NEW DRUGS, NEW HOPE

FIGHTING DRUG-RESISTANT TUBERCULOSIS IN GEORGIA
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ABOVE: An MSF vehicle waits in the parking lot outside the TB hospital in Zugdidi, Georgia.
Dear Friends,

MSF GETS PLENTY OF ATTENTION FOR ITS WORK RESPONDING TO FRONTLINE EMERGENCIES LIKE THE LATEST CHOLERA OUTBREAK IN YEMEN. FEWER PEOPLE ARE AWARE OF MSF’S LONGER-TERM MEDICAL RESEARCH AND ADVOCACY TO CONFRONT THREATS TO GLOBAL PUBLIC HEALTH, SUCH AS OUR AMBITIOUS EFFORTS TO FIGHT TUBERCULOSIS.

Tuberculosis (TB) killed 1.8 million people last year, overtaking HIV/AIDS as the world’s deadliest infectious disease. Another nine million people suffer from TB. The emergence of drug-resistant TB (DR-TB) presents even greater challenges, yet governments and pharmaceutical corporations worldwide systematically fail to make adequate investments in research and development to tackle these problems. There’s hardly any financial incentive to do so, with most of the TB burden in developing countries.

MSF is among the largest non-governmental providers of TB care in the world. We supported more than 20,000 patients on treatment in 2016—including more than 2,000 patients fighting DR-TB. We run 24 projects to treat the disease, in places from Swaziland to Tajikistan.

In this issue, you’ll get a rare look at the stories of MSF patients and staff fighting DR-TB in Georgia, in the heart of the Caucasus. After the collapse of the Soviet Union, TB resurfaced as a major threat to public health in the region—and Georgia is struggling to cope with a particularly high incidence of drug-resistant TB. Treatment options for people with DR-TB have ranged from bad to worse, often involving lengthy, expensive, and toxic drug regimens with no guarantee of success. MSF is working on a pioneering initiative with the Georgian health ministry to explore new treatment options for DR-TB using bedaquiline and delamanid, the first new tuberculosis drugs developed in nearly 50 years.

MSF’s project in Georgia is part of a larger initiative to “endTB” (Expand New Drug markets for TB), an international framework supported by Unitaid, an international organization that invests in new ways to prevent, diagnose, and treat HIV/AIDS, TB, and malaria. EndTB aims to find more effective and less toxic treatments for TB. Partners in the initiative plan to use bedaquiline and delamanid to treat 2,600 patients across 15 countries and collect vitally important data on the results. MSF is also involved in a separate international clinical research project called TB-PRACTECAL, which seeks to develop alternative regimens that will cure all forms of DR-TB within six months.

We are also at the forefront of efforts to provide more decentralized and community-based models of care, in some cases based on successful systems used for HIV treatment.

MSF advocates with governments, corporations, and multilateral institutions to push for more concerted action to fight tuberculosis. We are already gearing up for the 2018 UN High Level Meeting on TB, where we will push for policy changes that could help millions of TB patients to secure better treatment and a better chance to survive.

Finally, we are proud to bring you the first issue of a fully redesigned Alert in a new format, intended to better showcase stories from our staff and patients while also significantly reducing print costs. We are always looking for cost-effective solutions in order to devote more resources to our medical projects around the world. As always, thank you for supporting our essential work.

Sincerely,

John P. Lawrence, MD
President, MSF-USA Board of Directors
FIGHTING DRUG-RESISTANT TUBERCULOSIS IN GEORGIA

The morning sky is veiled by steel-gray clouds when Eldar arrives for his appointment at the local hospital in the town of Senaki, in rural western Georgia, deep in the Caucasus. Rail-thin and smartly dressed in a twill blazer and jeans, the 29-year-old has been battling tuberculosis (TB) since 2006.
Back then, Eldar’s doctor put him on treatment for multi-drug resistant TB, a long and complicated regimen he was unable to complete. In 2016, ten years after his original diagnosis, Eldar was still sick, and still tested positive for the disease. He was referred to the Doctors Without Borders/Médecins Sans Frontières (MSF) program near Senaki, where he was enrolled in a new treatment using bedaquiline and delamanid, the first new tuberculosis drugs developed in nearly 50 years.

After almost two more years of grueling treatment using these new compounds, Eldar recently received the news that he had finally tested negative. Light rain begins to fall as he climbs the crumbling cement steps of the hospital and enters the small consultation area, where he will meet with his MSF doctor and counselor for a follow-up. It’s an appointment he hopes will be one of his last.

Once considered all but defeated in Georgia, TB re-emerged as a major threat to public health after the collapse of the Soviet Union. During the years of conflict, displacement, and privation that came afterward, outdated and poorly followed treatment practices led to increased drug resistance. Though the incidence of tuberculosis is lower here than in some other countries in the region, Georgia is grappling with a particularly high burden of drug-resistant TB. For patients with these forms of the disease, the standard antibiotic treatments simply do not work.

Drug-resistant TB (DR-TB) is much harder to cure than ordinary, or “drug-sensitive,” TB. Treatment options for the disease are extremely limited and involve long, complex, expensive, and toxic drug regimens. Even with the promise of new drugs, most patients fighting DR-TB face a minimum of nine months of treatment, a period that often stretches to two years. They must swallow more than 10,000 pills over the course of their treatment and endure six to eight months of painful daily drug injections.

For patients like Eldar, the side effects of the treatment can be nearly as difficult to manage as the disease. The drugs can cause debilitating conditions
that range from nausea and joint pain to psychosis and partial or total hearing loss. Eldar experienced some hearing loss during his treatment, and struggles to make out the greetings he receives from staff members as he enters the Senaki Hospital. He smiles just the same, his gaunt face brightening as he greets the medical team who have become so familiar over the course of his long and difficult journey.

Eldar meets with his doctor, MSF physician Gocha Salia, in the facility’s small consultation room, a simply furnished space painted an old-fashioned pale peach. He lowers his thin frame onto the examination table. His voice is soft as he explains how he’s been feeling, as if he is afraid to speak out loud about his recovery for fear of tempting fate and inviting back the disease that has dogged his life for so long.

Though he now tests negative for TB, Eldar still suffers from terrible chest pain. He is concerned that his illness could be returning. Dr. Salia asks some questions about the nature of this pain: When exactly does it hurt? What does it feel like? Before he leaves, Eldar will also take a battery of other tests to check for side effects—“adverse events,” in the parlance of the MSF doctors currently studying the efficacy of the new drugs. A nurse will check his vision and hearing and test his reflexes to discern whether the drugs have left him with any nerve problems.

For now, Dr. Salia asks Eldar to lift his shirt and checks the young man’s breathing. All sounds well, and his temperature is normal too. “Don’t worry,” says Dr. Salia. “You’re doing much, much better.” The doctor reviews a recent X-ray with his patient. The translucent images reveal heavy scarring inside Eldar’s lungs—damage left by years of infection—but no new signs of disease. In fact, says Dr. Salia, comparing the image to an older X-ray, despite the chest pain that he will likely experience for the rest of his life, Eldar’s condition is steadily improving.
TUBERCULOSIS: 
A Global Public Health Crisis

According to the World Health Organization (WHO), 4,900 people worldwide die from tuberculosis (TB) every day—more than three every minute. Caused by the airborne bacteria *Mycobacterium tuberculosis* and spread when an infected person coughs or sneezes, TB can result in a chronic cough, fever, weight loss, lung damage, and, for many patients, death.

The global public health crisis posed by TB is exacerbated by the emergence of drug-resistant forms of the disease. As bacterial resistance to traditional “first-line” drugs increases, new and more effective medications and models of care are needed to treat patients and halt the spread of the disease. However, worldwide investments in such measures are woefully underfunded and underdeveloped.

MSF is one of the largest non-governmental providers of TB care in the world, treating the disease in 24 projects around the world and supporting more than 20,000 patients on treatment in 2016, including more than 2,000 patients fighting DR-TB. This work also includes partnering with national ministries of health, Unitaid, and other organizations to accelerate research and improve the quality and availability of treatment regimens for DR-TB.

Defining TB

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<td>TB that can be treated with standard drugs.</td>
<td>A general term used to describe all those forms of TB that show resistance to one or more of the common first-line drugs. The following are all forms of DR-TB:</td>
<td>Resistant to isoniazid and rifampicin, the two most powerful first-line TB drugs. <strong>52% of MDR-TB patients are successfully treated.</strong></td>
<td>Resistant to isoniazid and rifampicin and either a drug from the class of antibiotics known as fluoroquinolones or a second-line injectable drug (but not both).</td>
<td>Resistant to isoniazid and rifampicin and to second-line drugs, including fluoroquinolones, and at least one of the injectable second-line drugs (capreomycin, kanamycin, and amikacin). <strong>28% of XDR-TB patients are successfully treated.</strong></td>
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*Cure rate percentages are World Health Organization (WHO) estimates.*
As of October 2016, MSF, in partnership with national ministries of health, has initiated more than 1,000 DR-TB patients with bedaquiline and/or delamanid in 12 countries. Globally, there is still an unacceptable gap between those who would benefit from the new drugs and those who have been able to access them. To date, through programmatic or compassionate use, only 5,738 DR-TB patients have been able to access bedaquiline and just 405 have been able to access delamanid.
Visibly relieved, Eldar pulls his jacket back on and prepares to go to the next room, where he will meet with his MSF counselor to discuss the ways he can continue to protect himself from TB. “Of course, my life has changed,” he says as he stands up to leave. “Whenever you become ‘negative,’ everyone looks at you differently. When you have the disease people are afraid of you—now that I’m cured people don’t have as much fear.”

**A NATIONWIDE PROJECT**

Eldar is just one of many patients in Georgia who has benefited from receiving TB treatment with new drugs through a partnership between MSF and the Georgian Ministry of Labor, Health, and Social Affairs. “Here in Georgia, MSF is helping the government to implement these new drugs,” explains Dr. Sylvie Goossens, MSF head of mission in Georgia. Soon after the drugs became available in 2014, MSF began working with the health ministry to implement them within the framework of endTB (Expand New Drug markets for TB), a comprehensive international project that aims to find shorter, less toxic, oral-only, and more effective treatments for the disease. Through endTB and with MSF’s assistance, Georgia is adding the new drugs to treatment regimens, running an observational study on their safety and efficacy, and undertaking a clinical trial on new “user-friendly” treatments. [Read more about endTB and clinical trials on page 16.]

MSF currently provides and studies the effects of the new drugs in four tuberculosis hospitals in Georgia: Zugdidi in the west, near the border with the partially recognized state of Abkhazia; Batumi, a beach town on the Black Sea; Abastumani, on the southern slopes of the Meskheti mountains; and in Tbilisi, the nation’s capital. MSF teams also regularly visit several smaller health centers across Georgia, like the hospital in Senaki where Eldar received treatment. By the end of 2016, some 300 TB patients across Georgia were started on the new treatments.

Though the studies are still under way, initial outcomes seem very promising. Of the patients started on the new drugs from April 2015 to December 2016, 86.8 percent tested negative for TB after six months of treatment. To assess the efficacy of the treatments, “we look for what is called ‘culture conversion,’” explains Dr. Goossens. Sputum samples from patients are
cultured and tested for the presence of TB bacteria. “If the treatment is effective, then when we reanalyze the sputum, the culture will ‘convert’ from positive to negative, meaning that the bacteria is no longer active.”

**SOCIAL SUPPORT**

However promising their results, the new drugs are only part of the picture when it comes to effectively treating DR-TB in Georgia. Strict adherence to the long, difficult, and complex regimens is crucial to ensure that patients defeat TB—and that it stays defeated. “If patients are converting, it means they are on their way to being cured,” says Dr. Goossens. “But it doesn’t mean they won’t convert back to positive if they stop their treatment. It’s essential that patients continue their treatment for its prescribed duration and remain negative. Then we can declare them cured.”

This is where MSF’s adherence counselors come in. Working closely with the doctors and nurses, MSF counselors provide the support patients

**TOP TO BOTTOM:** MSF doctor Gocha Salia and a hospital nurse tend to a patient at Zugdidi TB Hospital; MSF nurse Maia Patsatsia checks a patient’s vision in Zugdidi; MSF head of mission doctor Sylvie Goossens.

**FACING PAGE:** MSF doctor Gocha Salia prepares to test a patient for neuropathic side effects at Zugdidi TB Hospital.
NEW DRUGS, NEW HOPE

need to stay on—or adhere to—their treatment. They connect patients with caregivers who can help support them after hospitalization, provide transportation stipends to ensure patients can reach health facilities for twice-daily appointments, and ensure they receive care for other medical conditions like hypertension, hepatitis, or chronic obstructive pulmonary disease. But beyond practical considerations, they also provide patients—many of whom come from precarious living conditions, or must endure extended hospital stays—with emotional support and encouragement.

At the health ministry’s TB hospital in Zugdidi, where the snow-capped Svaneti mountains loom on the horizon, MSF counselor and doctor Lika Jobava-Tchurgulia knocks gently on a door in the second-floor inpatient ward. Her bright yellow trench coat and chunky jewelry are a sunny contrast to the hospital’s drab plaster walls. She’s here to see Shota, an inpatient receiving treatment for extensively drug-resistant TB.

A thin, elderly man from a nearby village, Shota has been hospitalized here in Zugdidi for around six months. He is responding to his treatment, but Dr. Jobava-Tchurgulia is concerned about his mental health, and the limited support options available to him outside the hospital. She greets him and asks simple questions in a conversational tone about his day-to-day life, the care he receives at the hospital, and whether he has any family who could help to take care of him when he is discharged.

Shota explains that he has nephews in Zugdidi, but he hasn’t been in touch with them recently. Divorced from his wife and living alone before his hospitalization, he is most concerned about the state of his home.
FIGHTING DRUG-RESISTANT TUBERCULOSIS IN GEORGIA

and garden, which, he explains, have had no one to take care of them since he was admitted. Dr. Jobava-Tchurgulia listens carefully to his concerns and reassures him. She will get in touch with his nephews and visit Shota’s home to make sure things are in order. And she offers to take photos of his garden.

“BACK TO LIFE”

MSF team members aren’t the only ones who can provide essential support to TB patients struggling to adhere to their treatment. Sometimes knowing that someone has been in your shoes, and fought the same fight, can make all the difference. In Abastumani, a former resort town in the picturesque Meskheti mountains, MSF works in the local sanatorium, a grand but dilapidated building that now serves as the region’s TB hospital. It is here that Kale Mantkava defeated DR-TB—and where he now helps others fight it.

A wiry 55-year-old from the western city of Lanchkhuti, Mantkava was first diagnosed with TB in 1987. After a failed course of treatment, his disease became drug-resistant. For years he lived without symptoms, but his cough returned and his health began to fail in 2011. He was admitted as an inpatient to the hospital in Abastumani, where he was one of the first patients to be enrolled on treatment with the new drugs. During his time as an inpatient, the hospital staff noticed Kale’s determination to adhere to his treatment, and the encouragement he provided to his peers.

When Mantkava completed his treatment in November 2016, the hospital team offered him a position as a consultant. Now he lives and works at the hospital, supporting other patients as they struggle with their hospitalization and treatment. Among other responsibilities, Mantkava runs a small library from his room at the hospital, lending out books and magazines to the inpatients. He also has a green thumb—his room is festooned with all manner of plants, all of which are thriving in the sun that streams through his tall window. The plants are an important part of his work with the other patients. Throughout the hospital, Mantkava’s flowers and other decorative plants grow happily in pots on shelves and windowsills, providing splashes of color and life in the crumbling old sanatorium. “Caring for them helps patients take their minds off the hardships of the treatment,” he says.

“Because of what I’ve been through, I know the real picture of what TB is,” he says. “Patients always feel a stigma when they learn they have TB—I help to show them that it doesn’t have to be painful.” When the chilly weather improves, Mantkava hopes to start a flower garden outside on the hospital grounds for the inpatients to care for together. When the garden blooms, it will be a sign of hope for the future—like the hospital, his colleagues, and the other patients he’s seen recover from TB and “come back to life.”

“PATIENTS ALWAYS FEEL A STIGMA WHEN THEY LEARN THEY HAVE TB—I HELP TO SHOW THEM THAT IT DOESN’T HAVE TO BE PAINFUL.”

— Kale Mantkava, survivor of DR-TB and hospital consultant
“I have worked with so many patients who could have died for lack of treatment. Now they are alive, they are healthy and living. So every time I see them I feel proud, because I know how much work it took to recover.”

—MSF counselor Lika Jobava-Tchurgulia, from Zugdidi, Georgia

“When I was practicing medicine in the early 90s, tuberculosis was basically defeated in Georgia. If we found even one patient we were ‘happy,’ just to have the practice of treating the disease. When I found out that drug-resistant tuberculosis was becoming a problem in Georgia, I decided to find out how this happened, and what we could do to solve this problem.”

—MSF counselor Nino Kapanadze, from Tbilisi, Georgia

“I hope that in several years there won’t be any TB cases in Georgia, and that this program will manage to eliminate the disease. I’ve dedicated half my life to TB patients, and I’ve seen so many patients and so many stories. I hope doctors of my generation will be the last to treat TB and there won’t be any more need for TB treatment.”

—MSF doctor Gocha Salia, from Zugdidi, Georgia
“The endTB clinical trial is really a very innovative trial. For me, it’s a revolution in the treatment of tuberculosis. It would be great if patients could be treated for nine months instead of two years.”

—MSF clinical trial study coordinator
Nino Kiria, from Tbilisi, Georgia

“Before, patients didn’t believe that they could ever be cured. But MSF, with these new drugs, gave them hope for the future. Now they believe they can be cured. When MSF first brought these drugs into the country, they also gave training to the medical staff on how to administer them. Passing along that knowledge is important. These drugs work, and we’ve got the education and training on how to use them, so now it’s time to move to the next stage—a more supportive stage for the patients.”

—MSF doctor Marina Kikvidze, from Tbilisi, Georgia
Access to new drugs is limited due to high prices and the fact that manufacturers have not registered them for use in many countries with high burdens of TB. In addition, more research is needed on how to effectively use these new drugs in treatment regimens. To this end, MSF is participating in two clinical trials to find shorter, more effective, and less toxic treatments for multi-drug resistant and extensively drug-resistant tuberculosis: endTB and TB-PRACTECAL.
“In Georgia, one of my patients was infected with extensively drug-resistant tuberculosis (XDR-TB)—most likely from his son, who died of the disease a few years earlier,” says Paris-based Dr. Lorenzo Guglielmetti, MSF’s co-principal and investigator of the endTB trial.

Luka [patient name changed to protect anonymity] was 62 years old and, over the course of two grueling years of treatment, suffered terrible side effects and was twice told that his treatment had failed. “When I saw him, he was tired and very weak.”

As a last resort, Luka was put on a treatment regimen containing one of two new TB drugs, bedaquiline. “He responded very well and after just three months received the news that, for the first time, his sputum tested negative for TB,” said Dr. Guglielmetti. Luka spent a year in the hospital before going back to his village to finish his treatment. After two years of treatment—including six months using bedaquiline—he was cured.

However, a general lack of conclusive evidence on the safety and efficacy of these new drugs means that current World Health Organization guidelines on their use remain conservative. “They only recommend them to MDR-TB patients with no alternative treatment options, and additional resistance to most other drugs,” says Dr. Guglielmetti.
EndTB, a partnership between MSF, Partners in Health, Interactive Research & Development, and Unitaid that aims to use bedaquiline and delamanid to help improve treatment outcomes for MDR-TB, began the first of phase of the project—an observational study—in 2015. With a target of treating 2,600 patients across 15 countries, including Georgia, Bangladesh, and Kenya, MSF is collecting much-needed data that can inform policymakers and treatment providers on how to effectively use these two promising new drugs in TB treatment programs. “Phase one is not about revolutionizing treatment, it is about showing the efficacy of the new drugs,” says Dr. Guglielmetti.

Access to these new drugs is extremely limited: less than 5 percent of patients who need the new drugs currently receive them. “We need more evidence backing the use of these drugs and we need to push for them to be accessible everywhere in the world for all MDR- and XDR-TB patients who need them,” says Dr. Guglielmetti.

Preliminary results will be released later this year, but MSF teams have already witnessed dramatically higher cure rates and more tolerable side effects among the approximately 1,000 patients who have received the new drugs. Running in parallel to this study is phase two: a clinical trial. MSF and partners will implement the trial in six countries, including Georgia, Lesotho, and Peru. “The objective is to change the paradigm of treatment; to shorten treatment drastically,” explains Dr. Guglielmetti. “Of course, this is more difficult to accomplish because we need to show these new shorter regimens are at least as effective as the current two-year treatment.”

The clinical trial run by endTB will compare five new experimental nine-month treatment regimens and one control regimen (the standard 20-month treatment used in the phase one study). At least 750 MDR- and XDR-TB patients will be recruited on a voluntary basis and randomly assigned to one of the six treatments. The five new treatments use different drug combinations—including at least one of the new drugs—and contain no injectables, which are often extremely painful and difficult to administer under current treatment guidelines. The new combinations also use fewer pills (just five to ten per day, as opposed to up to 20 per day for current treatments). All of these drugs, except one, can be taken together once per day, and have more manageable side effects.
"We are trying to test a lot of different regimens to identify not just one treatment at the end of the trial, but many different alternatives that work for various forms of DR-TB, with the goal of finding at least one alternative that will work for each TB patient," says Dr. Guglielmetti.

The results will be finalized and released at the end of the five-year trial, which began in Georgia in February 2017.

“WE NEED MORE EVIDENCE BACKING THE USE OF THESE DRUGS AND WE NEED TO PUSH FOR THEM TO BE ACCESSIBLE EVERYWHERE IN THE WORLD.”

— Dr. Lorenzo Guglielmetti, MSF’s co-principal and investigator of the endTB trial

**ABOVE:** Delamanid tablets at the National Center for Tuberculosis and Lung Disease in Tbilisi.

**BELOW:** The hospital team meets to discuss patient care at Abastumani TB Hospital in Georgia.

**FACING PAGE:** MSF nurse Maia Patsatsia checks a patient’s eyesight at Zugdidi TB Hospital in Georgia. Vision problems can be a side effect of some TB medications.
NEW DRUGS, NEW HOPE

TB–PRACTECAL: A CLINICAL TRIAL FOR SHORT, EFFECTIVE, AND LESS–TOXIC TB TREATMENT REGIMENS

“The unique thing about PRACTECAL is that we are looking for regimens that will cure all forms of DR–TB within six months,” says Dr. Bern–Thomas Nyang’wa, MSF TB specialist and chief investigator for TB–PRACTECAL.

Launched in Uzbekistan in 2016, the first stage of the trial will compare the current standard treatment with three new six-month regimens containing different combinations with a backbone of bedaquiline, pretomanid (another new drug), and linezolid (a repurposed drug) for a total of 630 patients across four study sites in Uzbekistan, Belarus, and South Africa. “Pre-clinical testing of regimens using these three drugs at particular doses cured TB in mice in three months,” says Dr. Nyang’wa. “Nix–TB [a clinical trial run by the nonprofit organization TB Alliance] is using a similar regimen and, so far, the results have been extraordinary.”

Data will be collected from 240 patients after the first eight weeks of treatment. Once this quota is reached, the two most–promising regimens will be carried through to the second stage of the trial. Stage two will test the regimens for longer–term safety and efficacy. TB–PRACTECAL expects to release results within four years. “There has not been much progress since the new drugs were approved more than five years ago,” says Dr. Nyang’wa. “It remains critical to find new treatments that are shorter, more effective, and more tolerable as quickly as possible.”

Because of the increasing threat of DR–TB and its capacity to develop resistance to new antibiotics, there is an urgent need to develop a robust pipeline of new treatment options.

FACING PAGE: MSF counselor Nino Kapanadze meets with Kale Manikava, who recovered from TB at Abastumani Hospital.
MSF addresses models of care in two ways: how patients access treatment and how caregivers reach patients. When drug-resistant TB (DR-TB) emerged as a crisis, the standard model of care for all forms of DR-TB was compulsory hospitalization, from diagnosis to the completion of treatment—a total of 20 months. But this practice soon became unsustainable. Patients disliked being away from their families and it was impossible to continue working; it was not only isolating but the economic burden was enormous.
MSF tried to adapt. In Kenya, for example, MSF provided a stipend to patients to make up for lost income so they could continue to support their families. However, as TB proliferated, this approach became unsustainable, and there were not enough beds in treatment facilities. TB care providers were forced to rethink how to deliver treatment.

AMBULATORY CARE

Over the last five years, there has been a shift towards ambulatory care, in which patients still travel to the clinic or hospital, but, rather than being admitted, are diagnosed and treated as outpatients. “We actually started realizing ambulatory care was more feasible,” says Geneva-based Dr. Isaac Chikwanha, MSF Access Campaign medical advisor on TB, HIV, and hepatitis, who has also worked as a TB physician in Kenya. “In terms of cost effectiveness it was cheaper, and in terms of family support, it was better for the patients.”

“The main hesitation around this model was the fear of the disease spreading in the community, as well as concerns about managing daily injections and how to store some oral medications, which needed to be kept at cold temperatures,” says Dr. Chikwanha. “The cold chain is particularly challenging in rural settings, such as Homa Bay [Kenya], where we piloted the ambulatory model of care.”

A heat stable version of this medicine is now in use and, over the years, studies dismantled the fears and showed the benefits of the ambulatory model: it has improved adherence and cure outcomes and increased community awareness of TB. In fact, ambulatory care is now the World Health Organization’s recommended standard of care for TB.
Decentralized care takes the ambulatory model one step further. Transport is one of the biggest obstacles to accessing treatment. It is expensive and, at times, impossible for patients to travel to medical facilities. “In Papua New Guinea, the closest clinic is often a few days’ walk or an expensive boat ride away,” says Dr. Chikwanha. “So, if it is raining or the seas are choppy, people can’t travel and will miss out on a day, or more, of their treatment.”

Decentralization pushes for treatment to occur at the closest possible level to the patient—either at the nearest health facility or at the community level—eliminating barriers to access. Diagnosis remains centralized, as it is often only the larger hospitals that have the necessary capacity and authorized clinicians. But once a patient is diagnosed, treatment does not have to be facility-based and can occur at home with the support of family and community members.

“TB treatment is long and grueling, the side effects are discouraging, and patients think twice every single day before taking their medicine,” says Dr. Chikwanha. Because of this, decentralized care requires constant patient support from a health worker, friend, or community or family member—selected with the patient—to participate in directly observed therapy (DOT).

Treatment supporters not only observe treatment, they provide psychosocial counseling, collect supplies of medicine, report severe side effects to health workers, and encourage the patient to attend monthly check-ups. “The idea is to keep the link to the health facility but limit travel as much as possible and keep the care as community-based as possible,” says Dr. Chikwanha.

MSF implements decentralized and ambulatory models of care in all TB projects and the benefits are clear: the number of patients diagnosed has increased, treatment initiation is faster, cure rates have improved, and care is cost-effective.

But more can be done. For example, there is a rapid molecular test for TB, GeneXpert, that has enormous potential, but the machine’s cost and complexity mean it is not yet widely used. “GeneXpert is the gold standard to beat in TB diagnosis, but it is still not readily available at point of care. And, even though treatment can be decentralized, patients still have to travel long distances to be diagnosed,” says Dr. Chikwanha. “There are simpler, battery-operated diagnostics that could be used at peripheral facilities, closer to the patient, and MSF is pushing for these to be more readily available.”

Decentralized and community-based models of care have been successful, in part, because similar systems were already in place for HIV treatment. HIV models such as community adherence groups—where members provide each other peer support and take turns to collect medication for one another—have been successful for TB patients in many parts of Southern Africa. “We’re not re-inventing the wheel with ambulatory care, systems are already in place. This is actually just implementation of last-mile health delivery systems,” says Dr. Chikwanha.

This link between TB and HIV is also important on another level. TB is the leading cause of death for people living with HIV; in 2015, 400,000 people with HIV died from TB. The epidemics fuel each other; each infection worsens the other. To break this deadly link, MSF advocates for all TB patients to be screened for HIV and vice-versa, and for treatment to be offered in the “one-stop shop” model of care. One-stop shop emphasizes the need to deliver TB and HIV services at the same time in the same location to prevent the inconvenience of having to attend multiple follow-ups, sometimes at different health facilities or on different days at different times.

“The idea is to treat the person, not the disease; it should be a holistic approach,” says Dr. Chikwanha. “The advantage lies in the close interaction between HIV drugs and TB drugs; it’s very important that the same clinician or the same counseling team supports the patient throughout both treatments.” This is the ideal level of integration, but implementation is difficult and, often, beyond MSF’s control.

TB is now on the global political agenda leading up to the United Nations High Level Meeting on TB in 2018. MSF is pushing for policy changes that will make one-stop shop a reality, completely decentralize diagnosis and treatment, and improve health outcomes for all TB patients.
Health providers are often left empty-handed when the medicines, vaccines, and diagnostics needed to care for people living with tuberculosis don’t exist or are too expensive. These gaps are a result of a broken medical research and development (R&D) system that does not prioritize the creation of essential new tools to prevent, diagnose, and treat TB.
TB is one of the top 10 causes of death worldwide and disproportionately affects poor people living in developing countries. Pharmaceutical corporations, however, have systematically failed to sufficiently invest in new medicines and diagnostics over the last several decades. Up until 2012, when the United States Food and Drug Administration (FDA) approved Johnson & Johnson’s bedaquiline, it had been fifty years since a new TB drug was approved.

And when new medicines, vaccines, and diagnostics are created, companies often price them out of reach for those who need them the most. In fact, fewer than 5 percent of people in need are treated with the two newest TB drugs, delamanid and bedaquiline, even though it’s been several years since they hit the market.

Governments have also failed to sufficiently invest in new treatments for TB and other neglected diseases. When governments do fund medical research, they often neglect to ensure that the people most affected by a particular disease or condition will broadly benefit from these public investments.

The United States government is the biggest global funder of R&D for TB through direct grants and resources, as well as other incentives, though it doesn’t always ensure these resources and incentives work the way they are supposed to. For example, in 2007 the US Congress passed legislation that created the FDA’s Priority Review Voucher (PRV) program for neglected diseases, which was designed to incentivize the creation of medicines and vaccines for some of the world’s most neglected diseases, including TB. Yet, ten years later, no new products that are affordable for, and appropriately accessible to, those affected by neglected diseases have emerged from the program.

Under the PRV program, a company that registers an eligible neglected disease product with the FDA is awarded a voucher that can be used to fast-track any other drug through the FDA review process. This is an
important financial incentive, as companies have sold these vouchers for as much as $350 million.

If this incentive worked properly, drug developers would be rewarded for their investments in neglected diseases and people would benefit from new treatments. Instead, companies reap financial rewards from the PRV program time and time again without creating new or affordable products. Some companies have received vouchers for treatments that have been in use for years, so they’re not creating new treatments to help patients.

Johnson & Johnson received a PRV for the TB drug bedaquiline in 2012, as well as other US government incentives and rewards. Despite this, the drug is still not registered in all countries where it is needed, and it is priced too high for many patients.

The good news is that these problems can be fixed. It is possible to promote medical R&D that leads to new, lifesaving medicines that are affordable and will reach the people who need these drugs to survive.

To address the flaws in medical R&D at a global level, the former United Nations Secretary-General Ban Ki-moon created a High-Level Panel on Access to Medicines that included representatives from governments, pharmaceutical corporations, academics, and civil society organizations. In September 2016, the panel released a report that puts forth specific recommendations, including the need to promote better ways to conduct medical innovation that keep patient needs at the center of the process.

One initiative that MSF supports is the 3P Project, which offers drug developers incentives to invest in TB research and ensures that these investments will deliver new critically needed TB treatments. The 3P Project uses an open and collaborative medical R&D framework that aims to support the discovery and development of a one-month treatment regimen to cure all forms of tuberculosis. Specifically, the 3P Project offers grants to finance R&D activities and financial prizes for companies that meet specific objectives, and ensures that intellectual property and data are available for open collaborative research and fair licensing to support competitive production and affordability of the final products. The 3P Project aims to reward innovation while ensuring products will be appropriately available and affordable to all patients and treatment providers. A key part of the approach is “de-linking” R&D expenditures from
FEWER THAN 5 PERCENT OF PEOPLE IN NEED ARE TREATED WITH THE TWO NEWEST TB DRUGS, DELAMANID AND BEDAQUILINE, EVEN THOUGH IT’S BEEN SEVERAL YEARS SINCE THEY HIT THE MARKET.

expected product revenues, removing the need for R&D costs to be recouped through high-priced products.

Additionally, this innovative R&D approach—which MSF hopes will be supported by governments, pharmaceutical companies, and other relevant R&D organizations—reduces duplication of research efforts, saving time and money. Drug developers participating in the 3P Project will be able to more easily move promising drugs into clinical trials, preventing drugs from getting stuck earlier in the drug development pipeline due to lack of funding or profit incentives. By testing drugs together at an early stage, the 3P project also helps identify how different drugs interact with each other sooner in the process, which in turn accelerates the development of new treatment regimens containing the multiple drugs needed to cure TB.

THE 3P PROJECT
An Open Collaborative Approach to TB Regimen Development

PUSH
Direct upfront funding to finance R&D activities (i.e. through grants)

PULL
Incentivize R&D through the promise of financial rewards if certain objectives are met (i.e. through prizes)

POOL
Share intellectual property (IP) to ensure open collaborative research and affordability of the final products
Severe nausea, joint pain, psychosis, and permanent deafness are only some of the awful side effects that people being treated for drug-resistant tuberculosis (DR-TB) commonly endure. But the new drugs that are less toxic and more effective are too expensive or simply not available in countries with some of the highest burdens of DR-TB.
More new drugs are needed to further improve treatment outcomes and stay ahead of developing drug resistance. By doing research and development (R&D) differently, we can put patients’ needs first and expedite the creation of new treatments that work better for those most affected by TB.

After years of negotiations led by a coalition of public health groups including MSF, Johns Hopkins University (JHU) agreed in January to openly license the patents they hold on a promising new drug for TB, sutezolid, instead of granting an exclusive license to a single private company.

JHU agreed to a non-exclusive patent license that allows multiple drug developers, including product development organizations, companies, and governments, to conduct research and develop combination treatments that include sutezolid.

Licensing of the drug will be handled by the Unitaid Medicines Patent Pool (MPP), a UN organization that supports price-lowering competition for the production of HIV/AIDS medicines, and more recently for hepatitis C and TB medicines as well.

The benefit of an open, non-exclusive patent license is that more innovators are legally allowed to work on developing a drug, which could help get a product to market more quickly than if just one company was working on it. Exclusive patents are intended to help creators protect their creations, but they often hinder public health because they limit who can work on researching, developing, and testing a particular drug.

This marks the first time an American university has chosen an open innovation approach to TB, and is the first open license that the MPP has signed for a TB drug.

“This agreement has the potential to greatly improve current treatment options, but it can only be truly effective if the treatments created are made affordable and accessible to all people living with TB everywhere,” said Judit Rius Sanjuan, US manager and legal policy advisor for MSF’s Access Campaign.

The pharmaceutical company Pfizer also holds rights on sutezolid, though they abandoned development of this drug years ago. While the JHU deal is an important step towards bringing this new TB treatment forward, open access to existing clinical data is the necessary and urgent next step to avoid further delays in the clinical development of sutezolid and to avoid the unnecessary replication of clinical trials. MSF has asked both Pfizer and Sequella, another company that holds rights on sutezolid data through an exclusive contract with Pfizer, to share their data.

“We are asking for open access to existing clinical data so developers don’t have to redo studies that have already been done to replicate data that already exists,” Rius Sanjuan said. “Pfizer and Sequella shouldn’t make people living with TB wait any longer for new, lifesaving treatments. At MSF, we see every day the grueling side effects of the old medicines currently used to treat drug-resistant TB—we have no more time to wait.”

Sutezolid marks the first drug that, if developed with an open data policy and made affordable and available for people who need it, could implement the 3P Project approach to R&D, as explained in “Pushing and Pulling for Innovation” on page 24.

The effort to get JHU to agree to this open innovation approach was led by the student group Universities Allied for Essential Medicines (UAEM), and was supported by MSF, Treatment Action Group (TAG), the Global TB Community Advisory Board (TB CAB), Public Citizen, and JHU students and alumni. More advocacy is essential to get Pfizer and Sequella to contribute to this pioneering initiative.

“We are asking for open access to existing clinical data so developers don’t have to redo studies that have already been done to replicate data that already exists...”

—Judit Rius Sanjuan, US manager and legal policy advisor for MSF’s Access Campaign

OPPOSITE PAGE: Nurse Elmira Khositashvili works at her desk at Abastumani TB Hospital in Georgia.
In Memoriam
DAVID ROCKEFELLER

MSF-USA REMEMBERS WITH ADMIRATION AND APPRECIATION ONE OF ITS EARLIEST AND MOST FAITHFUL DONORS AND ADVISORS, DAVID ROCKEFELLER, WHO DIED MARCH 20, 2017, AT THE AGE OF 101 YEARS.

Beginning in 1989, David Rockefeller helped the nascent MSF-USA establish itself in the United States. Mr. Rockefeller generously hosted our small start-up team in his Rockefeller & Co. office at 30 Rockefeller Plaza in New York City. Founding Executive Director Chantal Firino Martell had been introduced to Mr. Rockefeller by Sebastien de la Selle, then a long-time member of the MSF-France board of advisors. Ms. Martell and executive administrator Leah Arnold worked out of the Rockefeller & Co. office until a separate space was eventually rented by MSF-USA.

Mr. Rockefeller not only donated office space, he also made the all-important introduction of Ms. Martell to his son, Dr. Richard Rockefeller. Thanks to that introduction, Ms. Martell and I, along with other MSF-USA founders, convinced Dr. Rockefeller to join MSF-USA’s initial board of advisors. Dr. Rockefeller not only joined the advisory board, he enthusiastically served as its chair for 21 years.

During that time, Dr. Rockefeller leveraged his and his father’s credibility within the US philanthropic community to make introductions and win support for MSF-USA throughout the country. Dr. Rockefeller regularly visited MSF programs abroad, including in Cambodia, Malawi, Niger, and Thailand. He also worked as a field doctor in Peru, and in northern Nigeria during a massive meningitis outbreak there in 2009. Dr. Rockefeller reported that he frequently discussed his MSF experiences with his father, who we know remained interested in MSF throughout his lifetime. Tragically, Dr. Rockefeller died in June, 2014 in an airplane accident.

MSF-USA is deeply grateful to David, Richard, and the entire Rockefeller family for their early and sustained faith in our mission. We will always honor David for his seminal role in launching MSF in the United States, and Richard, for his passionate dedication.

—Victoria B. Bjorklund
Member, Initial Board of Directors
Chair, Board of Advisors

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MSF-USA would like to thank all of our donors who have made commitments towards the Multiyear Initiative. With annual commitments of $5,000 or more over several years, these generous supporters help provide MSF with a predictable revenue stream, which strengthens our ability to respond rapidly to emergencies and to maintain operations of our programs. To date, we have received commitments totaling more than $57 million towards the initiative. To find out how you can participate, please contact Mary Sexton, director of major gifts, at (212) 655-3781 or mary.sexton@newyork.msf.org. Visit doctorswithoutborders.org/multiyear.
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MSF on the Road: Maine
“MSF on the Road: A Voice from the Field,” continues this summer in Maine with a series of speaking events with Dr. Gerry Bashein. For more information please call (212) 655-3759 or email OnTheRoad@msf.org.

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Summer Games Done Quick (SGDQ), MSF’s top fundraising event of the year, is a video game speed-running marathon. Last year, SGDQ raised $1.3 million for the work of MSF. The 2017 marathon will take place July 2–10 in Minneapolis, and you can watch live. For more information on SGDQ, visit gamesdonequick.com.

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LEFT: (From left to right) MSF team members Marina Kikvidze, Medea Oniani, and Nino Kapanadze stand outside Abastumani TB Hospital in Georgia.

FRONT COVER: MSF doctor Gocha Salia and a nurse from the Georgian Ministry of Health examine X-rays from a TB patient at Senaki Hospital.