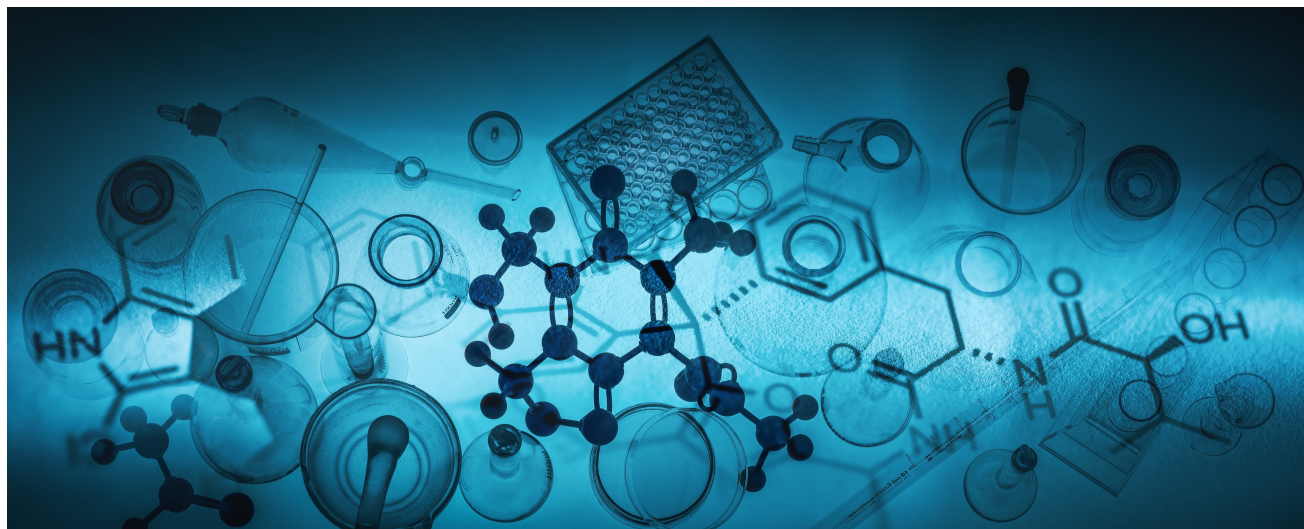


THE MONTHLY DOSE

Official Newsletter of The Mueller Health Foundation



WHAT'S NEW AT THE MUELLER HEALTH FOUNDATION:

We at The Mueller Health Foundation always try to stay up to date with the latest guidelines for TB care. Recently the World Health Organization (WHO) released a new operational handbook meant to provide practical guidance on how to put in place the recommendations at the scale needed to achieve national and global impact.

For the first time, the updated guidelines and the new operational handbook on TB care and support include implementation guidance on health education, counseling, and palliative care as well as on social support, treatment administration options, and digital adherence technologies.

You can access the WHO's Operational Guidebook here: <https://www.who.int/publications/i/item/9789240053519>

Stay tuned for more updates!

LATEST NEWS: SHOWCASING STORIES OF TB SURVIVORS

We at The Mueller Health Foundation continue to be deeply committed to sharing personal stories and giving a voice to TB patients, TB survivors, TB practitioners, and all the friends and family members of the people who have been affected by the disease. The organization *Doctors Without Borders* has put together a wonderful collection of stories from those affected by TB and this month we would like to highlight Nhlanhla Mshengu's story. Nhlanhla lives near Durban in South Africa. He had been diagnosed and put on a pulmonary tuberculosis (TB) treatment in his local clinic for over a year before it was discovered that he had multi-drug-resistant TB (MDR-TB). Here is his story:

After his MDR-TB diagnosis, Nhlanhla was referred to the *Clinical HIV Research Unit (CHRU)*, in *King Dinuzulu Hospital*. He was informed that the clinic had specialized services for the treatment of multi-drug-resistant and extensively drug-resistant TB (XDR-TB). At the clinic, he was recruited and enrolled in the *TB-PRACTECAL* clinical trial. Participants were randomly assigned to take either the standard treatment, or one of the new drug combinations. He was put in the group which received the new treatment. During the time before the trial, Nhlanhla was still using the standard TB treatment and he used to suffer a lot because his condition would stay the same for months. The doctors and nurses at the hospital informed him on how to follow the new trial procedures and processes accordingly. He carefully followed the instructions and used to visit the clinic for check-ups and other tests on a regular basis. After about three months the trial doctors told him that his health condition had gradually returned to normal and they were going to move him to another stage of the trial for follow-up. At this stage he had also started encouraging other patients to participate in similar trials, especially because the trial entailed only oral treatment, as opposed to the injections he was receiving previously. The injections as part of the standard TB treatment he received prior to the trial were very painful and the full course of the treatment took too long which led to many people to default. Nhlanhla is still participating in the trial and continues to adhere to treatment and attends all follow-up visits. He states that through the good work and patience of the trial staff that he now has hope that even MDR-TB can be addressed. He is now focusing on encouraging others, particularly those who have lost hope in the health system, to believe once again and give it a try. To read his full story please follow the link to the *Doctors Without Borders* website: <https://blogs.msf.org/bloggers/nhlanhla/tbme-i-had-already-written-will>

For more news, please also take a look at our top 3 picks for August in this newsletter, where we highlight novel research findings and news around the prevention and treatment of tuberculosis around the world.

MHF TOP PICKS FOR AUGUST

Every month, we at the Mueller Health Foundation like to showcase interesting news and updates in the field of tuberculosis. Below are our top 3 picks for August:

1. Systematic Review and Meta-Analysis of Infant BCG Vaccination and Risk of Pulmonary and Extrapulmonary Tuberculosis throughout the Life Course

A group of international researches funded by the National Institutes of Health (NIH) identified 14,927 original records from their database searches and included participant-level data from 26 cohort studies done in 17 countries in the meta-analysis. From this analysis, the researchers estimated the overall effectiveness of BCG vaccination against all tuberculosis to be approximately 18%. However, the research showed that when stratified by age, BCG vaccination only significantly protected against all tuberculosis in children younger than 5 years. Overall, the results suggest that BCG vaccination at birth is effective at preventing tuberculosis in young children but is ineffective in adolescents and adults. Additional resources should therefore be invested in research that provides new methods for boosting immunoprotection in older populations. To learn more about the research, you can access the full article at: <https://www.thelancet.com/action/showPdf?pii=S2214-109X%2822%2900283-2>

2. Creation of Data Compendium Associating Genomes of 12,289 TB Isolates with Quantitative Resistance Phenotypes to 13 Antibiotics

The study describes the collection and analysis of 15,211 M. tuberculosis isolates from CRYPTIC (Comprehensive Resistance Prediction for Tuberculosis: an International Consortium) partners in Asia, Europe, Africa, and South America. From this collection, 12,289 isolates belonging to the four main M. tuberculosis lineages were sequenced and had susceptibility to 13 different anti-tubercular drugs measured to capture their genotypic and phenotypic profile. Of the 12,289 isolates tested, 6,814 (55.4%) were resistant to at least one drug, including 4,685 that were resistant to the first-line drug rifampicin or were multidrug-resistant (RR/MDR). Of the RR/MDR isolates, 3% were extensively drug-resistant (XDR), and 38.8% were pre-XDR. The drugs with the highest percentage of resistant isolates were the first-line drugs isoniazid (49%) and rifampicin (38.7%). Resistance was low for the newer and repurposed TB drugs, like bedaquiline (0.9%), clofazimine (4.4%), delamanid (1.6%), and linezolid (1.3%). The main contribution of this study is that it provides an unparalleled view of resistance and resistance patterns among the panel of 13 anti-tubercular compounds studied. To learn more, you can read the paper here: <https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3001721>

3. Genome-Wide Association Studies of Global TB Resistance to 13 Antimicrobials in 10,228 Genomes Identify New Resistance Mechanisms

CRYPTIC (Comprehensive Resistance Prediction for Tuberculosis: an International Consortium) researchers analyzed the genomes of 10,228 M. tuberculosis isolates and investigated the association between resistance mechanisms and the minimum inhibitory concentration (MIC) for 13 TB drugs. MIC is a measurement of the lowest concentration needed of a drug to inhibit growth of bacteria. The purpose of using MIC was to find genetic mutations that may cause only subtle changes that reduce the effectiveness of a drug but could be overcome by using higher doses. This approach enabled the team to uncover a host of novel resistance determinants associated with both resistance and subtle changes in MIC, including those for newer and repurposed TB drugs. They then selected the 20 most significant resistance genes identified for each of the 13 drugs, including catalogued and previously uncatalogued genes, for further analysis. You can learn more and access the full article here: <https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3001755>

DID YOU KNOW?

Throughout history, tuberculosis has had a major impact on many famous works created by prominent writers, painters, and musicians. Many of these artists often suffered from tuberculosis themselves or had family and loved ones that were afflicted by the disease. Below are a few short stories of how tuberculosis shaped our literature, art, and music:

- While it is unclear whether the American Poet Edgar Allan Poe ever was afflicted with tuberculosis himself, the loss of his father, mother, adoptive mother, and wife Virginia to tuberculosis greatly influenced his poetry and writings. He wrote one of his most famous poems "Annabel Lee" for his beloved wife shortly after her death. The haunting phrase "...the wind came out of a cloud by night, chilling and killing my Annabel Lee" remains as a stark reminder of his wife's untimely death from the disease, which plunged him into a deep depression.
- The Czech writer Franz Kafka struggled with having tuberculosis throughout most of his life. During his lifetime, there was no cure for the disease, only palliative care and he was very much aware that the disease would ultimately end his life. In his diaries he often refers to himself as a "non-born, condemned to die, without having lived." While tuberculosis is never mentioned explicitly in his works, several characters embody his sentiment and feelings about suffering from tuberculosis: Many of his protagonists are condemned to death, but carry on completely ignorant of their fate and just like him they suffered but continued on their way, not caring and incurable.
- The Dutch painter Rembrandt, while not having suffered tuberculosis himself, was deeply affected by the death of his wife Saskia and young son Titus, who both were afflicted by tuberculosis. The portraits of his wife that he painted during her lifetime clearly show the progression of the disease. It was only the last portrait of his wife that he completed after her death that shows her as healthy and beautiful with a sprig of rosemary in her hand, which served as a symbol of remembrance. It was his final gift as an artist to his wife to remember her in her youthfulness and paint away her suffering from tuberculosis.
- Tuberculosis not only had a major influence on literature and art, but is often reflected in famous operas and musicals. The death of *Mimi* from consumption in *La Bohème* by Puccini is perhaps one of the most moving scenes in all of opera. In the musical *Les Misérables*, the character of *Fantine* also dies of tuberculosis. Similarly in the musical *Moulin Rouge*, the main protagonist *Satine* dies of tuberculosis, leaving the love of her life behind to tell her story.

Information Source:
<https://www.cambridge.org/core/services/aop-cambridge/core/content/view/EPF8C23B37CD4672222A3E464654/1002572730027642a.pdf/the-impact-of-tuberculosis-on-history-literature-and-art.pdf>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2439331/>
<https://sheffhallking.wordpress.com/2016/03/17/tuberculosis-in-music-and-film/>