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PERSPECTIVE

Communicable and non-communicable diseases: connections, synergies and benefits of integrating care

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There is a growing association between communicable and non-communicable diseases in low- and high-income countries and amongst the rich and the poor. In low- and middle-income countries especially, adults continue to be plagued by communicable diseases such as human immunodeficiency virus/acquired immune-deficiency syndrome (HIV/AIDS) and tuberculosis (TB), while at the same time being increasingly threatened by non-communicable diseases such as cardiovascular disease and diabetes mellitus (DM). Recent global data show that every year about 1.1 million people die from TB, 1.5 million people die from HIV/AIDS, nearly 5 million die from DM and over 9 million die from hypertension-related disease. Most of this mortality is premature.[1] Reducing these deaths on a global scale will require not only the implementation of specific treatments for each disease but also the recognition that there are important interactions between different diseases and useful synergies and benefits that can be gained from exploiting overlapping treatments and strategies. For example, there is a strong association between HIV and TB. HIV exacerbates the risk of TB, including recurrent disease, and increases morbidity and mortality in those with TB, while TB is one of the most important opportunistic infections and the cause of death in many persons living with HIV (PLHIV).

The most important strategy for preventing TB in PLHIV is antiretroviral therapy (ART),[2] and the impact of this intervention can be strengthened by the implementation of the 'Three I's' (intensified TB case finding, isoniazid preventive therapy and infection control). ART is also the most important strategy for reducing mortality in HIV-infected patients with TB, with its impact strengthened by concomitant use of cotrimoxazole and attention to the prevention, diagnosis and treatment of other opportunistic infections.[3] Maximising the benefits of these interventions requires expanded coverage and scale-up of quality-assured HIV testing to reach as many PLHIV and patients with TB as possible, especially those from vulnerable and marginalised groups; this activity is recognised in the UNAIDS recent 90-90-90 strategy.[4]

At the same time, PLHIV are also at increased risk of premature cardiovascular disease due to a higher prevalence of traditional risk factors such as smoking, alcohol and substance abuse, adverse effects of certain antiretroviral (ARV) drugs such as abacavir and some protease inhibitors and the direct effects of HIV itself. In HIV-infected persons, whether they are on ART or not, there is chronic activation of the innate immune system with excessive production of inflammatory markers that in turn are associated with an increased risk of atherosclerosis, coronary artery inflammation and all-cause mortality.[5] Markers of hypercoagulation are increased, and these are associated with systemic clotting, tissue damage and disease progression.[5] HIV-mediated breakdown of the integrity of the gut mucosa and chronic translocation of gut microbial products into the systemic circulation all contribute to this chronic inflammatory state.

Angiotensin converting enzyme (ACE) inhibitors and HMG-CoA reductase inhibitors ('statins') reduce cardiovascular risk through their anti-hypertensive and cholesterol-lowering properties, respectively, but both classes of drug also appear to have anti-inflammatory effects that may be especially beneficial for persons with HIV.[5] Smoking and hypertension are two important risk factors for cardiovascular and other non-communicable diseases for which it is potentially easy to screen, and they deserve far more attention than is currently the case in busy ART clinics in low- and middle-income countries. There is convincing evidence, for example, in Europe and North America, that smoking reduces the life expectancy in PLHIV on ART,[6] which suggests that smoking cessation interventions could have an important impact in improving longer-term outcomes. In a North American cohort of PLHIV, attention to lipid-lowering and anti-hypertension therapy combined with more lipid-friendly and less toxic ARV drugs has been shown to significantly reduce the risk of myocardial infarction,[7] suggesting the importance of including such interventions in the care package of PLHIV.

In another example, there are important associations between DM and TB. DM, both type 1 and type 2, increases the risk of TB by a factor of two or three, and 2012 estimates put the number of adult TB cases associated with DM at just over one million.[8] Persons with dual disease have worse TB treatment outcomes, with delayed sputum culture conversion and an increased risk of death, treatment failure or recurrent TB after successful treatment completion.[9,10] Conversely, TB, like other infections, can worsen blood glucose control and complicate the clinical management of DM. Bi-directional screening and integrated manage-

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ment should help to improve early diagnosis, treatment and health outcomes of both conditions. This was recommended in 2011 when the World Health Organization (WHO) and the International Union Against Tuberculosis and Lung Disease (The Union) launched the Collaborative Framework for Care and Control of Tuberculosis and Diabetes to guide policy makers and implementers in moving forward to combat the epidemic of TB and DM.[11] Some modifications are needed when treating DM in TB patients: sulphonylurea derivatives are best avoided in treating patients with dual disease because of their interaction with rifampicin, leaving insulin and metformin as suitable alternatives. There is preliminary evidence to suggest that metformin in its own right is a promising host-adjunctive therapy for TB, with studies showing in vitro action against *Mycobacterium tuberculosis* and in vivo activity in controlling tuberculous infection and modifying disease severity.[12]

The comorbidities associated with the communicable diseases of HIV/AIDS and TB and their links with non-communicable diseases are emerging research priorities.[13] However, more needs to be done at the implementation level to integrate care and treatment. The oft-quoted comments that TB and ART clinics are too busy to take on the additional tasks around non-communicable diseases or that clinics for non-communicable diseases do not understand or want to take on public health screening for infectious diseases must be acknowledged. However, maintaining the status quo will not help reduce the huge burden of premature mortality or unlock the potential improvements in outcomes of integrated care. Operational research or implementation science would help to pave the way forward by testing whether, for example, screening all PLHIV or TB patients for blood pressure or fasting blood glucose, respectively, is feasible and cost-effective or whether such screening should be targeted at certain individuals based on age, body mass index or smoking status. Depending on context, other non-communicable diseases such as cervical cancer, renal disease and mental illness could also be considered. To date, direct evidence of the benefits of integrated services remains scarce and this needs to change.[14]

Communicable and non-communicable diseases occur within the same patient populations, and it is vital to secure the necessary political and programmatic commitment for integrated, effective and sustainable action to address them. This in turn will help achieve the goal of healthy lives and wellbeing for all.

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