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How can integrated care and research assist in achieving the SDG targets for diabetes, tuberculosis and HIV/AIDS?

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SUMMARY

Integrating the management and care of communicable diseases, such as tuberculosis (TB) and human immunodeficiency virus/acquired immune-deficiency syndrome (HIV/AIDS), and non-communicable diseases, particularly diabetes mellitus (DM), may help to achieve the ambitious health-related targets of the Sustainable Development Goals (SDG 3.3 and 3.4) by 2030. There are five important reasons to integrate. First, we need to integrate to prevent disease. In sub-Saharan Africa, in particular, HIV infection is the main driver of the TB epidemic, and antiretroviral therapy combined with isoniazid preventive therapy (IPT) can reduce TB case notification rates. In Asia, DM is another important driver of the TB epidemic, and preventing or controlling DM can reduce the risk of TB. Second, we need to integrate to diagnose cases. Between a third to a half of those living with HIV, TB or DM do not know they have the disease, and bi-directional screening, whereby TB patients are screened for HIV and DM or people living with HIV and DM are screened for TB, can help to identify these 'missing cases'. Third, we need to integrate to better treat and manage patients who have a combination of two or more of these diseases, so that treatment success and retention on treatment can be optimised. Fourth, we should integrate to ensure better infection control practices for both TB and HIV infection in health facilities and congregate settings, such as prisons. Finally, we should integrate and learn how to monitor, record and report, particularly in relation to the cascade of events implicit in the HIV/AIDS and TB 90-90-90 targets.
KEY WORDS: TB; human immunodeficiency virus/acquired immune-deficiency syndrome; DM; integration; research

IN JANUARY 2016, the new Sustainable Development Goals (SDGs) replaced the 2000–2015 Millennium Development Goals (MDGs), ushering in a new era of ambitions to free the human race from poverty and improve health for present and future generations.[1] The overriding health-related goal, SDG 3, is to ensure healthy lives and promote well-being among all people at all ages. SDG 3 consists of nine main targets and four additional targets (summarised in Table 1); the aim of SDG 3.3 is to end the epidemics of the acquired immune-deficiency syndrome (AIDS), tuberculosis (TB), malaria and neglected tropical diseases by 2030, and that of SDG 3.4 is to reduce premature mortality due to non-communicable diseases (NCDs) by a third.[2]

The task ahead is enormous. According to the SDGs, ending the TB epidemic means reducing TB incidence by 80%, to less than 20 cases per 100 000 population, and TB mortality by 90% relative to 2015 in 15 years.[3] At the same time, no TB-affected families should face catastrophic costs due to TB—defined as spending $\geqslant$20% of an annual household income on TB care. Progress has undoubtedly been made over the previous years: TB incidence declined by 18% between 2000 and 2015, while TB mortality decreased by 47% between 1990 and 2015;[4] however, these downward trajectories will need to be steepened considerably if the SDG targets are to be met. Moreover, in terms of disease burden, the starting point in 2015 is already high. In that year,

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Table 1 Targets for health-related Sustainable Development Goals (SDGs)[2]

Goal 3. Ensure healthy lives and promote well-being for all at all ages
3.1 By 2030, reduce the global maternal mortality ratio to <70/100 000 live births
3.2 By 2030, end preventable deaths of newborns and children aged <5 years, with all countries aiming to reduce neonatal mortality to as low as 12/1000 live births and under-5 mortality to as low as 25/1000 live births
3.3 By 2030, end the epidemics of AIDS, TB, malaria and neglected tropical diseases, and combat hepatitis, water-borne diseases and other communicable diseases
3.4 By 2030, reduce premature mortality from non-communicable diseases by one third through prevention and treatment; and promote mental health and well-being
3.5 Strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol
3.6 By 2020, halve the number of global deaths and injuries from road traffic accidents
3.7 By 2030, ensure universal access to sexual and reproductive health care services
3.8 Achieve universal health coverage, including financial risk protection, access to quality essential health care services and access to safe, effective, quality and affordable essential medicines and vaccines for all
3.9 By 2030, substantially reduce the number of deaths and illnesses from hazardous chemicals and air, water and soil pollution and contamination
3.a Strengthen the implementation of the World Health Organization Framework Convention on Tobacco Control in all countries
3.b Support the research and development of vaccines and medicines for communicable and non-communicable diseases and provide access to affordable essential medicines and vaccines
3.c Substantially increase health financing and recruitment, development, training and retention of the health workforce in developing countries
3.d Strengthen the capacity of all countries, in particular developing countries, for early warning, risk reduction and management of national and global health risks

AIDS = acquired immune-deficiency syndrome; TB = tuberculosis.

there were an estimated 10.4 million new TB cases worldwide, 580 000 of whom had multidrug-resistant TB (MDR-TB, defined as *Mycobacterium tuberculosis* resistant to at least isoniazid [INH] and rifampicin [RMP] or RMP alone).[4] Although TB is potentially curable, there were 1.8 million TB deaths in 2015, 400 000 of which were associated with the human immunodeficiency virus (HIV).[4]

Ending the HIV/AIDS epidemic means that there should be less than one new HIV infection and one new AIDS-related death per 1000 population, so that HIV is no longer a major threat to public health.[5] Great progress has also been made, with a 30–40% decrease in the incidence of new HIV infections and HIV-related deaths during the MDG era.[6] However, as with TB, the public health burden is still immense, with an estimated 2.1 million new HIV infections and 1.1 million HIV-related deaths in 2015.[7] It is also of concern that HIV incidence has largely plateaued in the last few years. In some countries, such as in Eastern Europe, Central Asia, North Africa and the Caribbean, and among some key populations—people who inject drugs, transgender people, sex workers and men who have sex with men—HIV incidence is actually rising.[8] The world is far from being on top of this epidemic.

Finally, diabetes mellitus (DM) has emerged as one of the largest global health emergencies of the twenty-first century. According to estimates from the International Diabetes Federation, there were 415 million people living with DM worldwide in 2015, with numbers set to rise to 642 million by 2040.[9] Each year, another 10 million new people are estimated to develop DM and up to 5 million persons die from DM-related complications. This is a global pandemic that is clearly out of control.

THE NEED TO INTEGRATE

Reducing TB, HIV/AIDS and DM incidence and mortality on a global scale will require not only the implementation of specific preventive interventions and treatment for each disease, but also the recognition that there is significant interaction between the three different diseases, and useful synergies and benefits to be gained from taking advantage of overlapping diagnostic and treatment strategies. We wish to discuss five main areas where we believe that integrated care and research, particularly operational research, can help to achieve the ambitious goals and targets set by the global community.

Integration to prevent disease

HIV-associated tuberculosis

Sub-Saharan Africa, and particularly southern Africa, has been in the grip of an HIV-driven TB epidemic for more than three decades. Between 1985 and well into the late 1990s, TB case notifications rose by over 500% in some countries, and TB control efforts were severely disrupted due to HIV-associated drug reactions and increased morbidity and mortality.[10] The advent and subsequent scale-up of rapid HIV testing and antiretroviral therapy (ART) have been game changers in this regard. The use of rapid, simple-to-use tests meant that HIV testing could be decentralised, testing-related tasks were shared and information on HIV status was easily available. ART reverses the immune dysfunction associated with HIV, leading to rapid functional recovery of mycobacteria-specific immune responses, which in turn enhance the host's capacity to restrict mycobacterial growth.[11,12] As a result, ART has a potent TB preventive effect. A systematic review and meta-analysis of 11 studies from 2002 to 2011 showed that ART was associated with a 65% reduction in TB incidence across all baseline CD4 counts in people living with HIV (PLHIV).[13]

These data on individual PLHIV are further supported by mathematical models predicting the enormous benefit of early ART initiation on TB

prevention at the population level. Using data from the southern African HIV/AIDS epidemic, a strategy of universal HIV testing of adults, with immediate initiation of ART in those diagnosed as HIV-positive, might be expected to halve the incidence of HIV-associated TB within a 5-year period, both through a direct effect, as described earlier, and through an indirect effect, by reducing HIV transmission from infected to non-infected partners.[14] At the programme level, although PLHIV routinely initiate ART late, with advanced HIV-related disease and low CD4 cell counts, it has been shown in Swaziland, Zimbabwe and Malawi that when ART coverage in HIV-infected populations reaches a high level, national TB case notification rates decrease.[15–17] Furthermore, in Malawi and Kenya there is evidence to suggest that the reduction in HIV-positive TB cases has a beneficial effect on transmission of *M. tuberculosis* in the community as a whole, with fewer cases of TB also occurring in non-HIV-infected populations.[17,18]

In settings where HIV is prevalent, the administration of ART to PLHIV is therefore a key TB preventive measure, and modelling studies suggest that the earlier ART is started, the better the prevention effect.[14] The 2016 World Health Organization (WHO) guidelines, which recommend starting ART in any person diagnosed with HIV, regardless of WHO clinical stage or CD4 cell count, is a welcome intervention in this regard.[19] The positive effects of ART may be further augmented by the addition of IPT. Randomised controlled trials conducted in South Africa by Rangaka et al.,[20] and in Cote d'Ivoire by the TEMPRANO team,[21] have shown that the addition of INH to ART further reduces TB incidence by $\geqslant 30\%$. Analysis of other studies suggests that in high TB exposure environments IPT might need to be given indefinitely.[22]

While it is clear that giving ART and IPT to all PLHIV will reduce TB incidence, there are some important knowledge gaps in terms of implementing the interventions on the ground. What is needed from an integrated research programme is how best to deliver ART and IPT in the field, when is the optimal time to introduce IPT, whether this therapy should be given indefinitely under routine conditions, how to monitor for serious side effects such as hepatitis in large decentralised populations, how to retain people on treatment, particularly when they are feeling well, and how to measure the impact of these interventions in routine settings. Before the advent of ART, the administration of INH for 12 months after completion of anti-tuberculosis treatment significantly reduced the risk of recurrent TB,[23] but whether this holds true for patients already on ART is not certain, and requires further integrated research.

Diabetes-associated tuberculosis

In 2007 and 2008, two systematic reviews highlighted the significant risk among DM patients of developing active TB, with cohort studies showing a relative risk of 3.1 (95% confidence interval [CI] 2.3–4.3) and case-control studies showing odds ratios of 1.2 to 7.8.[24,25] These findings have since been confirmed, and there is now general agreement that the risk of TB in persons with DM is three times higher than in the general population.[26] Both type 1 and type 2 DM increase the risk of TB, but as type 2 disease accounts for $\geqslant 90\%$ of global cases of DM, the public health burden of comorbid disease from this type of DM dominates the interaction. In 2012, it was estimated that the number of adult TB cases associated with DM was 1 042 000, similar to what was observed for HIV-associated TB.[26]

The Asian subcontinent has the world's largest DM burden,[27] and the Asian urban poor are those most affected by both DM and TB. Pan et al. estimated in 2015 that if the DM epidemic continues to increase as it is currently doing, TB incidence will decrease by less than 10% in the next 15 years,[28] and there will be no chance of reaching the TB-related SDG goal. The precise reasons for the increased risk of TB in persons with DM are not clear, but there is growing evidence that individuals with uncontrolled hyperglycaemia are at higher risk for TB, suggesting that hyperglycaemia is an important determinant in this interaction.[29,30] This is supported by observations that the risk of TB is highest in the first 1–2 years after the diagnosis of DM, most probably because the disease is not well controlled at this time.[31,32] There is also some preliminary evidence to suggest that enhanced DM management and better DM control reduces the risk of TB.[33]

This growing body of knowledge suggests that in areas of high TB prevalence, better prevention of DM through improved attention to lifestyle management (including diet and exercise), possible use of metformin in those at risk of DM and better care of those with DM may help to accelerate a decline in TB cases. More evidence in this regard is needed. Randomised controlled trials should also be considered to determine whether TB preventive therapy to reduce the risk of TB is cost-effective in persons with DM. Finally, laboratory-based research, such as the TANDEM initiative,[34] which assesses the mechanisms of association between *M. tuberculosis* and type 2 DM at the cellular and genetic level, will be crucial to better understand the links between the two diseases.

Integration to diagnose disease

In the case of all three diseases (TB, HIV/AIDS and DM), many people either do not know they have the disease or, if they do know, they are not referred or registered for standardised treatment. In 2015, only

Table 2 WHO-recommended collaborative TB-HIV activities[37]

- A. Establish and strengthen mechanisms for delivering integrated TB and HIV services
  - A.1. Set up and strengthen a co-ordinating body for collaborative TB-HIV activities functional at all levels
  - A.2. Determine HIV prevalence among TB patients and TB prevalence among PLHIV
  - A.3. Carry out joint TB-HIV planning to integrate the delivery of TB and HIV services
  - A.4. Monitor and evaluate collaborative TB-HIV activities
- B. Reduce the burden of TB in PLHIV and initiate early ART (the *Three I's* for HIV-TB)
  - B.1. Intensify TB case finding and ensure high-quality anti-tuberculosis treatment
  - B.2. Initiate TB prevention with isoniazid preventive therapy and early ART
  - B.3. Ensure control of tuberculous infection in health care facilities and congregate settings
- C. Reduce the burden of HIV in TB patients
  - C.1. Provide HIV testing and counselling to patients with presumptive and diagnosed TB
  - C.2. Provide HIV prevention interventions for patients with presumptive and diagnosed TB
  - C.3. Provide cotrimoxazole preventive therapy for TB patients living with HIV
  - C.4. Ensure HIV prevention interventions, treatment and care for TB patients living with HIV
  - C.5. Provide ART for TB patients living with HIV

WHO = World Health Organization; TB = tuberculosis; HIV = human immunodeficiency virus; PLHIV = people living with HIV; ART = antiretroviral therapy.

Table 3 The activities recommended in the Collaborative Framework for the care and control of TB and DM[38]

- A. Establish mechanisms for collaboration
  - A.1. Set up the means and resources for co-ordinating DM and TB activities
  - A.2. Conduct surveillance of TB disease prevalence among persons with DM in medium and high TB burden settings
  - A.3. Conduct surveillance of DM prevalence in TB patients in all countries
  - A.4. Conduct monitoring and evaluation of collaborative DM-TB activities
- B. Detect and manage TB in patients with DM
  - B.1. Increase TB detection in persons with DM
  - B.2. Ensure TB infection control in health care settings where DM is managed
  - B.3. Ensure high-quality anti-tuberculosis treatment and management in people with DM
- C. Detect and manage DM in patients with TB
  - C.1. Screen TB patients for DM
  - C.2. Ensure high-quality DM management in TB patients

TB = tuberculosis; DM = diabetes mellitus.

6.1 million of an estimated 10.4 million new TB cases were diagnosed or notified to national authorities—a 4.3 million notification gap.[4] According to the Joint United Nations Programme on HIV/AIDS, more than half of PLHIV do not know their HIV status,[8] and about half of those with DM are similarly undiagnosed.[9]

The diagnosis of the three diseases is not difficult. HIV diagnosis depends on a rapid, easy-to-use dipstick, with results available in less than 30 min. DM can be diagnosed using fasting plasma glucose, 2-h plasma glucose following a 75 g oral glucose tolerance test (OGTT), random plasma glucose in a patient with classic hyperglycaemic symptoms or glycosylated haemoglobin (HbA_{1C}). Recommended cut-off values for each of these tests have been published by the WHO.[35] In most resource-poor settings, DM is diagnosed using a simple portable glucometer, along with a glucose test strip. TB diagnosis is more difficult, relying traditionally on sputum smear microscopy for acid-fast bacilli, with or without chest radiography. However, increased access to nucleic-acid amplification testing, such as the Xpert® MTB/RIF assay (Cepheid Inc, Sunnyvale, CA, USA), which provides results in less than 2 h, is beginning to facilitate TB diagnosis.[36]

Bi-directional screening will help to increase the numbers of patients being diagnosed. The 2012 WHO TB/HIV Policy Guidance recommends that all TB patients be tested for HIV, and this recommendation extends to persons with presumptive TB as well as the index patients' partners and family (Table 2).[37] In 2015, 55% of notified TB patients worldwide had a documented HIV test, with the highest uptake in the African region, at 81%.[4] Full implementation of this recommendation, with HIV testing uptake at 100%, would significantly increase the numbers of PLHIV who know their HIV status. Similarly, the Collaborative Framework for Care and Control of Tuberculosis and Diabetes, launched in 2011 by the WHO and the International Union Against Tuberculosis and Lung Disease (The Union), recommended that all TB patients be screened for DM (Table 3).[38] While there are no annual global figures for the number of DM persons who can be identified by this approach, two systematic reviews showed that screening TB patients for DM yielded a high prevalence of DM, ranging from 1.9% to 45%, with a median global DM prevalence of 16% among TB patients.[39,40] Implementation of this recommendation would increase the numbers of people with DM who know they have the disease.

The WHO TB/HIV Policy and the WHO/Union Framework for DM and TB also recommend that PLHIV or persons with DM be screened proactively for TB.[37,38] In 2015, in 12 high TB-HIV burden countries, 231 637 (10%) of 2.3 million people newly enrolled in HIV care were diagnosed with TB.[4] There are no global or regional data on the yield of TB among persons screened with DM. However, two large studies conducted in routine health service settings in China and India found that TB case notification rates ranged from 352 to 774 per 100 000 persons with DM screened in China, and from 642 to 956 per 100 000 persons with DM screened in India; these yields were significantly higher than those found from passive case finding among the general population.[41,42]

Integrated research is needed to guide the best way forward. Bi-directional screening for HIV-TB needs

to be assessed in TB hot spots such as urban slums, the mining industry, refugee camps and prisons, and among those vulnerable for HIV infection, such as persons who inject drugs and other key populations. Established diagnostic tools are available, but how and when they should best be used needs to be clarified. As sick, hospitalised HIV-infected patients with disseminated TB often cannot produce sputum, simpler specimens such as urine may need to be considered. Xpert testing of urine has been used successfully as a rapid screening investigation for TB among adult HIV-infected in-patients.[43] Measurement of urine-based lipoarabinomannan (LAM) as an additional rapid screening test for TB in HIV-infected in-patients with low CD4 cell counts and suspected TB has good sensitivity and specificity, and has been associated with reduced 8-week mortality in this group.[44]

New technologies for DM screening among TB patients also need to be investigated. Such methods should be rapid, should not require a fasting state, should allow the provider to differentiate between transient and longer-term hyperglycaemia, should be inexpensive and should require little specialised infrastructure. Several methods are currently under development, such as point-of-care glycated haemoglobin and glycated albumin assays.[45]

Integration to treat and manage disease

The WHO recommends that all TB patients undergo provider-initiated HIV testing and counselling, and that cotrimoxazole and ART be given as soon as possible after the start of anti-tuberculosis treatment in those diagnosed as HIV-positive.[19,37] ART substantially improves the prognosis of patients with HIV-associated TB, with excellent immunological and virological responses, reduction of mortality by 65–95% and reduced recurrence of TB after treatment is completed.[46] Cotrimoxazole preventive therapy further reduces mortality risk and results in fewer episodes of malaria and increased overall life expectancy.[47] Recent global estimates for the proportion of HIV-infected TB patients on cotrimoxazole are not available, but 78% of notified HIV-infected TB patients worldwide started ART in 2015, with some countries such as India, Malawi, Mozambique, Namibia and Swaziland having ART uptake rates of >90%.[4] The less than 100% ART uptake and delays in ART initiation are probably the two main explanations for the 75% treatment success rate among HIV-infected TB patients, which is lower than the 83% achieved in HIV-negative TB patients.[4] What is needed here is for TB and HIV programmes to work out how to achieve 100% HIV testing uptake, and for those patients with HIV-associated TB, 100% uptake of cotrimoxazole preventive therapy and ART.

Integrated HIV-TB services have a better chance of delivering better quality care and treatment and achieving these indicators compared with services that are isolated and focused only on TB or HIV-infected patients. There are successful examples of integrated TB and HIV care in the primary care setting in rural South Africa,[48,49] and good lessons can be learned from this and other parts of Africa about providing comprehensive HIV-TB care in the TB clinic for the duration of anti-tuberculosis treatment, followed by transfer to the HIV/ART programme after anti-tuberculosis treatment has been completed.[50]

Patients with DM-associated TB also fare badly on standard treatment. There is some evidence, although not consistent, that DM prolongs culture positivity at 2–3 months of treatment.[51] DM increases the risk of death during anti-tuberculosis treatment: 23 unadjusted studies showed a pooled relative risk (RR) of 1.89 (95%CI 1.52–2.36), and four studies that adjusted for age and other potential confounding factors found an effect estimate of 4.95 (95%CI 2.6–9.10).[51] DM also increases the risk of TB relapse: five studies reported a pooled RR of 3.89 (95%CI 2.43–6.23).[51] The mechanism of relapse remains unclear, and further research is needed to determine whether this is due to a reactivation of the former infection (true relapse) or re-infection with a new strain of *M. tuberculosis*. For several years, it was believed that there was no consistent association between DM and the development of MDR-TB. However, a recent systematic review and meta-analysis of 13 studies has shown that DM is an independent risk factor for the development of MDR-TB.[52] Poor treatment outcomes can be worsened by the addition of smoking: one study from Korea reported that smoking more than one pack of cigarettes per day significantly increased the risk of death in patients with dual disease.[53] Improved case management and better DM control appear to improve TB treatment outcomes,[33] although more work and evidence are needed in this area.

Some of the key clinical and programmatic areas in need of research to address the treatment of DM-TB are shown in Table 4.[54,55] Recent research has suggested that anti-tuberculosis treatment could be extended beyond 6 months in people with DM,[56] but the evidence is weak and needs to be strengthened, particularly as the WHO does not currently recommend a policy for extending treatment. Oral sulphonylurea derivatives interact with RMP, but more knowledge is needed on whether newer drugs such as pioglitazone, incretin-based therapies (glucagon-like peptide 1 receptor antagonists and dipeptidyl peptidase 4 inhibitors) and sodium glucose transporter 2 inhibitors have similar interactions. Based on current guidelines, DM is best managed with diet, lifestyle modification, metformin and insulin in case of simultaneous use of anti-tuberculosis medication.

Table 4 Key areas for clinical and programmatic research related to treatment and care of patients with both DM and TB

- Length of anti-tuberculosis treatment: is a 6-month treatment regimen adequate?
- Better control of DM during anti-tuberculosis treatment: how to achieve better control, and does this lead to better treatment outcomes?
- Drug-drug interactions: how does rifampicin interact with oral hypoglycaemic drugs and do the drug-drug interactions affect drug levels in vivo?
- Drug-drug toxicity: what are the principal toxicities observed in clinical practice and how can these best be prevented or treated?
- Medication adherence: what can be done to reduce the pill burden and side effects and ensure patients take medication on a daily basis?
- Integrated care clinics: is it feasible to run clinics providing integrated care for HIV/AIDS, TB and DM and include diagnosis and treatment for other non-communicable diseases such as hypertension and cardiovascular disease?
- Lifestyle advice: in integrated care clinics, is it feasible for health care workers to address dietary issues, proper daily exercise and persuade patients to quit smoking and reduce alcohol consumption?

DM = diabetes mellitus; TB = tuberculosis; HIV = human immunodeficiency virus; AIDS = acquired immune-deficiency syndrome.

There is some evidence that metformin may also be a useful adjunct to anti-tuberculosis treatment by augmenting protective host immune responses to *M. tuberculosis*, endorsing the use of this medication for treating patients with dual disease.[57]

There has been some reported experience of clinics that integrate treatment and care for communicable and NCDs, with feasibility and success being shown in Cambodia and Ethiopia.[58,59] Operational research or implementation science would help to pave the way forward by testing whether, for example, screening patients with HIV infection or TB for fasting blood glucose or other NCDs is feasible and cost-effective or whether such screening should be targeted at certain individuals based on age, body mass index or smoking status. A phased approach to DM screening and treatment would be advisable and, depending on context, other NCDs such as cardiovascular disease, cervical cancer, renal disease and mental illness might also be considered as part of the screening approach. Direct evidence of the costs and benefits of integrated services remains scarce, and further research in this area is essential.[60]

Integration to better implement infection control in health facilities and congregate settings

Infection control (IC) is the foundation for preventing exposure to tubercle bacilli among non-infected individuals in health facilities. Health facility exposure accounts for an appreciable proportion of the total risk of tuberculous infection among patients who are repeatedly attending health facilities for chronic care in high TB burden settings.[61] In high HIV prevalence areas, HIV-related TB accounts for a large proportion of hospital admissions and out-

Table 5 Infection control guidelines for reducing transmission of *Mycobacterium tuberculosis* in health facilities, particularly for ART and DM clinics[65]

Facility-level measures:
- Rethink and redesign the use of available spaces, renovate existing facilities or construct new facilities
- Conduct on-site surveillance of TB disease in health workers, particularly those working in ART or DM clinics
- Communicate about TB transmission to health workers, patients and visitors
- Monitor and evaluate the package of TB infection control measures

Administrative measures:
- Promptly identify people with TB symptoms, keep infectious patients separate from others, institute cough etiquette and respiratory hygiene and minimise time spent in health care facilities
- Provide a package of prevention and care interventions for health workers, including HIV prevention, ART and isoniazid preventive therapy for HIV-positive health workers

Environmental protection:
- Ensure good natural ventilation (open windows and doors, enlarged or additional windows, open skylights for cross-ventilation)
- Use ultraviolet germicidal irradiation fixtures (if applicable and affordable)

Personal protection:
- Use particulate respirators

ART = antiretroviral therapy; DM = diabetes mellitus; TB = tuberculosis; HIV = human immunodeficiency virus.

patient consultations, resulting in intense TB transmission within congested facilities and presenting a difficult challenge for IC, particularly in case of transmission of MDR-TB and extensively drug-resistant disease.[62,63]

There is less experience or knowledge about TB transmission within DM care facilities, although a recent meta-analysis highlighted the association between DM and the increased risk of primary transmission of MDR-TB, which raises concerns about the possibility of health facility-based transmission.[52] A rapid assessment of 10 DM clinics in China showed poor TB IC practices.[64]

The most recent WHO TB IC guidelines are focused on early identification, isolation and treatment of those presumed to have TB, personal protective measures for health care workers combined with infrastructure modifications (such as enlarged windows, open skylights, open-air waiting rooms) and better organisation to avoid congestion and ensure appropriate air flow and patient flow within facilities (Table 5).[65] More work is needed to assess current IC practices in HIV/ART and DM clinics, and regular supervision should be undertaken to ensure that guidelines are adhered to.

Integration for monitoring, recording and reporting

Finally, there is an urgent and imperative need for programmes to learn from each other about how to monitor, record and report. Both TB and HIV/AIDS programmes have good recording and reporting

Table 6 90-90-90 targets for HIV/AIDS and TB[66,67]

90-90-90 targets for HIV/AIDS
• 90% of those living with HIV should know their HIV status
• 90% of those diagnosed with HIV should be on sustained ART
• 90% of those on ART should have undetectable viral loads
90-(90)-90 targets for TB
• Reach at least 90% of all people with TB
• As a part of this approach reach at least (90%) of the key populations
• Achieve at least 90% treatment success for all people diagnosed with TB

HIV = human immunodeficiency virus; AIDS = acquired immune-deficiency syndrome; TB = tuberculosis; ART = antiretroviral therapy.

systems that each year result in up-to-date global reports on patients diagnosed and enrolled for treatment, along with treatment outcomes.

Since the start of the SDG era, the TB and HIV/AIDS communities have pledged to end their respective epidemics by 2030, and both UNAIDS and the global TB caucus have signed up to 90-90-90 targets (Table 6).[66,67] In the case of HIV/AIDS, if the 90-90-90 target strategy is achieved, nearly three quarters of all PLHIV will be on treatment and virally suppressed. Modelling studies suggest that achievement of this outcome will enable the world to end the AIDS epidemic by 2030, defined as less than one new HIV infection and one new AIDS-related death per 1000 population.[5] Similarly, for TB, achievement of the 90-(90)-90 targets (see Table 6) should facilitate the ending of the TB epidemic by 2030.

The 90-90-90 targets imply a cascade whereby patients enrolled in their monthly, quarterly or annual cohorts move from one step to the next. There are currently no established monitoring systems in place within routine services to track this movement. As their denominator for treatment outcomes, many programmes use the patients who are registered for either TB treatment or ART, and despite calls to change this paradigm[68] there seems little enthusiasm for moving this denominator upstream and starting with patients diagnosed with TB or HIV. Changing the denominator will mean that rates of TB treatment success or retention in ART will inevitably worsen, as pre-treatment attrition in many TB programmes and ART programmes is considerable.[68,69] This is nevertheless the honest approach, and the way to start monitoring the 90-90-90 cascade through the routine services.

In the case of DM, it is fair to say that no cohort monitoring or assessment of treatment outcomes takes place for most patients. Studies in Malawi and Jordan have shown the feasibility of using the TB DOTS approach for monitoring quarterly and cumulative registrations and treatment outcomes in persons with DM,[70,71] but these have yet to be widely accepted in practice.

Tracking large numbers of patients with TB, HIV/AIDS or DM from one step to another and reporting regularly on cumulative treatment outcomes will require another paradigm shift away from paper-based recording tools to robust, simple, cheap and real-time electronic medical record systems, even in low-resource settings.[72] Without electronic medical record systems, too much time will be spent matching data from different paper-based records or tally-counting on treatment outcomes, time that could be better spent providing patient-centred care.

CONCLUSION

For the diagnosis, care and prevention of TB, HIV/AIDS and DM, we already have many of the tools in hand and we have undertaken pilot studies to learn about integrated services to provide better quality care for our patients. However, we seem unable to use these tools and lessons learned to our best advantage. The so-called 'Know–Do' gap is large. This has to change. Researchers will need to work much more collaboratively with national and non-governmental field-based staff and communities to ensure optimal delivery of health services for patients.

Is there a need for new tools? For TB, the answer is certainly yes. TB care and prevention would be greatly enhanced with better point-of-care diagnostic tests, better and safer drugs, shorter treatment regimens and a vaccine that is safer and more effective than bacille Calmette-Guérin.[73] For HIV/AIDS, much can be done with the tools already available. Considerable efforts are being made to identify a cure for HIV/AIDS, either through a sterilising cure (whereby all latent HIV-infected cells are eliminated) or a functional cure (whereby latent HIV persists, but viraemia is very low or absent without the use of ART).[74,75] However, these approaches are currently either not feasible for scale-up or have met setbacks,[76] and research continues. Some argue that the only guaranteed way to end the AIDS epidemic is through the deployment of a safe and effective vaccine, but here again there has been limited success. To date, only three vaccines have completed clinical trials, with two of the three vaccines failing their efficacy trials and the third showing modest efficacy of only 31%.[77,78] For DM, the task is inherently more difficult, with a fundamental need to help populations to change their lifestyles to prevent the rising incidence and prevalence of type 2 DM.[79] Without new public health legislation to tackle the food and beverage industry, it is unlikely that significant progress will be made.

Many of the SDGs focus on poverty, hunger, education, clean energy, employment, cities, climate change and ecosystems,[2] and by seriously addressing these upstream issues we can hope to reduce both incidence and mortality from the disease triad. Strengthening the implementation of the WHO

Framework Convention on Tobacco Control cuts across TB, DM and HIV/AIDS and would lead to a reduction in incident TB and improved outcomes for all three diseases. There is a need to work within the SDG framework, to take risks and to think out of the box, and if we are able to do this the SDG goals and targets might just be achieved.

Disclaimer: The views expressed in this document are those of the authors and may not necessarily reflect those of their affiliated institutions.

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RÉSUMÉ

Intégrer la prise en charge des maladies transmissibles, comme la tuberculose (TB) et l'infection par le virus de l'immunodéficience humaine (VIH) ou syndrome d'immunodéficience acquise (SIDA), et non transmissibles, particulièrement le diabète (DM), peut contribuer à atteindre les cibles sanitaires ambitieuses des Objectifs de Développement Durable (ODD 3.3 et 3.4) d'ici 2030. Il y a cinq raisons majeures à cette intégration. En premier lieu, cette intégration est nécessaire à la prévention des maladies. En Afrique subsaharienne en particulier, l'infection à VIH est le principal moteur de l'épidémie de TB et le traitement antirétroviral combiné au traitement préventif par isoniazide peut réduire les taux de notification des cas de TB. En Asie, le DM est un autre important moteur de l'épidémie de TB, et la prévention ou la lutte contre le DM peut réduire le risque de TB. Deuxièmement, nous devons réaliser cette intégration pour diagnostiquer les cas. Entre un tiers et une moitié des personnes vivant avec le VIH, la TB ou le DM ne savent pas qu'ils sont atteints de ces maladies ; un dépistage dans les deux directions—grâce auquel les patients tuberculeux bénéficient d'un dépistage du VIH et du DM ou les personnes vivant avec le VIH et le DM bénéficient d'une recherche de TB—peut contribuer à identifier les « cas manqués ». Troisièmement, cette intégration est nécessaire pour mieux traiter et prendre en charge les patients qui ont une combinaison de deux ou plusieurs de ces pathologies afin d'optimiser le taux de succès du traitement et la rétention sous traitement. Quatrièmement, cette intégration doit assurer de meilleures pratiques de lutte contre l'infection à la fois pour la TB et l'infection à VIH dans les structures de santé et les lieux de promiscuité comme les prisons. Enfin, nous devons intégrer ces maladies et apprendre comment les suivre, les enregistrer et les déclarer, surtout dans le cadre de la cascade d'événements implicites dans les cibles 90-90-90 des cibles du VIH/SIDA et de la TB.

RESUMEN

Integrar la gestión y la atención de las enfermedades transmisibles, como la tuberculosis (TB) e infección por el virus de la inmunodeficiencia humana (VIH) y síndrome de inmunodeficiencia adquirida (SIDA) y las enfermedades no transmisibles, sobre todo la diabetes (DM), contribuiría a alcanzar las ambiciosas metas relacionadas con la salud de los Objetivos de Desarrollo Sostenible (ODS 3.3 y 3.4) hacia el 2030. Existen cinco razones importantes para la integración. En primer lugar, la integración es necesaria con el fin de prevenir las enfermedades. En especial en África subsahariana, la infección por el VIH constituye el principal factor determinante de la epidemia de TB y la asociación del tratamiento antirretrovírico y el tratamiento preventivo con isoniazida puede disminuir las tasas de notificación de casos. En Asia, la DM representa otro factor determinante de la epidemia de TB y la prevención o la estabilización de la DM puede reducir el riesgo de contraer la TB. En segundo lugar, la integración es necesaria al diagnóstico de los casos. De un tercio a la mitad de las personas que sufren la infección por el VIH, la TB o la DM desconocen su diagnóstico y la detección bidireccional, en la cual los pacientes con TB participan al cribado de la infección por el VIH y los pacientes con DM o infección por el VIH participan al cribado de la TB, puede contribuir a detectar estos 'casos pasados por alto'. En tercer lugar, la integración es necesaria para atender y tratar mejor a los pacientes en quienes concurren dos o más de estas enfermedades, con el propósito de optimizar la eficacia terapéutica y la fidelización al tratamiento. En cuarto lugar, la integración es indispensable con el fin de garantizar mejores prácticas de control de las infecciones en materia de TB y también de infección por el VIH en los establecimientos de atención de salud y los entornos colectivos como las prisiones. Por último, es esencial integrar y aprender los métodos de supervisión, registro y notificación, sobre todo en relación proceso asistencial continuo del VIH/SIDA y la TB frente a las metas '90-90-90′.