The 1/4/6x24 campaign to cure tuberculosis quickly

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The "right of everyone to enjoy the benefits of scientific progress and its applications," also known as the right to science, is enshrined in the Universal Declaration of Human Rights and international human rights law. People with and at risk of tuberculosis (TB) are eager to realize this right[1,2]. Among the essential "applications of scientific progress" are the long-awaited shorter, less toxic TB treatment regimens. Thanks to two decades of renewed investments in TB drug development and research, it is now possible to treat TB infection in as little as one month and most forms of drug-sensitive and drug-resistant TB in four and six months, respectively[3,4,5,6,7,8]. However, these shorter treatments are futile until they reach the people who need them. Thus the 1/4/6x24 (one, four, six by 2024) campaign was launched at the AIDS 2022 conference in Montreal (see Table 1).

Table 1 | The 1/4/6x24 campaign

	1	4	6	x24
Description	1-month or once weekly treatment regimens for TB prevention	4-month treatment regimens for drug-sensitive TB	6-month treatment regimens for drug-resistant TB	By the end of 2024
Details	1 month of daily isoniazid and rifapentine, 3 months of once-weekly isoniazid and rifapentine, and 3 months of daily isoniazid and rifampicin	4 months of daily isoniazid, rifapentine and moxifloxacin, given with pyrazinamide for the first 2 months; for children with non-severe TB, 4 months of isoniazid and rifampicin, given with pyrazinamide, and in certain circumstances with ethambutol, for the first 2 months	6 months of bedaquiline, pretomanid and linezolid, given with or without moxifloxacin depending on drug susceptibility	A deadline for having in place the "staff, stuff, space, systems, and support" needed for shorter TB regimens to be made accessible to everyone, everywhere, as a human right

This should proceed together with priority research to extend the benefits of short treatment and prevention regimens to any groups that cannot currently use them due to data gaps or research exclusions.

The campaign calls for every eligible person with TB infection or disease to have access to evidence-based, short-course treatment regimens. For this to happen, the community of people affected by TB and their allies must refuse to accept the malaise and mediocrity of duty bearers (state and non-state actors obligated to respect, promote and realize human rights) and demand timely accountability from governments, global health actors and the pharmaceutical and diagnostics industries to ensure that these new standards of care are expeditiously brought to scale.

There is no time to waste. According to the World Health Organization (WHO), in 2020, the number of TB deaths increased for the first time since 2005, wiping out more than a decade of progress in just 12 months. This trend continued in 2021, and estimated TB incidence also increased, reversing a long (if slow) decline in the number of people believed to develop TB each year. The 1/4/6x24 campaign offers a new, unified framework around which to rally the energy, political will and funding needed to course-correct the global fight to end TB and avert unnecessary suffering and death. With the science behind all regimens under the 1/4/6x24 campaign now reflected in WHO guidelines, the current task is implementation at speed and scale.

Paul Farmer, whose legacy inspired the 1/4/6x24 campaign, insisted that the best available prevention and treatment options be made available to everyone, everywhere[9]. Farmer regularly called for the full healthcare infrastructure necessary for delivering person-centered care — what he referred to as the '5 Ss': staff, stuff, space, systems and support[10]. This approach requires a multisector and fully financed TB response.

On the heels of the replenishment of The Global Fund, which raised an unprecedented US$14.25 billion, more investment in TB is still needed. The Global Fund allocates just 18% of its funding to TB, $1.2 billion per year. Yet, the Global Plan to End TB 2023–2030 estimates that $250 billion is needed between now and 2030. Investments must increase markedly to bridge this gap and ensure that corresponding national strategic plans are fully funded. The financial and economic implications of implementing 1/4/6x24 at scale need to be rigorously evaluated, but temporary increases in drug and implementation costs are expected to be offset by savings in human resources, given the shorter duration of the regimens. Savings and benefits can also be expected from improved adherence, outcomes and safety that enable people to rejoin the workforce sooner and avoid treatment interruptions that can generate drug resistance. The costs of inaction are clear: according to the Global Plan, failure to scale up the full range of available innovations would result in 6.6 million additional TB deaths and economic losses of $1 trillion by 2030.

Steps must be taken to make short-course regimens available to everyone eligible as a human right. National governments and duty bearers must take action to put in place the 5 Ss necessary for implementing these regimens by the end of 2024. This includes rapidly updating policies and treatment guidelines, ensuring the availability of the diagnostics, medicines and human resources, and increasing investments in TB programming. National governments must generate demand for shorter drug regimens through multisectoral approaches to closing gaps in TB testing, including improving access to rapid molecular diagnostic tests and imaging.

Donors must step up funding to mitigate anticipated higher medicine costs and address increased needs of health systems and laboratory networks. Donors should fund civil society and community organizations to work on national 1/4/6x24 campaigns and accountability initiatives.

Pharmaceutical and diagnostics corporations must take corrective action to create better and more affordable diagnostic tests; lower the prices of rifapentine, bedaquiline, pretomanid, linezolid and delamanid (an important component of shorter regimens for population groups that cannot yet benefit from access to pretomanid-based regimens for drug-resistant TB); and develop fit-for-purpose formulations, such as a pediatric rifapentine and fixed-dose combinations to support the four-month regimen for adults, and must register them with regulatory authorities.

Researchers and funders also must prioritize inclusive clinical research, as key groups of people affected by TB, such as children and pregnant people, cannot yet benefit from scientific advances that have enabled treatment to be shortened owing to the lack of clinical trials in these cohorts. We condemn the practice of excluding people from studies under the guise of protecting them — on the contrary, evidence is urgently needed. More work should also center on the preferences and needs of people affected by TB for treatment and adherence support.

We adamantly reject the shameful, persistent indifference toward TB. Survivors, community and civil society groups, scientists and clinicians, and their allies must build global solidarity

to generate political will and substantial resource commitments from governments, donors and industry. We urge others to join us and support the 1/4/6x24 campaign.

Competing interests

J.F. received grant funding from the Stop TB Partnership's Global Drug Facility to support the rollout of child-friendly formulations of second-line drugs. M.P. has no financial or industry conflicts to disclose; he serves as an advisor to the WHO, Foundation for Innovative New Diagnostics, Stop TB Partnership and Bill & Melinda Gates Foundation. B.-T.N. is employed by Médecins Sans Frontières, the sponsor of the TB-PRACTECAL trial that developed a 6-month multidrug-resistant/rifampicin-resistant TB (RR-/MDR-TB) regimen. Through grants to her institution, C.D.M. receives research funding to study all-oral shortened regimens for treatment of drug-resistant TB containing bedaquiline, delamanid, linezolid, clofazimine, levofloxacin, moxifloxacin and pyrazinamide.

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