Simple stool-based diagnosis could be a global life-saver by enabling millions more children at risk from TB and MDR-TB to be tested

Other scientific studies released at today’s official MDR-TB press conference at the 49th Union World Conference on Lung Health includes data from multiple countries showing impact of innovative MDR-TB treatment effort with Bedaquiline curing hundreds of cases of MDR-TB in Eastern Europe and Central Asia

Thursday, 25 October 2018, (The Hague, The Netherlands) – A simple method for processing stool samples for Xpert MTB/RIF testing using minimal equipment has been announced at the 49th Union World Conference on Lung Health and could enable the identification of thousands of children with tuberculosis (TB) and multidrug-resistant TB (MDR-TB) disease - drastically reducing the numbers of children under five dying from TB.

Currently, an estimated 239,000 children die every year from tuberculosis (TB). Children with TB rarely die when they receive standard treatment for the disease, but 90 percent of children who die from TB worldwide went untreated.

Young children cannot spit up a sputum specimen and other methods are needed to get a sputum sample off them, which are complex, invasive, stressful and painful and often need the children to be hospitalised overnight (usually for the smallest children (<5y)

Children
gastric aspiration is used, in which a tube is brought into the child’s stomach via his or her nose.)

Stool sampling has in recent times been under investigation but it has been widely considered that stool is a difficult sample, because it contains so many other bacteria and debris, and it is believed that the *Mycobacterium tuberculosis* bacilli are fully "encapsulated" by other materials in the sample, making it difficult to "free" the bacilli. It was previously believed that good quality DNA material could only be obtained from stool in multiple cleaning steps using sophisticated equipment.

A new simple method developed by researchers at the KNCV Tuberculosis Foundation involves mixing a sample of stool with a sample of the SR (Sample Reagent) buffer (which comes with every Xpert machine cartridge in bottles of 8 ml). This simple Xpert stool test was positive (showing TB) in all children who also had positive respiratory samples – there were no false negative stool samples. The work was done in collaboration with Ethiopian and Indonesian research institutes, and the respective national TB control programs.

The test also identifies resistance to rifampicin which is a marker for MDR-TB.

“No child should die from TB,” said José Luis Castro, Executive Director of The International Union Against Tuberculosis and Lung Diseases (The Union). “There is an urgent need to drastically step up investment in research and development that can deliver new and better diagnostic tools such as this stool test. Promising breakthroughs of this kind are needed if we are to make inroads into preventing illness and death from both drug-susceptible TB and MDR-TB.”

Kitty van Weezenbeek, Executive Director of the KNCV Tuberculosis Foundation which developed the method in collaboration with the National Tuberculosis Programs of Ethiopia and Indonesia, said: “If further testing confirms the preliminary findings in Indonesia and Ethiopia, the potential of this method is enormous and means that being
able to diagnose TB and MDR-TB from stool would mean that we have a method in our hands that can diagnose TB at the lowest health care level and can bring testing to hundreds of thousands of people. In that way, children can now get a microbiologically confirmed TB diagnosis at primary health centres, where that is currently not possible.”

Currently, to obtain a sputum test, children are referred to specialised service providers, as testing is not possible at the community level.

Additionally, current stool processing methods use sophisticated centrifugation and filtration that are only available in referral laboratories, usually attached to referral hospitals.

Today’s press conference highlighted four abstracts (shown below) being presented at the 49th Union World Conference on Lung Health 2018. (Note: Press summaries are based on abstracts; final data presented at the conference may change).

Simple stool processing method for the diagnosis of pulmonary TB using GeneXpert

The diagnosis of pediatric pulmonary tuberculosis (pTB) is difficult and often relies on clinical signs and symptoms, as obtaining respiratory specimens for testing of young children is challenging. GeneXpert MTB/Rif can be applied on stool samples for diagnosing pTB, but until now, this method is not routinely implemented due to the complexity of the available processing methods.

Petra de Haass, Laboratory Advisor at the KNCV Tuberculosis Foundation in The Hague, The Netherlands, reported on a simple method for processing stool samples for Xpert MTB/RIF testing using minimal equipment. This method was tested in vitro using TB-negative stool samples from children in Ethiopia, and on stool samples from 36 children with presumptive pTB aged <15 years in a tertiary care hospital in Bandung, Indonesia. From these children, respiratory samples (RS) were also obtained by gastric
aspiration for children aged 5 or below and by sputum induction for older children and tested with Xpert for comparison.

The *in vitro* tests showed the potential of the method; using a very simple method, omitting homogenization and filtration steps, reliable results were obtained and no significant inhibition of amplification, a critical step in the GeneXpert process, was observed.

The median age of the children with presumptive pTB was 17 months (interquartile range: 5.5-78 months). pTB was diagnosed among 6 of them (17%); 27/29 submitting stool and RS had an interpretable test result on both samples, the results being concordant in 24 (89%, 95% confidence interval: 71-98%). The three children with discordant results all had an MTB-positive result on stool only.

This groundbreaking work shows that a simple and low-cost method, using similar processing steps as are applied for sputum, can diagnose TB at any GeneXpert site using stool samples, and can even diagnose additional children. The method has the potential to make a bacteriological diagnosis of TB in children at the lowest levels of health care.

**Abstract:** Simple stool processing method for the diagnosis of pulmonary TB using GeneXpert MTB/Rif: promise for improved access to a bacteriological diagnosis for children.

**Session:** CDC Late-Breaker Session on TB, Mississippi Room, Friday 26, 16.00-17:30

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**Excellent outcomes for drug-resistant TB in Belarus**

A cohort study analysing the use of bedaquiline to treat patients with multi- and extensively drug-resistant TB has reported 80 per cent of the participants cured.
Presenting the data, Alena Skrahina, Deputy Director of the Republican Research and Practical Centre for Pulmonology and TB in Minsk, noted the satisfactory safety and effectiveness of the Belarus national TB programme. Particularly the excellent outcomes for a significant proportion of people with extensively drug-resistant TB.

**Abstract:** Bedaquiline containing regimens in the treatment of multi- and extensively drug-resistant tuberculosis at the programmatic level. Prospective cohort study

**Session:** Innovative treatment for MDR-TB, Amazon 360, Friday 26, 16:00-17:30

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**National roll out of shorter treatment for MDR-TB in Kyrgyz Republic**

The preliminary results of a study assessing the use of shorter treatment regimen for multi-drug resistant tuberculosis in Kyrgyz Republic has found the treatment to be effective.

The study, which took place between January and June 2017, has reported 74 per cent of patients to have had negative culture results for TB, even in a country with a high level of resistance.

Presenter Aimgul Duishekeeva, Technical officer of the KNCV Tuberculosis Foundation Branch Office in Bishkek, Kyrgyz Republic, concluded the shorter treatment regimen will be introduced in all regions of the country in 2018.

**Abstract:** Shorter treatment regimen (STR) for multi-drug resistant tuberculosis (MDR-TB) - first outcomes in the Kyrgyz Republic

**Session:** Innovative treatment for MDR-TB, Amazon 360, Friday 26, 16:00-17:30

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**Positive results for shorter treatment regimen in Tajikistan**

An analysis of shorter treatment regimen for multi-drug-resistant TB in Tajikistan has shown promising preliminary results.
Presenting the data, Mavluda Makhmudova, Country Director of KNCV Tuberculosis Foundation in Tajikistan, noted that 72 per cent of the patients successfully completed treatment between December 2016 and June 2017.

As with the results of the study in Kyrgyz Republic, implementing shorter treatment regimen is possible even in countries with high levels of drug resistance.

**Abstract:** First results of shorter treatment regimen used in treatment of multi-drug resistant patients in Tajikistan

**Session:** Innovative treatment for MDR-TB, Amazon 360, Friday 26, 16:00-17:30

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Across a four–day conference programme, the Union World Conference looks not only at scientific advances, but also at the obstacles to developing safe and user-friendly forms of TB prevention and the delivery of drugs to treat the disease and at strategies to address the barriers to making effective prevention and treatment available to all. The global conference features more than 1,000 scientific presentations, including oral and poster abstract sessions, plenaries by the world’s leading lung health researchers, symposia, workshops, satellites and a Community Space, De Ontmoeting, open to the general public.

For the first time in the Conference´s history a pre-Conference event TB Science2018 will be held, focusing on Basic Science.

For journalists who cannot attend in person, all press conferences will be livestreamed on YouTube and available for playback on The Union´s Facebook Page. The conference offers complimentary registration, a fully staffed media center and extensive professional support.

Details on media registration for WCOLH2018 are available here.
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About the 49th Union World Conference on Lung Health

The Union World Conference on Lung Health, convened by the International Union Against Tuberculosis and Lung Diseases (The Union) is the world's largest gathering of clinicians and public health workers, health programme managers, policymakers, researchers and advocates working to end the suffering caused by lung disease, with a focus specifically on the challenges faced by low-and lower-middle income populations. Of the 10 million people who die each year from lung diseases, some 80 percent live in these resource-limited settings.

Organising international conferences on TB and related subjects has been a core activity of The Union since its founding in 1920.

About the International Union Against Tuberculosis and Lung Disease (The Union)

The Union was founded in 1920 and is the world's first global health organisation. We are a global leader in ending TB, we fight the tobacco industry, and we solve key problems in treating major diseases. We use science to design the best treatments and policies for the most pressing public health challenges affecting people living in poverty around the world. The Unions members, staff and consultants operate in more than 150
countries and embody our core values of accountability, independence, quality and solidarity.

**About KNCV Tuberculosis Foundation**

KNCV Tuberculosis Foundation is an international non-profit organization dedicated to the fight against tuberculosis (TB), the deadliest infectious disease in the world. By developing, testing, evaluating and scaling up country specific, patient and community centred TB strategies and interventions we work to impact public health and save lives. KNCV was established in 1903 by civil society organizations. Presently our team includes over 400 professionals, working from a central office in The Hague, The Netherlands, and country offices in Africa and Central and South East Asia.