiosis: a drug that is safe and effective in populations most severely affected, including immunocompromised individuals, such as HIV patients, and malnourished children.

Cutaneous leishmaniasis: a safe, topical, or oral well-tolerated, self-administered and affordable treatment that could cure the lesions without leaving deep scars.

Dengue: New therapeutic solutions, including direct acting antivirals and broadly neutralising monoclonal antibodies to treat dengue fever and prevent progression to severe disease.

HIV & AIDS: a safe, effective, scalable, and globally available and accessible cure (providing for remission and eradication), developed with communities, with a special focus on children who cannot swallow tablets or alcohol-based syrups. Ideally, it would also protect against reinfection.

Leprosy: new post-exposure chemoprophylaxis (PEP) regimens are needed to improve effectiveness and reduce the risk of AMR.

Lymphatic filariasis (elephantiasis), and **onchocerciasis** (river blindness): a drug that can kill adult worms to be used in elimination efforts.

Malaria: novel combination therapies that are active against resistant strains are needed, and improved, easy-to-take, possibly single-dose cures to support compliance, particularly in children, that ideally would have the ability to block transmission of the parasite and provide post-treatment prophylaxis.

Mycetoma: research to understand the exact route of infection, and more effective and affordable treatment options for the fungal form of the disease.

Pneumonia: develop and test ways to power oxygen concentrators to improve access to oxygen at secondary health facilities and in hard-to-reach areas, develop innovative devices and ways to improve pneumonia treatment.

Snakebite: there is a dire need for innovation at every point in the continuum of care, from the improvement of antivenom manufacturing to post-treatment wound management.

Tuberculosis: a novel, short (2-4 months) treatment for all patients needs to be developed, that is successful irrespective of resistance against current drugs, with once-daily fixed dosing; and an ultra-short and effective therapy for latent infection.

Visceral leishmaniasis: an oral, safe, effective, low-cost treatment of short course active against resistant strains and suitable for all populations (including pregnant women and immune-compromised patients).



NEED FOR MORE RESEARCH TARGETING WOMEN

There has been a reluctance to include women susceptible to becoming pregnant in clinical trials because of the potential risks involved. This results in a lack of data on the safety of some tools against PRNDs for pregnant women. There is, therefore, an urgent need to address the lack of pregnancy safety trials and to include pregnant and breastfeeding women in the research process, including in clinical trials - in a safe and ethically sound way.

Diseases such as HIV, TB, and malaria are closely linked to direct causes of maternal mortality, such as postpartum haemorrhage and sepsis, and there is a lack of tools that can be safely used during pregnancy. Despite advances in prevention and treatment, women remain at an alarming risk of HIV infection, in particular, young women aged 15 – 24 years, who are twice as likely to be living with HIV than men¹⁸.

In HIV prevention, there is an especially urgent need for **new tools that come in discreet forms and allow women to reduce their infection risk** on their own terms, without the need for partner negotiation. This includes investing in the introduction of **long-acting prevention products such as a monthly vaginal ring** that has been recommended by the WHO and approved in several African countries, with additional regulatory reviews pending, and **a bimonthly injectable** that has been approved in the US and will be submitted for review in African countries. Also in development are **multipurpose vaginal rings and other formulations that are designed to prevent both HIV and unintended pregnancy, and in some cases, other STIs**. Expanding women's prevention choices is critical so they have the options they need to protect their sexual and reproductive health.

In malaria treatment and prevention, **new medicines are needed to treat and protect pregnant women**, particularly in the first trimester of pregnancy. There is also an urgent need for basic and clinical research to better understand the interconnection between causes of maternal mortality and HIV, TB, and malaria infection, and to **develop and test the efficacy of new treatments to reduce maternal mortality**. Pregnant or breastfeeding women must also be included in clinical trials in a safe and ethically sound way, focusing on women as part of a process but also as separate research subjects, so that they can benefit from new drugs earlier in the process¹⁹.



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¹⁴ TB claimed 1.3 million TB deaths among HIV-negative people according to the WHO Global Tuberculosis Report (2021), available at: <https://www.who.int/publications/i/item/9789240037021>

¹⁵ Cf. WHO Towards zero leprosy. Global leprosy (Hansen's Disease) strategy 2021–2030: <https://www.who.int/publications/i/item/9789290228509>

¹⁶ For more information on NTDs and product gaps, please see the WHO website available at https://www.who.int/neglected_diseases/diseases/en/ and the Drugs for Neglected Diseases Initiative's (DNDi) website at <https://www.dndi.org/diseases-projects/>

¹⁷ Cf. Pedrique et al.: The drug and vaccine landscape for neglected diseases 2000-2011: a systematic assessment, *The Lancet* (2013); 1(6) e371–e379, available at: [https://www.thelancet.com/journals/langlo/article/PIIS2214-109X\(13\)70078-0/fulltext](https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(13)70078-0/fulltext)

¹⁸ UNAIDS Global HIV & AIDS statistics factsheet 2021, available at: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf

¹⁹ Cf. DSW: PRNDs through a gender lens, 2021, available at: https://www.dsw.org/en/wp-content/uploads/2021/05/PRNDs_Gender_Study.pdf

²⁰ Cf. ESSENCE, Seven approaches to investing in implementation research in low- and middle- income countries (2020), available at: https://www.google.com/url?q=https://www.who.int/tdr/publications/seven-approaches/en/&sa=D&source=docs&ust=1639645421547000&usg=AOvVaw1k_bB09Jh3uijbFNX2W3E6



NEED FOR IMPLEMENTATION RESEARCH

The coverage of many life-saving and innovative tools remains low in most affected countries. A better understanding of what drives, or hampers sustainable acceptance of tools, as well as the impact of intervention strategies on disease burden, are essential for reaching global targets. The EU should allocate resources to support operational and implementation research into effective, affordable, and acceptable models for scaling up access to existing interventions²⁰. In parallel, investing in quality health services is key to ensuring research extends from publications to populations in need.



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LMICs WILL BEAR THE GREATEST BURDEN

The 2019 World Bank report on AMR made clear that LMICs will bear the greatest burden of AMR's rising social and economic impacts. Around 5.7 million people die annually from lack of access to antibiotics²¹, while over 700,000 people die from drug-resistant infections, including TB. The latest WHO review of the antibiotic pipeline indicates it is nearly empty to address identified priority pathogens. There is also rising concern about resistance to antiviral drugs against HIV & AIDS, and first-line treatment for malaria (artemisinin-based combination therapies)²². Without novel therapies, malaria could become untreatable in some parts of the world. Furthermore, drug resistance has also been reported for most of the medicines used for leprosy²³, as well as against azithromycin, the first-line treatment against yaws. There is also a real threat of drug resistance in soil-transmitted helminthiases.²⁴ Such resistance could have the potential to further constrain an already limited therapeutics pool for NTDs.

²¹ Isabel Frost, Jessica Craig, Jyoti Joshi, Kim Faure, and Ramanan Laxminarayan. 2019. Access Barriers to Antibiotics. Washington, DC: Center for Disease Dynamics, Economics & Policy.

²² Cf. Fairhurst R. and Dondorp A. (2016) Artemisinin-Resistant Plasmodium falciparum Malaria. Microbiol Spectr. available at: <https://pubmed.ncbi.nlm.nih.gov/27337450/>

²³ Cf., WHO, A guide for surveillance of antimicrobial resistance in leprosy: 2017 update, 2017, available at: <https://www.who.int/publications/i/item/9789290225492>

²⁴ Cf., WHO, Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030, 2020, available at: <https://www.who.int/publications/i/item/9789240010352>

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Deutsche Stiftung Weltbevölkerung (DSW) is a global development organisation that focuses on the needs and potential of the largest youth generation in history. We are committed to creating demand for and access to health information, services, supplies, and economic empowerment for youth. We achieve this by engaging in advocacy, capacity development, and reproductive health initiatives, so that young people are empowered to lead healthy and self-determined lives. With our headquarters in Hannover, Germany, DSW operates two liaison offices in Berlin and Brussels, as well as maintaining a strong presence in Ethiopia, Kenya, Tanzania, and Uganda. DSW also advocates for investment in research and innovation to fight poverty-related and neglected tropical diseases – diseases that continue to disproportionately affect women and girls.

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