might need to be considered to address regional heterogeneities in the epidemiology and transmission of tuberculosis.[14] Although wide population coverage might be justified in settings with intense transmission, risk-targeted strategies might be more suited in other settings. Health-economic modelling and a comprehensive evaluation of the public value of the candidate vaccine should support and guide responsible investments towards vaccine availability.

In conclusion, a promising new vaccine against tuberculosis seems to be on the horizon. Transforming this research success into a tool for global health will require long-standing and continuous efforts from governments, funders, industries, civil society, advocacy groups, health-care practitioners, and international agencies. Early planning is required, and WHO has called for concerted efforts and a wide mobilisation of resources and know-hows. There is no better time to echo the need for solidarity than now, with bold commitments on tuberculosis research and development endorsed by all UN member states during the first UN high-level meeting on ending tuberculosis, and supported by partners in public health.[15] The imperative to achieve the Sustainable Development Goals and End TB targets demands that we use the existing political momentum to increase and sustain support for tuberculosis vaccine research. Ongoing research and evaluation of other tuberculosis vaccine candidates must also continue. We should collectively consider ways to shorten the time to availability of effective vaccines and to mobilise resources to ensure future equitable access and affordability.

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Drugs and vaccines in the 21st century for neglected diseases

Neglected diseases are a diverse group of infectious conditions prevalent in tropical and subtropical areas, and affect billions of people worldwide, disproportionately among the poorest populations and those living in remote, rural areas or conflict zones, almost exclusively in the developing world. Neglected diseases include malaria, tuberculosis, diarrhoeal diseases, and the 20 neglected tropical diseases defined by WHO. As major public health problems, these diseases are a focus of the WHO Sustainable Development Goals programme, which aims to end the epidemics of tuberculosis, malaria, and neglected tropical diseases by 2030. Other commitments—including the WHO Roadmap on neglected tropical diseases and the 2012 London Declaration on Neglected Tropical Diseases—have established action plans to control, eliminate, or eradicate ten diseases by 2020. A central focus of these agreements is the development of novel therapeutic agents. By incorporating cutting-edge science and technology, drug research and development for neglected diseases have progressed considerably.

Nonetheless, a profound gap persists between disease burden and the development of therapeutic assets for such diseases. Although neglected diseases are responsible for about 11% of the global disease burden, the development of therapeutic products for these diseases is disproportionately low.[1] Between 1975 and 1999, only 1·1% of all approved drugs targeted neglected diseases.[2] A survey[2] published in 2013 showed that, of the 850 therapeutic products that reached the market between 2000 and 2011, only 37 (4·3%) were developed for neglected diseases. Among the 336 new chemical entities developed in this period, only four compounds (1%) were indicated for neglected diseases: three for malaria and one for tuberculosis. No new chemical entities were developed for neglected tropical diseases in the 2000–11 period, and the five products approved for these diseases were repurposed compounds, new formulations, or drug combinations.

In light of the goals set for 2020, it is appropriate to examine the current drug research and development landscape for neglected diseases. Between January, 2012, and September, 2018, 256 therapeutic products reached the market, but only eight (3·1%) targeted neglected diseases. The 157 small-molecule compounds, only two new chemical entities (1·3%) were approved for neglected diseases: bedaquiline for tuberculosis and tafenoquine for malaria. Bedaquiline, which reached the market in 2012, is used as part of a combination therapy for multidrug-resistant tuberculosis.[3] This diarylquinoline was the first drug to be approved for tuberculosis after 1998 and the first with a novel mechanism of action to be approved in 40 years. The US Food and Drug Administration (FDA) approved tafenoquine in July, 2018, as a radical cure for *Plasmodium vivax* malaria—the first treatment for this indication in 60 years. Tafenoquine prevents disease relapse in patients aged 16 years and older with a single dose, which is a crucial improvement over the other available treatments.[4]

The list of approved new chemical entities will expand in 2019 with the development of fexinidazole, the most advanced oral drug for human African trypanosomiasis. Fexinidazole entered clinical trials in 2009 and is currently being registered as a treatment for early-stage and late-stage human African trypanosomiasis caused by *Trypanosoma brucei gambiense* in adults and children older than 6 years.[5] Importantly, for the first time, human African trypanosomiasis can be cured with the use of pills alone. Moreover, no drugs have been developed for this condition since 1990 when eflornithine was repurposed from a clinical trial for cancer.

The remaining six products registered between 2012 and 2018 are repurposed drugs, new formulations, and biologicals. In 2014, miltefosine reached the market as a broad-spectrum therapy for leishmaniasis. Developed in the 1980s for cutaneous metastases of breast cancer, this alkylphosphocholine was repurposed for leishmaniasis and at present is the only oral drug available to treat all clinical forms of the disease.[6] In another instance of repurposing, the veterinary drug moxidectin was approved by the FDA to treat onchocerciasis (river blindness) in patients aged 12 years and older in June, 2018,[7] which rendered this macrocyclic lactone the first drug to be registered for onchocerciasis in 20 years. Another advance was the development of paediatric benznidazole to treat Chagas disease in children aged 2–12 years,[8] which was granted FDA approval in 2017.

The other three registered products are biologicals. In 2016, Vaxchora—a single-dose attenuated virus vaccine indicated for active immunisation against *Vibrio cholerae* serogroup O1—was the first vaccine to be approved by the FDA for the prophylaxis of cholera.[9] The other biologicals are human rabies immunoglobulins (KedRab and a new formulation of HyperRAB) indicated for post-exposure prophylaxis of rabies infection.[10,11]

The numbers above represent a rate of 1·1 products targeting neglected diseases approved per year from 2012 to 2018, which is lower than the three products per year approved in the 2000–11 period. Notably, the proportion of new chemical entities among the registered products for neglected diseases increased from 2000–11 (10·8%) to 2012–18 (25%); this proportion was 13·3% for the entire 2000–18 period, highlighting the need for intensified research on the development of new chemical entities. Of the six new chemical entities approved in 2000–18, four are indicated for malaria, reflecting a concentration of drug research and development efforts on this disease. No new chemical entities were approved for neglected tropical diseases in this period.

These developments have actively contributed to a gradual but consistent reduction of the neglected disease burden in this century, reflecting progress towards the endorsed global health agendas.

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