INNOVATION AND UNIVERSAL HEALTH COVERAGE

Universal health coverage presents an enormous, complex challenge that calls for the expertise of many partners, all working together. In the series of articles that follows, some of the world's prominent global health innovators explain how their collaborations are creating the kinds of tools and approaches that will be indispensable to meeting the challenge of health coverage for all.

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AURUM INSTITUTE/ IMPAACT4TB

Although we've known how to treat and prevent Tuberculosis (TB) for over 70 years, it remains the world's deadliest infectious disease, killing more than 4,000 people every day. People being successfully treated for HIV are now dying from TB in high numbers, as TB remains the leading cause of death for people living with HIV. TB is a disease of poverty and inequitable access to care. Most of these deaths occur in low- and middle-income countries, where access to TB prevention and treatment remains limited, and is often constrained by people's ability to pay.

A lesser known fact is that almost a quarter of the globe is infected with TB, which can lie dormant for decades before it strikes. People with TB infection have no symptoms, are not contagious and most often don't even know they're infected. But they're at risk of developing active TB at some point in their life. That risk is particularly acute among people living with HIV and children under the age of five.

This time last year, the United Nations High-Level Meeting on TB produced a historic declaration where national leaders committed to a new set of targets in the fight against TB, including putting 30 million people on TB preventive treatment by 2022.

Later this month, world leaders will meet in New York again, this time to discuss Universal Health Coverage and the importance of ensuring health for all—a goal that goes hand-in-hand with efforts to provide TB preventative therapy to everyone in need, regardless of their ability to pay.

The fact is that without addressing the seedbed of the TB epidemic—latent TB—we will never achieve our elimination goals. And focusing on prevention is a game-changer in other ways. When we emphasize the right to prevention, TB elimination becomes rooted in the needs of individuals and families and becomes a core part of achieving Universal Health Coverage. Preventing people from becoming ill also prevents them—and their health systems—from having to suffer the consequences of catastrophic health expenditures in the future.

To contribute to the target of putting 30 million people on TB preventive treatment by 2022, Unitaid is investing US$59 million in the Aurum Institute's IMPAACT4TB project. The four-year grant prioritizes short-course TB preventive therapy for people living with HIV and children under five, and subsequently all those in close contact with TB patients, in 12 high-burden countries—who represent 50 percent of the global TB burden.

The target groups will receive an affordable short-course TB preventive therapy known as 3HP, consisting of high-doses of two antibiotics (isoniazid and rifapentine) given weekly for three months. The 3HP regimen offers a shorter,

safer alternative to the older standard of care— isoniazid preventive therapy (IPT)—in which people take isoniazid every day for between six and 36 months.

The Aurum Institute and its partners are preparing to start 400,000-600,000 people on 3HP across 12 countries in order to catalyze an increase in supply, demand for and uptake of 3HP. The next few years will focus on reducing the price of 3HP and addressing barriers to supply at the global level.

South Africa's Aurum Institute is spearheading the TB prevention project and is working with the Clinton HIV/AIDS Access Initiative, KNCV Tuberculosis Foundation, John Hopkins University, the Global Drug Facility-Stop TB Partnership, and the Treatment Action Group.

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THE ROLE OF COMMUNITIES IN IMPROVING ACCESS TO NEWER AND BETTER HIV MEDICINES

Sitting and talking with other people living with HIV at a health facility in Uganda, Zane* no longer felt alone. Unlike many of the others there who remained on efavirenz (EFV), he had recently switched to a new treatment regimen that includes dolutegravir (DTG) and could not believe how much better he felt. On DTG, he had more energy to hang out with his friends, participate in sports and he was able to focus in school in ways that he couldn't when he was taking EFV. For several years, the Clinton Health Access Initiative (CHAI) and other partners have worked to bring the highly optimal DTG, a best-in-class medicine, to market at a more affordable price to improve the quality of life for millions of people living with HIV, just like Zane.

The meeting Zane attended in Uganda was organized by a group called the Optimal ARV Community Advisory Board (CAB). With encouragement from a strong network of civil society leaders and support from donors, such as Unitaid, CHAI, in partnership with AfroCAB and HIV i-Base, created the board in 2016 as a core part of its HIV treatment optimization work. It has since become an integral part of CHAI's work in supporting introduction of, and building demand for, HIV treatment products.

By definition, a CAB usually consists of individuals from the general public who meet with representatives of an institution to relay information from the community. Using AfroCAB's network of civil society organizations across Africa and Asia, 17 community members across 11 countries – Benin, Togo, Senegal, Cameroon, Cambodia, Malawi, Kenya, Nigeria, Uganda, South Africa and Zimbabwe – were selected to serve on the Unitaid-CHAI Optimal ARV CAB to support demand generation for new and better HIV treatment regimens and strengthen the community's role in how these regimens are planned and rolled out.

At the annual CAB meeting in May 2018, several CAB members shared experiences about visiting facilities in their countries and hearing both the challenges that many patients are facing on EFV, and the success stories of patients, like Zane, who were able to switch to DTG in part as a result of the CAB's work. In sharing these experiences and identifying solutions to address specific challenges through consultations, treatment literacy trainings, workshops, and materials, CAB members have been able to build demand among people living with HIV so that everyone can experience the benefits of DTG and access the information they need to make decisions about their health.

For example, in Zimbabwe, CAB members held five regional awareness meetings with networks of people living with HIV to ensure they are well-

informed about HIV treatment options and can advocate for access to more effective regimens, such as those including DTG. In one of these meetings, a young person living with HIV requested to have a separate meeting for youth to safely voice their experiences, which resulted in another gathering with 65 young people in attendance from across the country. Many young people were able to find support from other youth. For example, one attendee was able to find others in similar situations after sharing an experience with EFV: "I took EFV at night and I would hallucinate. I could see the bed spinning and other things that did not exist."

CAB members in many countries are also directly engaging with the community to develop information, education, and communication materials to improve civil society's understanding of new HIV treatment options and generate demand for new optimal products. For example, Nigeria CAB members convened a meeting with their community to create treatment literacy videos that will be distributed and played in health facilities in early 2019. In Malawi, patient materials that were developed by the CAB members in partnership with other key stakeholders were adopted by the Ministry of Health as the official national treatment literacy materials, and CAB members in Benin and Togo produced radio programs to inform the public on the availability and use of new antiretroviral drugs.

To move toward the goal of Universal Health Coverage (UHC), countries will need to make decisions on which medications or services will be covered. These decisions must be informed by the best available evidence and by civil society. Community voices will play a critical role in ensuring that their needs are met. The CAB can serve as a model on how to incorporate these views.

Optimal ARV CAB members already began implementing more treatment optimization workshops and consultation meetings in 2019 to further strengthen partnerships and build demand for access to optimal HIV treatment. As they continue to work with partners to provide unique perspectives on barriers and opportunities within the HIV space, they also recognize the need to develop even more innovative solutions to address some of the most complex challenges in order to bring the world one step closer to ending HIV and helping people living with HIV, like Zane, achieve the best quality of life possible.

*Name changed to protect identity

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HOW EARLY INFANT DIAGNOSIS POINT-OF-CARE TESTING FOR HIV CAN SAVE LIVES

After five hours hunched in a crowded minibus, three hours trying to soothe a crying baby, and one hour waiting to see a healthcare worker, a Malawian mother finally made it to a health facility to have her baby tested for HIV. Despite the hours of travel, she soon learned that she may have to wait up to three months for a test result because the facility had to send the test sample to one of the country's few centralized labs to be processed. With additional children and responsibilities at home, she worried if she would be able to make it back to find out if her baby had HIV.

Of all HIV-exposed infants worldwide, only 50 percent receive a timely early infant diagnosis (EID) test. Of those, only half receive their results due to long turnaround times and high rates of loss-to-follow-up. Unfortunately, without treatment, nearly half of HIV-infected children die by the age of two, with 20 percent dying in the first two to three months of life.

Recognizing that timely diagnosis and initiation to treatment are critical to reducing the number of infants dying from HIV, Unitaid is funding the Clinton Health Access Initiative (CHAI), UNICEF, and the African Society for Laboratory Medicine (ASLM) to accelerate access to point-of-care (POC) testing for EID of HIV across 10 countries in sub-Saharan Africa.

POC technologies are smaller, simpler, robust devices that can be used by non-laboratory staff at clinics within communities. Test results are ready onsite, the same day. If strategically placed, POC EID could significantly increase the number of HIV-positive infants who are identified and initiated on treatment and broaden the community's access to care.

Access to affordable, quality health-care services is critical to in the fight against HIV/AIDS and to accelerate progress toward the goal of Universal Health Coverage (UHC). POC technology offers an innovative solution to ensure HIV positive newborns in the poorest countries, especially in sub-Saharan Africa where the HIV burden is highest, have access to rapid diagnosis so they can start life-saving treatment when they need it most.

With Unitaid support, CHAI collaborated with its partners, including UNICEF and the ministries of health (MOHs) in Malawi and Mozambique, to launch pilots to demonstrate how POC EID successfully reduces result turnaround time and increases the number of HIV-positive infants identified and initiated on antiretroviral therapy (ART).

The pilots found that strategic placement and implementation of POC EID devices can increase the number of HIV-positive infants on ART. The pilot in

Malawi showed that 91.1 percent of infants diagnosed with HIV using POC EID were initiated on treatment, compared to the 45.8 percent of those who were diagnosed using the conventional, referral-based system. Additionally, with POC EID, 99 percent of results were returned to infants and caregivers within the same day, compared to 0 percent using conventional EID.

In Mozambique, a CHAI study with the National Institute of Health showed that 89.7 percent of infants diagnosed using POC EID were initiated on treatment within 60 days, compared to the 12.75 percent through conventional EID. Furthermore, 99.2 percent of POC EID results were returned within 60 days, compared to just 7.2 percent in conventional testing. Both studies showed that the cost to administer POC EID may also be lower than conventional tests.

With support from Unitaid, CHAI and partners continue working toward a future free of pediatric AIDS by helping Ministries of Health introduce and scale up POC EID testing programs. With the potential to reduce result turnaround times, increase the percentage of results returned to patients and improve linkage to treatment, POC EID provides an opportunity to close the HIV testing and treatment gaps for infants. This way, more mothers, like the one in Malawi, will be confident that their healthcare systems can deliver results and the medical care that their babies need.

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COALITION PLUS / HIV/ HCV DRUG AFFORDABILITY PROJECT

In 2015, Coalition PLUS started a project with Unitaid to make HIV/HCV drugs affordable in 7 countries (Brazil, Colombia, India, Indonesia, Morocco, Malaysia, Thailand) and contribute to universal access to HCV care in low and middle-income countries.

Embedded in our community-based approach, developed over the years in the fight against HIV and then HCV, our goal is to provide the means for increasing communities' empowerment and informing technical experts of communities' needs. This allows to generate demand for and uptake of HCV services, and strengthen community-based services for outreach and care. It is crucial to understand that there is a complementarity and not a competition between community-based health system and national health system, in the fight against these pandemics to reach the 2030 goals.

Created in 2008, Coalition PLUS is a network of over 100 partners in 40 countries, amongst which, 15 members sit at board level for a genuine shared governance. We raise awareness about HCV care services, harm reduction, education and treatment. We also advocate with and for people who are infected, or particularly vulnerable to HIV or HCV to be involved in the design, implementation and evaluation of HIV and HCV national programs, by providing evidence on community needs through activities including outreach, education and counselling.

At the time of implementing UHC, coordination and alignment between all stakeholders (government, technical international partners, CSOs) are key. It is our collective duty to coordinate better with national government, international institutions AND in-country skilled community representatives that through their experiential knowledge can contribute to review of models of care and make impactful health policies that integrate the needs of affected people (i.e the "community").

We foster policy dialogue with government officials to increase commitment of national public authorities to well-funded and efficient o f s pecific n eeds in care, and advocate to remove remaining barriers to access to care for vulnerable, criminalized and stigmatized populations. Increasing knowledge-building and coordination, to inform the global discussion is needed to create synergies and share good practices.

In terms of the needed innovation and impact to make UHC real, providing a global approach of health to those people who do not go to the public health system, is a momentum action to be taken seriously. Key populations need to be approached where they are, to be brought to health care and be provided with customized care (In Morocco the ALCS, one of our founder NGO,

is identified to implement HCV screening because of their experience with PWID but also train healthcare workers to reducing stigma in areas where the concentration of PWIDs is high). This is what many local NGOs already do in their country, and this has to be scaled-up for longterm impact. This is not a choice but a moral responsibility if we want real impact on the epidemics and not only short-term data-driven results.

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DNDi
Drugs for Neglected Diseases *initiative*

THE TREATMENT REVOLUTION CHILDREN WITH HIV HAVE BEEN WAITING FOR

A long-awaited revolution in HIV treatment for children is coming, and it has already started at the Regional Referral Hospital in Mbarara, Uganda. This August, researchers in this western Ugandan city kicked off the last studies for what could become one of the first truly "child-friendly" treatments specifically designed for infants and young children with HIV.

Until recently, the main treatment recommended by the World Health Organization was only available as a foul-tasting syrup that requires refrigeration and contains 40% alcohol. Children struggled to take the medicine, often vomiting it back up; caretakers in rural areas buried the treatments in the ground to keep them cool.

Despite successful efforts to reduce mother-to-child transmission of HIV, kids are still slipping through the cracks with 160,000 new infections among newborns in 2018. Innovation for these children has lagged behind that of adults because most children born with HIV are in countries that don't constitute a "lucrative market." Today there are 1.7 million children living with HIV, and about 300 die every day – one main reason has been poor treatment options.

New treatments and improved diagnostics for young children are now being introduced, many of them supported by the global health initiative Unitaid. Since it was created in 2006, Unitaid has supported access to treatment for hundreds of thousands of kids with HIV. In 2012, Unitaid partnered with the nonprofit research and development organization, Drugs for Neglected Diseases initiative (DNDi), to help close the treatment innovation gap for children with HIV.

To replace the syrups, DNDi, supported by Unitaid, worked with partners to launch one of the largest implementation studies ever for children with HIV in Africa. Called LIVING, this study provided key evidence that an easy-to-take treatment for kids containing a specific class of antiretrovirals (ARVs) in the form of "pellets" can lead to excellent treatment outcomes for kids. The study helped countries like Uganda phase out syrups and other countries are following suit.

Although the pellets are an improvement over the syrups, they are still not ideal. So DNDi and the Indian generic company Cipla have been developing a "4-in-1" treatment that contains all four ARVs children with HIV need and does not require refrigeration. Researchers in Mbarara recently began testing the 4- in-1, with caregivers easily sprinkling the sweet-tasting granules over food or milk. If all goes well, the 4- in-1 should be available in 2020 – and

will be the first of several long-awaited and improved therapeutic options for children with HIV to become available.

Although there has been an unacceptable delay of decades, the HIV treatment revolution is finally on the horizon for children. Our duty now is to ensure the rapid introduction and scale up of new tools and technologies for children with HIV and other diseases as part of the global push toward universal health coverage – and make certain the days of children being left behind and neglected by advances in science, medicine, and public health are over.

FOUNDATION FOR INNOVATIVE NEW DIAGNOSTICS (FIND) / HEAD-START

Hepatitis C is one of the world's most common infectious diseases, affecting 71 million people and killing hundreds of thousands every year. Yet **4 out of 5 people infected with the hepatitis C virus don't know it.** Breakthroughs in hepatitis C treatment mean that the disease is curable, and following dramatic drug price reductions, accurate, timely diagnosis is today the major roadblock in the path to care.

The disease is usually contracted through unsafe healthcare or injection drug use; HIV co-infection is not uncommon and can speed up hepatitis C disease progression. The vast majority of those infected live in low- and middle-income countries with weak health systems. Where services do exist, hepatitis C screening and diagnosis remain largely centralized and siloed because current diagnostics are just too complex and expensive for countries with limited budgets and poor infrastructure.

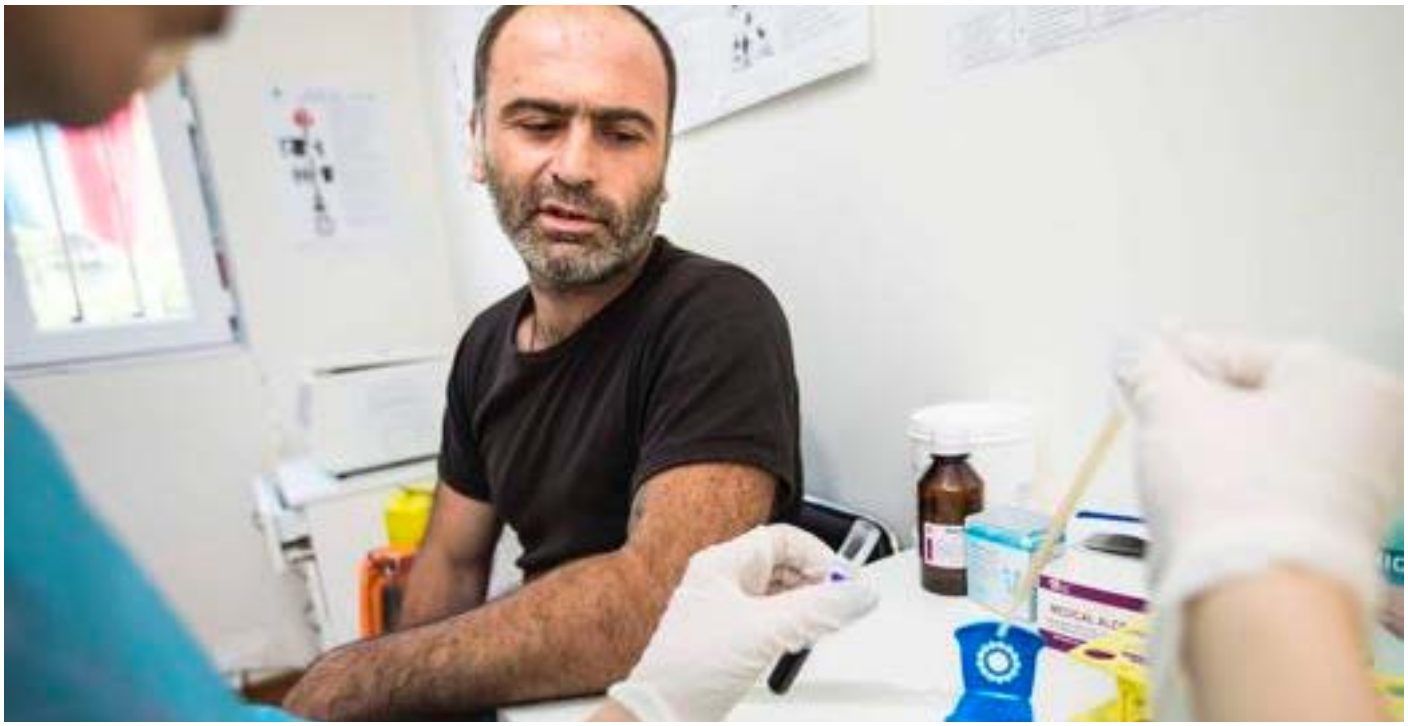
Universal health coverage (UHC) depends on even the most marginalized and remote populations being able to access the care they need. The Unitaid-funded HEAD-Start project (Hepatitis C Elimination through Access to Diagnostics) is rethinking the whole diagnostic pathway, aiming to simplify the diagnostic tools needed for hepatitis C and ensure they are accessible where they will have impact, through increased efficiencies and reduced costs.

A prime example is ongoing in Cameroon and Rwanda, where **HEAD-Start is assessing novel technologies that can identify the hepatitis C virus in a dried blood spot from a finger prick**, removing the need to draw and transport a vial of venous blood. Special paper with dried blood spot samples collected in the most rural of settings can be sent easily and cheaply to laboratories for testing using these innovative new tools. Activating learnings from the HIV community, **HEAD-Start is also exploring the feasibility of self-testing for hepatitis C, in South Africa and Kenya.**

Alongside the development of urgently needed new tools, HEAD-Start is building the evidence base that will drive a change in global implementation guidelines and national policies in several highburden countries. Demonstration studies are showing the impact of decentralizing diagnostic services by making them available for the first time ever in existing antiretroviral treatment centres and harm reduction sites (HRS) – allowing people like Zurab* (pictured) to be tested locally at the Imedi HRS in Batumi, Georgia, when like many HEAD-Start study participants, he would not have considered traveling to a centralized clinic far from home for the test. **In Georgia, HEAD-Start data have already spurred the government to make a policy change and decentralize hepatitis C care.**

HEAD-Start activities are being conducted in collaboration with multiple partners, from WHO to ministries of heath and diagnostic developers. In Malaysia, FIND is also working with another product development partnership (PDP): people found to be infected with the hepatitis C virus through decentralized screening initiatives are linked to care either as part of a Drugs for Neglected Diseases *Initiative* clinical trial, or in government hospitals.

Hepatitis C is just one example of the critical diagnostic gaps that threaten the achievement of UHC. When diagnostics are not acknowledged as an essential component of the healthcare system, they get little attention, budget, and support for development and implementation. If tests are not explicitly listed in national health plans or benefits packages, there is no mechanism for procurement, supply, and reimbursement. But, as the Unitaid investment in HEAD-Start recognizes, you can't treat what you don't know, and every patient, regardless of their financial status, deserves to know their diagnosis.



Zurab*, a beneficiary of the Imedi harm reduction site in Batumi, Georgia, watches his blood sample being processed for hepatitis C diagnosis.
Photo © 2019 FIND / John Rae (download photo: *https://photos.app.goo.gl/g1o32w4Y8297X86g8)*

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*Zurab's name has been changed.

ISGlobal
Barcelona
Institute for
Global Health

The new challenge to malaria control

The world is not on track to achieve the goals proposed by WHO in the Global Technical Strategy for Malaria 2016-2030 (GTS), and the currently available tools are unlikely to suffice. Vector control, our most effective strategy, is now challenged by insecticide resistance and mosquitoes that avoid insecticides in bednets and indoor sprays by biting outdoors, feeding upon animals or changing their biting times resulting in “residual transmission” even after good bednet and spraying coverage. There are few tools available and recommended to address these challenges.

Innovation into practice: repurposing an old tool

The BOHEMIA project (Broad One Health Endectocide-based Malaria Intervention in Africa) is developing an innovative strategy to complement the existing tools: administer ivermectin to humans and livestock to reduce malaria transmission.

Ivermectin is an established anti-parasitic drug that can also kill mosquitoes feeding on treated people or animals. BOHEMIA is testing the mass drug administration of ivermectin to humans and/or livestock to prove this novel strategy can tackle residual malaria transmission. It targets mosquitoes that feed on treated humans regardless of the place and time of biting, as well as mosquitoes that feed partly on livestock and are not routinely exposed to insecticide within the home.

The four-year project funded by Unitaid will conduct two clinical trials in different ecological and epidemiological settings in east and southern Africa, specifically Tanzania and Mozambique. Ivermectin will be distributed in mass drug administration campaigns to people and livestock, for two consecutive years, to try to reduce the mosquito populations that transmit malaria.

This innovative One Health approach offers an opportunity for preventing neglected tropical diseases in humans (intestinal helminths, scabies and filariae among others), which will also have a positive impact on households. Application to livestock reduces the burden of intestinal helminths and ecto-parasites in domesticated herds, thereby increasing income and food security.

BOHEMIA’s goals

The main goal of BOHEMIA is to contribute to the global public health goals for malaria control by developing a complementary strategy for vector control.

Since ivermectin is already used in mass campaigns for direct treatment of two neglected tropical diseases, once the intervention is proven to be safe and effective, BOHEMIA will work to align the campaigns in collaboration with the other disease communities and drug producers.

The first scientific evidence is expected late 2021, with full results in 2023.

The Consortium

BOHEMIA is a consortium led by the Barcelona Institute for Global Health (ISGlobal) and funded by Unitaid. It includes two African institutions: the Centro de Investigação em Saúde de Manhiça (CISM) in Mozambique, and the Ifakara Health Institute (IFI) in Tanzania, and three academic partners: the University of Basel, the University of Oxford, and Virginia Tech.

innovating to save lives
Jhpiego
an affiliate of Johns Hopkins University

COMMUNITY HEALTH WORKERS DELIVER KNOCK-OUT BLOW TO MALARIA-IN-PREGNANCY

In sub-Saharan Africa, more than 25 million pregnant women are at risk of malaria—10,000 women and approximately 200,000 newborn babies die each year because of malaria-in-pregnancy. Although malaria is preventable and treatable, many women don't know that and can't get safe, effective medicine or miss opportunities at antenatal care to stay healthy.

To achieve universal health coverage, women's primary health care needs, including addressing malaria in pregnancy must be at the forefront of comprehensive country policies and strategies that reach all women at risk for malaria — no matter where they live.

Since 2017, Jhpiego, with financial support from Unitaid and in coordination with partners, is leading Transforming Intermittent Preventive Treatment for Optimal Pregnancy (TIPTOP) —an innovative, ambitious pilot project that uses community health workers to reach tens of thousands of pregnant women in their own communities, provide quality-assured preventive antimalarial treatment and link them to nurse-driven antenatal care in health facilities for follow-up. This "no missed opportunities" approach is at the forefront of TIPTOP's pioneering solutions to advance the prevention of malaria in pregnancy and save lives.

In the Democratic Republic of the Congo (DRC), Dorcas was infected with malaria during her pregnancy and delivered twins—one healthy, and one in need of lifesaving treatment to survive, because of the disease. In her most recent pregnancy, she connected with her TIPTOP-trained community health worker, Seba Mambo.

"I got involved in TIPTOP to help the community, because malaria is silently killing people," Seba says. "We work with pregnant women by administering antimalarial medication to keep them healthy, so that when they deliver their children, they are healthy. We don't want any more deaths."

Seba took malaria care right to Dorcas's door, and the young mom is staying healthy because of it. "With previous pregnancies, I started antenatal care after 6 or even 7 months, but with this pregnancy, I started in my third month," Dorcas says. "Now, I have already taken my malaria medicine twice."

TIPTOP isn't just reaching Dorcas, or her community, or even her country. In collaboration with Ministries of Health in the DRC, Nigeria, Madagascar and Mozambique, TIPTOP's combination of making the right medicine and the right care available at the right time to pregnant women in their communities sets the stage for replication and scale up to help accelerate country plans to deliver equitable access to achieve Universal Health Coverage for all. Working in collaboration with ISglobal, MMV and the World Health Organization,

TIPTOP is on track to reach more than a hundred thousand pregnant women in high-burden countries with the care they need to have healthy, malaria-free pregnancies and thriving newborns.

And the project is contributing vital evidence to potentially update global recommendations on preventing malaria in pregnancy, if the evidence permits.

“By preventing malaria in pregnant women, we are protecting them from death, or from their child contracting malaria,” Seba says.

TIPTOP is just one of Unitaid’s investments in innovative, lifesaving care dedicated to solving the worlds’ most chronic health challenges, from malaria to HIV to cervical cancer.

See more here: *https://spark.adobe.com/page/GadRPEQ3XQpxc/*
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FIRST NEW DRUG FOR RELAPSING MALARIA IN MORE THAN 60 YEARS

First new drug for relapsing malaria in more than 60 years

Over 2.5 billion people around the world are at risk of *P. vivax* malaria – the second most common malaria species, leading to around 7.5 million clinical infections each year.1 More than half of these infections occur in the Americas while about one-third are in South East Asia.*(1)*

P. vivax malaria is particularly debilitating because of its recurrent infections, also known as relapses, which pose a substantial economic burden on families and nations.*(2)* Recent research estimates that the global economic burden of *P. vivax* malaria is USD 330 million per year.*(3)*

P. vivax can be present, and infectious to mosquito vectors, even when the infected person shows no symptoms. It can also be difficult to detect since it usually circulates at low levels in the blood. These factors pose significant challenges for countries such as Mexico, Ecuador, Nepal and the Republic of Korea that are pressing towards malaria elimination where *P. vivax* can be responsible for more than of 70% of malaria cases.*(4)*

In spite of this, the development of new drugs able to stop the relapse has been neglected. Since 1952, primaquine has been the only medicine able to prevent vivax malaria from relapsing. However, patients often do not comply with the WHO-recommended 14-day treatment regimen, leading to reduced efficacy.*(7)* A more compact-dosing regimen to improve compliance was therefore urgently needed.

In 2018, the US Food and Drug Administration and the Australian Therapeutic Goods Administration approved the single dose cure, tafenoquine, developed by GSK and Medicines for Malaria Venture (MMV) for the radical cure of *P. vivax* malaria.*(5,6)* As a single-dose cure, tafenoquine, addresses the compliance challenges of primaquine and will support endemic countries as they move towards malaria elimination.*(7)*

Case study: Pring's story

Pring Chon is a soya bean and cassava farmer from Oslev Village, Cambodia, where he lives with his wife and children. He has suffered with malaria more than 12 times in his life; on one occasion it led to severe malaria and he had to be hospitalized. Pring has been infected with *P. vivax* malaria that lies dormant in the liver only to relapse periodically, without warning and in the absence of a new infective mosquito bite. "I feel bad with this illness," Pring explained. "When I'm infected, I can't work and my wife can't work."

In Cambodia, artemisinin-based combination therapies (ACTs) are used to treat blood-stage malaria infections, leading to relief of symptoms; but there are no medicines routinely used to cure malaria relapses. The approval of new anti-relapse medicines like tafenoquine could help relieve the suffering experienced by patients like Pring.

Injectable artesunate for severe malaria

Injectable artesunate is a major innovation for treating severe malaria in adults and children, recommended by the World Health Organization (WHO).*(8)*

Malaria is an infectious disease that is preventable and treatable. Severe malaria is the harshest form; if left untreated, the case fatality rate can be very high. The disease claimed the lives of more than 435,000 people in 2017,*(9)* the majority were children under 5 years old, living in Africa. A child dies from malaria every 2 minutes.*(10)*

The landmark AQUAMAT(*11)* and SEAQUAMAT clinical trials revealed that treatment of severe malaria with injectable artesunate results in a 23% and 35% reduction in deaths in African and Asian patients, respectively, in comparison to the alternative intravenous quinine treatment.*(12)*

MMV collaborated with Guilin Pharma, a Fosun Pharma company, to help achieve WHO prequalification for its injectable artesunate formulation, Artesun®, in November 2010. This approval represented a critical turning point, making it possible for the first time for donor funds to support the procurement of injectable artesunate as WHO's preferred treatment for severe malaria. In December 2018, a second injectable artesunate product, Larinate® 60, manufactured by Ipca received WHO prequalification with support from MMV, helping to ensure a healthier marketplace for this lifesaving drug.

Between 2010 and 2018, an estimated 128 million vials of injectable artesunate have been delivered to malaria-endemic countries resulting in an estimated 840,000 additional young lives have been saved compared to if they had received treatment with quinine.*(13)*

A 2017 paper in PLoS ONE ranked injectable artesunate as one of the 29 most cost-effective health interventions to improve the quality of children's lives. *(14)*

Case study: Desmond's story

Four-year-old Desmond Oming from Awir in northern Uganda had "serious fever with a lot of diarrhoea and vomiting", explained his mum, Jennifer Alwin, when she brought him to Apac District Hospital.

After a lengthy wait in the crowded outpatient department, Desmond was seen by Dr Josephine Apio who suspected malaria and sent him for testing. The results came back positive. It was the fourth time he had suffered from malaria in his young life and this time it was severe malaria.

Fortunately, Apac's hospital is one of the 339 health-care facilities in Uganda that now receive injectable artesunate (Inj AS) for the treatment of severe malaria, through the MMV-led Improving Severe Malaria Outcomes project funded by Unitaid.

Rectal artesunate: buying time to save lives

Pre-referral treatment with Rectal Artesunate (RAS) has been shown to halve disability and death in children less than 6 years old with severe malaria and living more than 6 hours from a referral centre. In 2005, the WHO recommended the use of RAS for the pre-referral management of severe malaria in such children, and in 2017, RAS (100 mg) was added to the WHO Essential Medicines List and Essential Medicines List for Children.[1]

Despite these guidelines, no WHO prequalified (WHO-PQ), quality-assured RAS product was, until recently, available – denying millions of children access to its life-saving benefits.

Supported by Unitaid grants, MMV has worked with Cipla Ltd and Strides Pharma Science Ltd, over the past 5 years, to bring to market quality assured RAS (100 mg) products.[2] In February 2018, Cipla's product received WHO-PQ and is now approved for use in seven countries in Africa. In June 2018, the Strides product was also prequalified by WHO and is now approved in eleven countries. RAS has been enthusiastically welcomed by countries such as Zambia who are scaling it up at the community level, with the aim of making it available nationwide.

WHO-PQ of the Cipla and Strides products has accelerated procurement of RAS in endemic countries, with the latest data showing an upward trend in its use. In 2018, an estimated 1.7 million RAS suppositories were ordered by endemic countries – a substantial increase compared with 2017, and of those orders, 1.5 million were for WHO-prequalified quality-assured RAS 100 mg.[3]As such, over 85% of RAS procured in 2018 by the three largest international buyers – The Global Fund, President's Malaria Initiative and UNICEF – was quality-assured.

With funding from Unitaid, MMV is working to support the introduction and scale-up of RAS. This work is further supported by the community access to rectal artesunate for malaria (CARAMAL) project, led by the Clinton Health

1 The WHO followed this up with an 'information note' in October 2017, describing when, and how, to administer the treatment

2 Building on work initiated by the WHO's Special Programme for Research and Training in Tropical Diseases (TDR), not funded by Unitaid.

3 Instead of alternative, non-WHO approved 50 mg and 200 mg formulations.

Access Initiative. The project is focused on three high-burden countries – Democratic Republic of the Congo, Nigeria and Uganda – and is piloting community case-management schemes and multi-country observational research to identify the operational and health system-related factors affecting the introduction of RAS.

Mervis' story: Surviving severe malaria

One night in May 2018, 3-year-old Mervis from Kebumba, Serenje District, Zambia had a high fever. By the next morning, she had begun convulsing. Priscilla Chibuye, Mervis' mother, rushed her to the nearest community health volunteer, Idess, who had been trained through the MAM project. Idess quickly suspected severe malaria and administered two artesunate suppositories. These helped to stabilize Mervis until she could get to a health facility.

Justina, an ETS bicycle rider, was called. The journey to Mulilima Rural Health Centre took an hour and a half. It was confirmed that Mervis was suffering from severe malaria. She was promptly given injectable artesunate. Mervis was already feeling better after her second dose that evening. She received her third and final dose of Injectable artesunate in the morning and was soon discharged. Her mother, Priscilla was given oral medication to complete Mervis' malaria treatment at home.

Priscilla remarked that before the MAM project came to her community, many children used to die from severe malaria. She was grateful the situation had changed.

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THE MEDICINES PATENT POOL

AN INNOVATIVE MODEL ENABLING THE WORLD'S MOST VULNERABLE TO ACCESS GAME-CHANGING MEDICINES

Nearly 2 billion people around the world – most of them in low- and middle-income countries – lack access to essential medicines and basic health technologies. Each year, 100 million people are driven into poverty because healthcare costs are too high. This lack of affordable access is a fundamental barrier to achieving universal health coverage and reducing inequality.

In 2010, Unitaid set up the Medicines Patent Pool (MPP) as a first-of-its kind innovative solution for rapidly getting effective and affordable medical treatments into the hands of those who most need them. Although patent pooling had been applied in other fields, it had never been tried in health. No one was sure it would work.

The concept

Disease experts, including the World Health Organization (WHO), civil society and patient groups, help MPP identify the drugs that people need most. MPP then approaches companies that hold the patents for those drugs and negotiates non-exclusive licences, allowing generic companies to manufacture those treatments for sale in lowand middle-income countries.

What makes MPP model particularly innovative are the unique, pragmatic public health-oriented features that differentiate it from other access to medicines initiatives. First, *sustainability*: generic companies do make profits, but because multiple companies are given the same licence and thus encouraged to compete, those profits – and, as a result, prices – are kept low. Second, *quality assurance*: generic versions of drugs must be approved by a stringent regulatory authority such as USFDA or WHO. Third, *freedom to innovate*: the way the licences are pooled allows generic manufacturers to produce new combinations of the original drugs better-adapted for patients, including inventing new formulations for the needs of specific groups like children. Finally, the *licences are completely transparent*: available in full on MPP website – unprecedented in the pharmaceutical field.

The impact

In less than a decade, the innovative work of the MPP's small but dedicated team has had an outsized impact. Through its licences, 8 billion pills have been sold at affordable prices, generating more than USD 1 billion in global savings and enabling countries and organisations to procure larger quantities of high-quality generic medicines. The territories covered by these licences mean that HIV treatments licensed through MPP, for example, are now available to approximately 94% of adults and 99% of children in developing countries.

The most recent example of the real-life impact of MPP licences is the new WHO-recommended best-in-class HIV treatment dolutegravir (DTG). This licence has allowed the development, registration and manufacture of TLD (an innovative combination of tenofovir disoproxil fumarate, lamivudine and DTG). Thanks to their freedom to innovate under MPP licences, generic manufacturers who held rights to these molecules developed a new, single pill, once-a-day treatment for HIV – one that is both clinically superior and less expensive than existing therapies. Just five years after the licence was signed, 3.9 million people across 61 developing countries have had access to DTG at dramatically lower prices – with many more countries about to make the switch.

DTG and TLD are game changers with affordable price tags - patients take fewer pills, experience fewer side effects, and are more likely to adhere to their regimens.

"Just a few small pills, and a simple regimen to adhere to... after fifteen years of always remembering to carry all your pills, it's really like fresh air, a new life."

Anton Basenko, advocate and person living with HIV, Ukraine

Read more stories:
Patients and advocates from around the world discuss the real life impacts of affordable access to these treatments

Looking forward

Thanks to the demonstrated impact of MPP's work in quickly delivering access to high-quality but affordable HIV, tuberculosis, and hepatitis C treatments – and the support of organisations such as WHO and G7 – MPP announced in 2018 that it will expand its mandate to cover essential medicines (the safest and most effective medicines required to meet the basic needs of a health system, as determined by WHO). This means potentially working in areas such as cancer, heart disease and diabetes, and contributing further to the goal of universal health coverage – leading to improved health and socioeconomic outcomes for the world's poorest and most vulnerable.

Contact for media enquiries Sophie Thievenaz, Head of Communications a.i., *sthievenaz@medicinespatentpool.org*
Learn more about how the MPP works *www.medicinespatentpool.org*

MTV STAYING ALIVE FOUNDATION (MTV-SAF) – MTV SHUGA

Young people and adolescents continue to face acute risk of HIV infection: in 2018, there were over 500,000 new HIV infections among young people and 3.5 million living with HIV. The vast majority of HIV infections among young people occur in sub-Saharan Africa and with a rapidly rising youth population in the continent, if current progress is maintained, new HIV infections are set to rise. Business as usual is not working: we need effective ways of reaching young people, and innovative methods to direct them to services.

MTV-SAF is a global leader in developing youth-focused behavior change mass media, with MTV Shuga being its flagship campaign. MTV Shuga is a multi-award winning TV drama, accompanied by radio, digital, social media, and mobile elements, which weaves life-saving HIV and wider sexual health information into storylines that reflect the lives of youth audiences. Through relevant storylines and characters, high-quality production and the MTV brand, the content attracts substantial audiences and drives behavior change by immersing them into entertaining sexual health content.

MTV Shuga is distributed cost-free and rights-cleared to global broadcasters. To-date, MTV Shuga has aired on 180 broadcast platforms, including major terrestrial broadcasters across Africa. This cost-free distribution model equates to huge audiences, as well as substantial cost benefits. The World Bank have recently undertaken a cost benefit analysis of MTV Shuga and found that the benefits, in terms of HIV DALYs in five African countries, equated to US$300 million over 30 years, a return of $150 per $1 invested and an internal rate of return of over 700%.

Since 2018, with financial support from Unitaid, MTV-SAF has been developing three new seasons of MTV Shuga in South Africa and Cote d'Ivoire (two seasons), to drive demand for HIV Self-Testing (HIVST), PrEP and wider HIV innovations among African youth. Utilizing the power of the MTV Shuga brand, extensive and engaged youth audiences, and relationships with global TV broadcasters, we are increasing awareness, acceptability and demand for groundbreaking HIV innovations, and driving audiences to service providers to secure uptake.

MTV Staying Alive UK, 17–29
Hawley Crescent, London, NW1 8TT, United Kingdom
Staying Alive Foundation Inc., 1515 Broadway, New York, USA

IMPROVING ACCESS TO TOOLS THAT DETECT SEVERE ILLNESS: KEY STEP TOWARD BETTER PRIMARY HEALTH CARE AND ACHIEVING UNIVERSAL HEALTH COVERAGE

Devices like pulse oximeters (POX), which measure oxygen saturation in the blood, or electronic clinical decision support tools (eCDSTs) that help process patient information and symptoms through digital applications, are essential for alerting health workers to signs of severe disease and need for urgent treatment. These critical tools are available and accessible in high-income countries, but barriers related to demand, adoption, supply, and delivery prevent access in some low-resource settings (LRS). When danger signs are overlooked or not adequately addressed, children's lives are at risk. Lack of appropriate diagnostics often leads to misuse of medicines and antibiotics, contributing to the rise of antimicrobial resistance.

In 2017, an estimated 5.4 million children died before their fifth birthday, most from diseases that can be prevented and treated, like pneumonia, diarrhea, and malaria. **To achieve universal health coverage (UHC), one of the most effective steps that governments can take is to improve management and treatment of sick children by making sure that tools to identify severe illness and decrease mortality are available and accessible at the primary health care (PHC) level.**

The potential impact of this step is significant. It is estimated that effective use of POX and eCDSTs at the PHC level over the next ten years could result in up to 358,000 lives saved and more than 4.7 million complications averted,[1] a as well as lead to increased health worker confidence and motivation.

That's why PATH, with $28 million in financial support from Unitaid, is partnering with the Swiss Tropical and Public Health Institute, national ministries of health, and international thought leaders on the Tools for Integrated Management of Childhood Illness (TIMCI) initiative. This ambitious four-year project sets out to innovate how frontline health workers detect severe disease in sick children—by improving access to important diagnostic tools like POX, and making those tools smarter and more relevant to LRS.

1 Effectiveness of the intervention among both children with pneumonia and children with fever not caused by pneumonia. Model results were generated for lives saved across the five focus countries between 2019-2028. Further modeling information can be provided as needed.

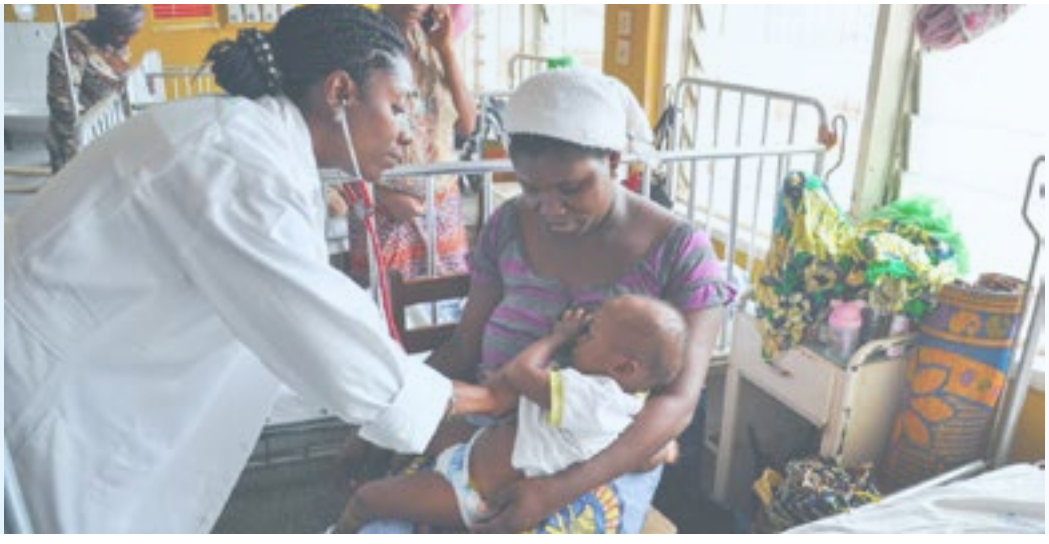
The overall goal: leverage effective, lean innovations to make PHC service delivery more accessible, accountable, affordable, and reliable. The underlying resolve: help establish progress toward UHC goals by improving PHC systems.

TIMCI aims to strengthen the market for critical diagnostic tools in LRS through action, evidence, and innovation:

- First, in coordination with ministries of health, we will integrate POX and eCDSTs into local childhood illness management guidelines and put them in the hands of frontline health workers in almost 200 PHC facilities across five countries in Africa and Asia.
-
- Second, we will generate important and missing data on the feasibility, cost-effectiveness, and health impact of these devices.
-
- Third, we will leverage health technology innovations to augment the features of standard POX to measure additional vital signs, such as respiratory rate, hemoglobin, and temperature—and validate these new multimodal devices in the field.

Ten years from now, this work will help drive the estimated coverage of POX and eCDSTs in the five focus countries from nearly 0 up to 65 percent. By demonstrating that these tools improve the management of childhood illness and can be sustainably implemented, TIMCI will generate evidence-based demand, increase donor engagement, and provide incentives for manufacturers to innovate and for governments to pursue adoption.

Starting with five countries, we hope to then empower others to replicate this work as one of the key drivers toward improving PHC systems and achieving UHC targets mandated by United Nations Sustainable Development Goal 3.8 by 2030.



Dr Mame Nyarko examining a child that is held by his mother at Princess Marie Louise Children's Hospital.
Credit: PATH/Doune Porter

For inquiries, please contact Elena Pantjushenko,
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ENDTB TACKLES DRUG-RESISTANT FORMS OF WORLD'S DEADLIEST INFECTIOUS DISEASE, EXEMPLIFIES WHAT'S TRULY NEEDED TO PROVIDE UNIVERSAL HEALTH COVERAGE

Dmitry Makarov, a 30-year-old Kazakhstan man, moved so quickly through worsening, debilitating forms of tuberculosis that by March 2016, the only care he was receiving was palliative.

"He was prepared to die," Yekaterina Sakhabutdinova said. She's a drug safety specialist for Partners In Health, the lead implementer of the revolutionary, $80 million partnership Expand New Drug Markets for TB, known as endTB.

The seven-year, Unitaid-funded partnership began in 2015 and spans 17 countries, including Kazakhstan. EndTB's goal is to revamp management of multidrug-resistant tuberculosis (MDR-TB) by introducing new drugs; expanding access to them; developing shorter, safer treatment regimens; and ultimately, improving quality of life for all patients.

MDR-TB kills more than 200,000 people every year and is a particularly cruel and hard-to-treat version of TB, which became the world's deadliest infectious disease in 2015.

Makarov's story—including the innovative clinical trials and technologies that helped save him—is one of hundreds, and soon will be one of thousands as successful treatments expand.

It's also a stark example of why the upcoming political declaration on universal health coverage (UHC), to be approved at the UN's High-Level Meeting on Sept. 23, faces critical questions.

If UHC truly is to be transformative, it must address the full extent of a population's health needs, with special attention to the poorest and most vulnerable. The realization of the right to health for all requires public financing, public provision of care, and critically, closing the financing gap for low- and middle-income countries. Failure to address these fundamental issues would advance the privatization of care, which—time and again—has only increased inequities and costs, while decreasing quality.

Partners In Health, Unitaid, and endTB collaborators are taking a different approach.

Dr. Michael Rich, endTB co-leader and clinical investigator for Partners In Health, noted that while 600,000 people globally contract MDR-TB every year, clinical trials that test regimens against each other have been scarce.

Finding the best drug combinations can improve treatment outcomes and boost markets for specific medicines, lowering costs for all. And most importantly, it can save more lives.

“EndTB’s innovation is that while the regimens for MDR-TB in general are about 50 percent successful globally, and about 30 percent for extensively drug-resistant (XDR) TB, we’re getting success rates above 80 percent,” Rich said.

Along with improved guidelines and better, more affordable drugs, endTB also is working to ensure universal access to treatment for MDR-TB patients. GeneXpert machines in endTB labs for all 17 countries are improving diagnosis, and outreach efforts including a mobile TB van in Peru and nationwide education programs in Lesotho are finding more patients, raising awareness, and reversing societal stigmas.

And in Kazakhstan, mobile phone apps for treatment reminders and accompaniment methods through Skype, Viber, and WhatsApp are helping patients—like Makarov—stay in daily treatment and recover from a disease that used to be a death sentence.

HIV SELF-TESTING AFRICA (STAR) INITIATIVE

Some 770,000 people lost their lives to the HIV epidemic last year. With 1.7 million new cases arising annually, eradicating HIV remains one of the world's most daunting public health challenges.

The international community has set ambitious targets to eliminate the virus by 2030. Ensuring all people living with HIV are aware of their status is paramount.

Yet, approximately one in four people worldwide are unaware that they are HIV-positive. Even with more people getting tested than ever before, key populations, men and young people are still being left behind at alarming rates. Persistent challenges for men, including testing and treatment coverage and increased mortality risk, require rethinking the current service delivery models to ensure that men's needs are at the center.

Enter HIV self-testing (HIVST), which offers millions of people a way to learn their HIV status in private requiring 20 minutes or less. As newer HIVST kits have received WHO prequalification, a test can take just one minute, using either an oral swab or finger pinprick test kit.

Since 2015, Population Services International, with funding support from Unitaid, is leading the largest global HIVST endeavor, known as the Self-Testing Africa (STAR) Initiative. Now in its second phase, STAR has generated compelling evidence on the effective distribution of HIVST products and linking self-testers with treatment or prevention services. There is a groundswell of momentum at the global and country levels; the World Health Organization adopted guidelines on HIVST in 2016; 32 countries are piloting self-testing programs; 59 countries now have policies in place that support self-testing as a key health care strategy; and 53 have new policies under development.

Self-care interventions such as HIVST hold the potential to increase individuals' autonomy, strengthen countries health systems, and ultimately pave the way toward universal health coverage.

Governments are increasingly recognizing the systemic benefits of HIVST in making the most cost-effective use of scarce resources—namely more efficient prevention and treatment efforts, and more affordable products.

As of July 2019, the STAR Initiative had distributed 3.6 million HIVST kits in the six project countries of eSwatini, Lesotho, Malawi, South Africa, Zambia, and Zimbabwe, with a target of 5 million kits by 2020. With additional investment by other donors such as the Global Fund and PEPFAR, the number of HIVST kits to be distributed in these six countries alone has doubled.
Each kit is helping to shift the narrative—from one of people beholden to

health systems that may not serve their needs to one where they are armed with the knowledge and tools to take their care into their own hands. As more people opt into self-testing, learn their status, and are linked with appropriate treatment, the goalpost of ending the HIV epidemic is closer than ever.

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NO MORE EXCUSES: PROTECT PREGNANT WOMEN THROUGH RESEARCH, NOT FROM IT!

Safety and efficacy of new drugs in pregnancy is poorly studied with pregnant and breastfeeding mothers routinely excluded from trials; even when available, clinical data lag behind any introduction of drug into market by many years. Carefully conducted clinical trials in pregnancy are challenging to undertake, with a commonly held misconception that pregnant women cannot be ethically enrolled onto drug trials (understandable, in the light of prior experience with drugs like thalidomide). Consequently these drugs may become widely deployed in women in resource-limited settings where monitoring is sparse and harms to mother and infants pass unrecognised. In the case of HIV drugs, what little data around pregnancy and breastfeeding which exist emerge only around 7 years after the drug has been introduced. In low and middle income countries where access to healthcare may be patchy, there exist neglected populations of pregnant women such as mothers who engage late with health services in pregnancy, and who might not access any benefits from new and better treatments. Alongside the humanitarian prerogative to provide medicines across all populations lies an ethical imperative to ensure treatment is safe, effective and evidence-based, with equal opportunity for access.

The **DolPHIN-2 trial** was funded by Unitaid to address a critical gap in evidence surrounding the proposed global transition to dolutegravir (DTG)-based regimens: *is DTG beneficial in pregnant mothers who initiate HIV treatment late in pregnancy*?

In sub-Saharan Africa, it is not uncommon for HIV-positive women to present to health services for the first time in late pregnancy, and consequently conventional HIV treatment may simply not have sufficient time to reduce the amount of HIV in the blood (viral load) by the time of delivery. Late initiation of HIV treatment in pregnancy (affecting approximately 1 in 5 of HIV-positive pregnancies in S Africa) is associated with a 7-fold increased risk of mother-to-child transmission of HIV, and a doubling of infant mortality in the first year of life. However, studies in non-pregnant adults confirm that DTG acts very quickly, reducing HIV viral load considerably faster than standard (efavirenz-based) regimens. Since viral load at delivery is the most important single determinant of infant transmission risk, there is reason to study whether DTG is both safe and effective in pregnancy in order to estimate any potential impact on mother-to child transmissions globally. The DolPHIN-2 trial randomized 268 pregnant women initiating treatment in the third trimester of pregnancy to DTG-based regimen or standard-of-care. Detailed and careful follow-up of mothers, and their newborn infants was undertaken.

DolPHIN-2 findings were presented at the CROI conference in March 2019, and widely reported in conference live-feeds, post-meeting reports, and in the press, including the NY Times. We found pregnant mothers assigned to

the DTG arm were significantly more likely to have suppressed viral load by delivery, and moreover DTG was well-tolerated in both mothers and their newborn infants. The large differences in rates of virological suppression between both regimens suggest that significant public health benefits could accrue if dolutegravir-based ART is widely implemented. Our data support the recent revision to WHO guidelines recommending transition to dolutegravir in first line ART for all adults, regardless of pregnancy or child-bearing potential. All mothers and infants enrolled onto DolPHIN-2 are under longer-term follow-up.

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POLICY BRIEF: THE DOLPHIN-2 STUDY (NCT03249181)

Background

- **1.5M HIV+ women** become pregnant every year.
- A significant proportion of HIV-infected women in Africa **initiate ART late**, in the third trimester of pregnancy.
- Late ART initiation associated with a **seven-fold increased risk** of infant transmissions, and **doubling of infant mortality** in the first year of life.

The DolPHIN-2 Study

- HIV+ pregnant women initiating ART in the **third trimester** randomised to **dolutegravir (DTG) vs efavirenz (EFV)** based therapy.
- **Primary endpoint was VL<50 copies/mL at delivery** for efficacy, and occurrence of **drug toxicity in mothers and infants.**
- Efficacy and safety (to 31.1.19) data presented at Conference on Retroviruses and Opportunistic Infections (CROI) in Seattle on the 3rd March 2019.

Results

268 mothers (137 DTG, 131 EFV) included for safety, and 250 mothers (125 DTG, 125 EFV) for efficacy analyses

- **DTG associated with superior virological response when initiating ART in the third trimester**: VL<50 copies/mL in 74% (89/120) DTG versus 43% (50/117) EFV arm at delivery visit.
- Risk ratio was unaffected by baseline VL, CD4 count, gestation at enrolment, maternal age, study site, and was 1.64 (95% CI 1.31 – 2.06) after a median of 55 days on ART.
- **DTG was well-tolerated in late pregnancy**; no differences in frequency or organ class of severe adverse events compared with EFV. No significant differences in gestational age, pre-term delivery, IRIS .
- **No difference in congenital anomalies** between arms.

Poor outcomes related to late presentation included:

- **Four stillbirths** none thought to be related to drug.
- **Eight infant deaths** none thought to be related to drug.
- **Three HIV infected infants** all likely to have occurred before ART initiation.

Conclusion

- **DTG is well-tolerated and achieves superior virological suppression** before delivery compared to EFV when initiated in late pregnancy.
- Late presentation in pregnancy is associated with **poor outcomes** despite ART and regardless of arm.

What might this mean for policy makers?

- For National Programmes where DTG is used as first-line (including pregnant women after the first trimester), no immediate change in policy is indicated, the availability of additional safety data is reassuring.
- National Programmes which discourage use of DTG in all pregnant women may wish to re-evaluate risk-benefit considerations. For women who present late in pregnancy, when fetal development has largely been completed, there are clear benefits in the rapid VL reduction achieved with DTG.
- National Programmes which do not routinely offer DTG to women of child-bearing potential may wish to re-evaluate the potential benefits of DTG outside the first trimester of pregnancy.
- Regardless of country policy, National Programmes should endeavour to **collect birth outcome data** on all pregnancy exposures to anti-retroviral drugs (including stillbirths and transmissions), contributing whenever possible to **international collaborative registries.**

Notes

1) DolPHIN-2 was funded by Unitaid
2) DTG was donated by ViiV Healthcare
3) The DolPHIN-2 Consortium includes the Infectious Diseases Institute (Kampala), The University of Cape Town, Radbourd University, Liverpool School of Tropical Medicine, and University of Liverpool

For further information, see:
http://www.croiwebcasts.org/
@UoLDolphin2

SIMPLIFYING HIV TREATMENT TO IMPROVE GLOBAL ACCESS

People diagnosed with HIV can now live long and healthy lives, but only if they have access to effective treatments. Improving health outcomes for people living with HIV is an essential component of achieving Universal Health Coverage and is vital to reduce the spread of HIV. Globally, there are almost 38 million people living with HIV, most of whom are in low income countries. For one in ten of these people, the initial HIV treatment offered to them will not keep their infection in check. These people need an alternate, 'second-line', HIV treatment.

There is an urgent need to simplify second-line treatment for people living with HIV. Current second-line treatment options are complex and impractical in poorer countries. They require multiple pills, ideally selected using specialised tests that are often not available, and the medicines have many more side effects. As a result, many people who need second-line treatment do not receive it.

With the support of Unitaid and other partners, the Kirby Institute is implementing an international clinical trial called D2EFT*, which will determine the most efficient second-line HIV treatment. The randomised controlled trial tests two simplified second-line treatment options against the current standard-of-care.

The simplified treatments being tested will have significant benefits if they prove to be as effective as the current standard. They:

- allow second-line treatments to be formulated as a single pill with fewer side effects
- avoid the need for specialised tests (HIV gene drug resistance testing)
- reduce the costs of the medication
- simplify fragile heath care supply chains
- allow nurses and assistants to prescribe second-line treatment (as they do initial treatment)

These innovations would dramatically improve access to second-line HIV treatment, especially in low-income countries, and allow more people to be treated within the existing funding environment.

While most clinical trials are undertaken only in wealthy countries with established infrastructure, D2EFT is being conducted in 14 mostly low-income countries – the places where simplified treatment is most urgently needed. In several of these, including Mali, Guinea and Indonesia, the Kirby Institute is working with local teams to develop the capacity to undertake clinical trials. This collaboration ensures that study results are relevant to those most affected, assists in the implementation of the study's findings by building local understanding and advocacy, and strengthens health care systems.

We will arrive at UHC more swiftly if we can harness innovation and evidence to ensure every health care dollar is spent to maximum effect. **The ultimate goal of D2EFT is to develop a second-line treatment option that is simpler for patients and cheaper for health care systems.**

This innovative research will save lives, and deliver essential evidence needed to achieve Universal Health Coverage for people living with HIV.

For more information on the D²EFT trial visit the Kirby Institute website:
kirby.unsw.edu.au
For media enquiries contact:
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D²EFT is funded by Unitaid, with additional funding from the Australian National Health and Medical Research Council (NHMRC), the U.S National Institute of Allergy and Infectious Diseases (National Institutes of Health) and ViiV Healthcare, and in-kind support from Janssen Pharmaceutical.

*Dolutegravir and Darunavir Evaluation in adults Failing Therapy.

UNITAID'S WORK ON THE VANGUARD OF HEALTH INNOVATION

Unitaid is an international organization that turns great ideas into groundbreaking global health solutions. It goes about this by piloting the most promising inventions and approaches from the worlds of science and medicine, then working with large funding partners such as PEPFAR, USAID and the Global Fund to introduce them on a sweeping scale in lower-resource countries. The innovations range from affordable, accessible medicines and diagnostic tools to prevention measures.

Unitaid's work is highly collaborative, recognizing that to achieve the momentous goal of universal health coverage, many entities must work together like the parts of a single organism. Unitaid coordinates closely with scale-up partners, with the World Health Organization, with countries, with communities, and with the 127 partner organizations involved in implementing $US 1.3 billion in Unitaid grant projects all over the world.

Since it was founded in 2006, Unitaid has focused on bringing new weapons into the fight against the epidemics of HIV/AIDS, malaria and tuberculosis in low- and middle-income countries. In 2015, Unitaid began work to introduce affordable HIV self-testing in Africa; the market for self-testing kits was virtually nonexistent, but today, as the result of Unitaid's investments, 59 countries have policies on selftesting. In 2016, Unitaid introduced the world's first child-friendly TB medicine, which is now being used in more than 100 countries. In 2018, Unitaid demonstrated that 18 million pediatric malaria cases could be avoided in the Sahel region of Africa through a few doses of oral medication per child. Partners have taken that result and are widely introducing the preventive medicine.

As it moves into a new decade, Unitaid is building on its work with a view to supporting the global drive for universal health coverage. Three-quarters of the organization's projects support new ways to integrate health services—TB testing in pediatric clinics, malaria prevention with prenatal care, multiple diseases diagnosed by a single machine—a streamlining seen as essential to meeting the goal of universl health coverage and the UN Sustainable Development Goals for health.

At the same time, Unitaid is participating in an enormous push by the entire global health community to stop the advance of drug-resistant microbes. Drug-resistant forms of TB, HIV and other diseases have brought illness, death and financial ruin to many thousands of people and are a threat to every country. Unitaid's role is to find and bring in innovative drugs, tests and prevention methods to help tackle superbugs. More than 60 percent of the organization's portfolio is dedicated to projects that fight antimicrobial resistance. Unitaid also invests heavily in innovations to eradicate malaria-carrying mosquitoes that are resistant to insecticides.

Unitaid has 48 grant projects under way. New and notable among these are initiatives to:

- Avert cervical cancer. One-dollar screen-and-treat solutions using artificial intelligence aim to fend off this major killer of HIV-positive women. • Protect people from malaria in sub-Saharan Africa with new-generation insecticide-treated nets.
- Use mobile technology and “smart” pillboxes to help patients adhere to long TB treatments.
- Equip primary health care workers with easy-to-use devices to measure oxygen in the blood so they can better identify severely ill children.
- Pilot a powerful new technology for TB diagnosis. Next-generation gene sequencing provides fast, accurate diagnosis of drug-resistant TB, helping clinicians prescribe the correct medicine from the outset of treatment.

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