Shorter Regimen for Preventing TB Found to Have Lasting Protective Effect in People Living with HIV

New study finds there is no need to repeat short-course TB preventive therapy after one year and finds that shorter regimen nearly doubles treatment completion rate

BOSTON (11 March 2020)—A new study finds a single course of weekly rifapentine and isoniazid for three months (3HP) provides lasting protection against tuberculosis (TB) and does not need to be repeated year after year. The WHIP3TB trial, led by the Aurum Institute and partners, was presented today at the Conference on Retroviruses and Opportunistic Infections (CROI). The clinical trial showed that repeat annual administration of 3HP did not provide additional benefits when compared to the single, three-month treatment course. The trial involved over 4,000 adults with HIV infection receiving antiretroviral therapy (ART) across three African countries.

“We knew that 3HP was as effective as longer treatments for preventing TB disease in people with HIV, but there were doubts about the duration of protection in high-burden TB settings,” said Gavin Churchyard, group CEO of the Aurum Institute and principal investigator on the study. “What this study demonstrates conclusively is that there is no need to repeat a course of 3HP annually, a finding that has huge implications for health programs caring for millions of people with HIV globally.”

The study was led by the Aurum Institute and sponsored by the KNCV Tuberculosis Foundation and funded by USAID through the Challenge TB project. The WHIP3TB trial was implemented by the Aurum Institute and Perinatal HIV Research Unit (PHRU) in South Africa, the Ohio State University, Global One Health initiative in Ethiopia, and by Centro de Investigação de Saúde de Manhiça (CISM) in Mozambique. Other senior investigators were from the London School of Hygiene and Tropical Medicine and Johns Hopkins University Center for TB Research.

The study had two parts. The first part compared the effects of a single three-month course with two three-month courses given annually (for two years) to people living with HIV. The second arm compared 3HP to daily isoniazid for six months. Researchers enrolled 4,027 adults with HIV (and on ART) but without active TB and divided them into three groups: one group received 3HP for three months, another received 3HP for three months in year one and again in year two, and another received daily isoniazid for six months. After two years of follow up, rates of TB were virtually the same in participants who received either one (three-month) course or two (three-month) courses of 3HP. The 3HP regimen was found to be safe, with similarly low rates of adverse effects in both 3HP arms of the trial.
After one year, the researchers found adherence to be higher among patients who were assigned to the 3HP groups than among patients who were prescribed six months of isoniazid. Completion of the treatment course in the combined 3HP arms (3610 people) versus isoniazid (404 people) arms was 90.4% versus 50.5%, respectively.

“When we’re asking people who are not sick to take medicines, adherence can be a huge problem,” said Professor Katherine Fielding, from London School of Hygiene & Tropical Medicine and senior statistician on the study. “This study confirms what we already suspected—that it’s easier for people to take pills once a week, for three months, than once a day for six months. Shorter regimens lead to higher adherence, which ultimately improves treatment outcomes.”

**TB Prevention**

Tuberculosis, a disease that still kills around 1.5 million people every year, can lie dormant for decades before it strikes; this is called “latent TB infection.” People with latent infection—almost a quarter of the globe—have no TB symptoms, are not contagious, and most of them don’t know they are infected. If left untreated, latent infection can develop into active TB, the form of TB that makes people sick and is capable of being transmitted from one person to another.

“Latent TB infection is the breeding ground for the TB epidemic, and preventing new cases is critical if we want to end the TB epidemic,” added Churchyard.

People living with HIV are at high risk of developing TB and are 20 to 37 times more likely to move from latent infection to active TB. Treatment of TB infection is referred to as TB preventive therapy (TPT) and is one of the most powerful ways to prevent TB. At the United Nations High-Level Meeting on Ending Tuberculosis in September 2018, heads of states committed to providing preventive treatment to at least 30 million people, including 6 million people living with HIV by 2022. That year, only 65 countries had reported initiating 1.8 million people living with HIV (PLHIV) and 349,487 children < 5 years on isoniazid preventive therapy (IPT).

“The fact that there is no need for a repeat dose of the medicines is good and timely news for all patients receiving 3HP as well as for public health practitioners,” said Dr. Gidado Mustapha, director of Challenge TB and head of the project management unit at the KNCV Tuberculosis Foundation.

The 3HP regimen offers a shorter, safer alternative to the older standard of care (IPT) in which people take isoniazid every day for between six and 36 months. In February 2018, the World Health Organization (WHO) released consolidated guidelines for the treatment of latent TB infection that recommend the use of 3HP for people living with HIV and people who are in close contact with TB cases.

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**About Aurum**

*Established in 1998, the Aurum Institute is an African Public Benefit Organisation whose mission is to improve the health of people and communities living in poverty through innovation in global health*
research, systems and delivery. It is rooted in Africa is dedicated to researching, supporting and implementing innovative, integrated approaches to Global Health with their headquarters in South Africa with offices in the USA, Ghana and Mozambique. The Aurum Institute has developed itself into a leading player, bridging the worlds of research, policy and implementation for impact. www.auruminstitute.org

**About KNCV**
KNCV Tuberculosis Foundation (KNCV) was established in 1903 as an umbrella organization for Dutch tuberculosis control, supporting community-based initiatives across the country and facilitating the exchange of best practices. KNCV was among the founding members of the UNION and STOP TB Partnership. During the 115 years of its existence and to this day KNCV plays a key role in eliminating TB in the Netherlands and supporting high prevalence countries in strengthening and optimizing TB control within national health strategies. Whereas the Netherlands has reached the pre-elimination phase, TB remains the deadliest infectious disease worldwide. KNCV has been indispensable in the evolution towards a robust and watertight TB control system in the Netherlands, building on technical expertise and placing patients and families’ social support at the center: our patient-centered approach. https://www.kncvtbc.org/

**About John Hopkins Center for TB Research**
The Johns Hopkins Center for Tuberculosis Research was founded in 1998 to contribute to global tuberculosis control through innovative research and training. Its research efforts span the fields of epidemiology, clinical trials, diagnostics and basic science, with faculty from six departments in the Johns Hopkins University School of Medicine, Bloomberg School of Public Health, and School of Nursing. Clinical research collaborative sites are located in Baltimore City, Maryland, as well as sites in Brazil, South Africa, India, and other TB high burden countries.

**About Centro de Investigação em Saúde de Manhiça**
The Manhiça Health Research Centre (Centro de Investigação em Saúde de Manhiça, CISM), created in 1996 is a research institution managed by Manhiça Foundation, whose mission is to promote and conduct biomedical research in health priority areas to promote and safeguard the health of the population. The CISM is located in the district of Manhiça, in Maputo province, southern Mozambique. Since its foundation, the center has contributed to generate knowledge and scientific evidence that has contributed to guide health policy in Mozambique and at global level. The activities of CISM stand on three pillars: research, training and healthcare. http://www.manhica.org

**About PHRU**
The Perinatal HIV Research Unit (PHRU)-Matlosana is located at the Tshepong Hospital, Matlosana Municipality, South Africa and conducts research in the Hospital and in surrounding communities. Established in 2007 by Drs Martinson and Varieva, with just two employees conducting an observational study assessing mortality in admitted patients with TB, PHRU-Matlosana has grown substantially capable of conducting both simple and complex medical studies, and has built a research infrastructure to service clinical research while supporting the activities of the health services. A satellite site of PHRU-Soweto, the Matlosana site has a close relationship with the North West Department of Health and the Department of Medicine at Tshepong Hospital. Many of our research projects address severe clinical problems faced by similar hospitals and communities in Southern Africa.
About GOHi
The Ohio State University, Global One Health initiative (GOHi)’s mission is to expand capacity for a One Health approach via applied education, training, research and outreach to address causes and effects of diseases at the cross-road or interface of humans, animals, plants and the environment more efficiently and effectively. GOHi is head-quartered at The Ohio State University (OSU) in Columbus, Ohio (USA) with a non-governmental organization (NGO) affiliated-entity based in Addis Ababa, Ethiopia (Eastern Africa). GOHi works in partnership with national, regional and international academic, research, governmental, non-governmental, private companies, industries and regulatory bodies. GOHi is an affiliate entity of the Ohio State University (OSU) which is Founded in 1870 as a world-class public university
https://globalonehealth.osu.edu

About The London School of Hygiene & Tropical Medicine
The London School of Hygiene & Tropical Medicine (LSHTM) is a world-leading centre for research and postgraduate education in public and global health. LSHTM’s mission is to improve health and health equity in the UK and worldwide; working in partnership to achieve excellence in public and global health research, education and translation of knowledge into policy and practice. LSHTM has 3,000 staff based all around the world with core hubs in London and at the MRC Units in The Gambia and Uganda.