Precision Medicine and Tuberculosis

Merging precision medicine and precision public health to address a global health challenge more precisely

Note: The organizer will have speakers and participants will have discussion on precision medicine and Tuberculosis.

Precision Medicine, a disease treatment and prevention approach that tailors interventions for individuals based on individual variability in genes, environment, and lifestyle, holds the promise of revolutionizing healthcare delivery. However, concerns have been expressed that precision medicine, with its focus on detecting and curing disease at the individual level, neglects important factors such as social determinants of population health, and will drive away investments in efforts to advance public health and reduce health disparities. On the other side, counter arguments to these concerns have emerged, indicating that a population perspective enhances the output of precision medicine and ensures that premature or inappropriate adoption of technologies is minimized, and that the same technologies that fuel precision medicine can be used to advance public health. This rapidly evolving concept, designated "precision public health", involves the collection, assessment and handling of more accurate population- and individual-level data on genes, exposures, behaviors, and other social-economic health determinants. Through this process, public health action for improving health in subpopulations in need of recommended prevention measures is enhanced; and, by using more precision data for action, health disparities in the population are addressed and reduced. Finally, precision approaches involving multiple sectors and disciplines are now also a focus in global health and recent research - yet to be published - has defined how application of precision medicine and precision public health principles can contribute to manage global health challenges like tuberculosis (TB) more precisely and effectively.

With an estimated 10 million people developing TB disease and 1.6 million TB-related deaths globally in 2017, TB remains a major public health burden and the top infectious killer throughout the world. Within this larger epidemic, drug-resistant TB (DR-TB) is today a public health crisis. The World Health Organization (WHO) estimated that, in 2017, 558,000 cases of multidrug-resistant and rifampin-resistant TB (MDR/RR-TB) emerged globally, 230, 000 people died from it, and MDR-TB prevalence in new cases in some countries is as high as 35%. At the same time, the number of MDR/RR-TB cases notified and treated according to international standards are about a quarter of those estimated, revealing a major gap.

At present, the treatment of TB is largely through standardized, empirical combination regimens administered for essentially arbitrary periods that do not take into consideration detailed drug-susceptibility information, individual variabilities in drug metabolism processing, or pathogen-host interaction. Challenges in the care and treatment of TB include: incomplete understanding of the pathophysiology of infection, lack of optimal and rapid diagnostics usable at the point of care; lack of a robust armamentarium of effective drugs with a favorable safety profile; and the long and arduous currently recommended treatment duration.

Potential solutions have been articulated to face the DR-TB crisis. They include: (i) first of all, prevention of development of drug resistance through high-quality treatment of drug-susceptible TB; (ii) scaling-up of rapid molecular diagnostic tests for detection of DR-TB cases; (iii) prompt access to appropriate DR-TB treatment; (iv) implementation of infection control measures; and (v) high-level political commitment and adequate financing to sustain the efforts over a long period of time.

Emerging scientific and technological advancements hold the promise of introducing precision medicine into the care and control of TB and improve individual and population level of outcomes by addressing the shortcomings of current surveillance, diagnostics, treatment, and monitoring. Several precision medicine tools, some already available and others in exploratory stage, have the potential to enhance TB care and control efforts. These include: pharmacogenomics to optimize dosing of drugs for individual patients and identify potential risks for drug adverse events; biomarkers to discriminate between TB infection and disease, to determine risk of reactivation, to monitor treatment effect, to optimize duration of therapy, and to guide host-directed therapies; prediction of drug susceptibility using genome sequencing techniques; tools to enhance real-time surveillance of drug resistance burden and transmission patterns through linkage of geospatial information and patient-derived data. Furthermore, given the intricacies and complexities of proper treatment of DR-TB, the application of clinical decision support systems, enhanced by artificial intelligence connected with a central database storing the essential information on the mycobacterial strain and the patient, could provide a replicable and scalable solution to precise regimen formulation.

We plan to conduct a workshop on “precision medicine and tuberculosis”, which will convene experts from academia, public health, industry, and policy makers, to explore the ways in which precision approaches can be applied to TB care, control, and research and to identify what infrastructure and frameworks are required to achieve this goal. Participants will also include technology experts who are not at present engaged in TB-related research or activities. Relevant advances in technology as well as unmet

challenges in TB care and control and how they might benefit from application of precision medicine and public health tools will be discussed.

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