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NOTES FROM THE FIELD

Decline in national tuberculosis notifications with national scale-up of antiretroviral therapy in Malawi

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From 2000 to 2012, Malawi scaled up antiretroviral therapy (ART) from <3000 to 404905 persons living with HIV/AIDS (human immunodeficiency virus/acquired immunedeficiency syndrome), representing an ART coverage of 40.6% among those living with HIV. During this time, annual tuberculosis (TB) notifications declined by 28%, from 28234 to 20463. Percentage declines in annual TB case notifications were as follows: new TB (26%), recurrent TB (40%), new smear-positive pulmonary TB (19%), new smear-negative pulmonary TB (42%), extra-pulmonary TB (19%), HIV-positive TB (30%) and HIV-negative TB (10%). The decline in TB notifications is associated with ART scale-up, supporting its value in controlling TB in high HIV prevalence areas in sub-Saharan Africa.

Human immunodeficiency virus (HIV) infection is the strongest risk factor for developing tuberculosis (TB), and in the last two decades it has fuelled the resurgence of the disease, particularly in sub-Saharan Africa. In 2012, an estimated 1.1 million people living with HIV/AIDS (acquired immune-deficiency syndrome) (PLHIV) developed TB, of whom 320000 died.[1] A systematic review of 11 studies from around the world found that antiretroviral therapy (ART) in PLHIV was strongly associated with a reduction in TB incidence, and that this effect was found across all CD4 count strata.[2] At the programme level, it has also been documented in Thyolo District, rural Malawi,[3] and in Cape Town, South Africa,[4] that when ART scale-up achieves a high level of coverage in a population TB notification rates decline. In rural Malawi, this reduction was noted for both new and recurrent TB.[3] The finding in Malawi of a reduction in recurrent TB is in line with other systematic review evidence showing that ART reduces the risk of TB relapse in PLHIV.[5]

As far as we are aware, there have been no reports comparing national TB notifications with national scale-up of ART. Malawi has an excellent national recording and reporting system for both TB patients as well as for PLHIV on ART.[6] We took the opportunity of using these reporting systems to describe the association between ART scale-up and annual national TB case notifications in Malawi from 2000 to 2012.

ASPECT OF INTEREST

This was a retrospective descriptive study using national reports. Malawi is a poor country in central-southern Africa with a current population of approximately 16 million and a severe HIV/AIDS epidemic, with an estimated 1 million HIV-infected persons. ART scale-up started in 2004, with quarterly reports of numbers of patients alive and retained on treatment. PLHIV are eligible for ART if they have World Health Organization clinical stage 3 or 4 disease or a CD4 count below the nationally agreed threshold (⩽250 cells/μl before 2010 and ⩽350 cells/μl thereafter). In the first 6 years of scale-up, first-line treatment comprised mainly a fixed-dose combination of stavudine+lamivudine (3TC) + nevirapine; however, since 2011 there has been a gradual change to tenofovir+3TC+efavirenz. Malawi has had a well-respected DOTS-based National TB Programme (NTP) since 1985, with case finding, diagnosis, registration, treatment and treatment outcomes following agreed international guidelines.[7] TB patients are classified as new or previously treated disease, and divided into smear-positive pulmonary TB (PTB), smear-negative PTB and extra-pulmonary TB (EPTB).[7]

The study population included all adults and children with HIV who were recorded as alive and retained on ART at the end of each year (2000–2012), and all adults and children registered nationally each year with TB (2000–2012). Data sources were national reports from the NTP and the HIV Department, Ministry of Health, Lilongwe, Malawi. Given the change in national ART eligibility criteria during the course of the study, ART coverage was calculated using the total HIV population as the denominator (from national epidemiological projections using Spectrum). TB data were further stratified by new and previously treated disease, types of TB and HIV status. Data were analysed descriptively, and the highest and lowest annual numbers of TB patients were compared using χ^2 tests, odds ratios (ORs) and 95% confidence intervals (CIs) where appropriate. Levels of significance were set at 5%.

The number of people alive and retained on ART from 2000 to 2012 increased progressively from <3000 to 404905, with the population coverage of ART increasing from <0.5% to 41% (Figure 1). The trend in TB case notifications is shown in Figure 2. Over the last 6 years, there has been a clear downward trend in the numbers of all TB cases and of those stratified by category, type of TB and HIV status, with the lowest numbers observed in 2011 or 2012. When comparing the highest with the lowest numbers of cases in 2011 or 2012, the per cent decreases were as

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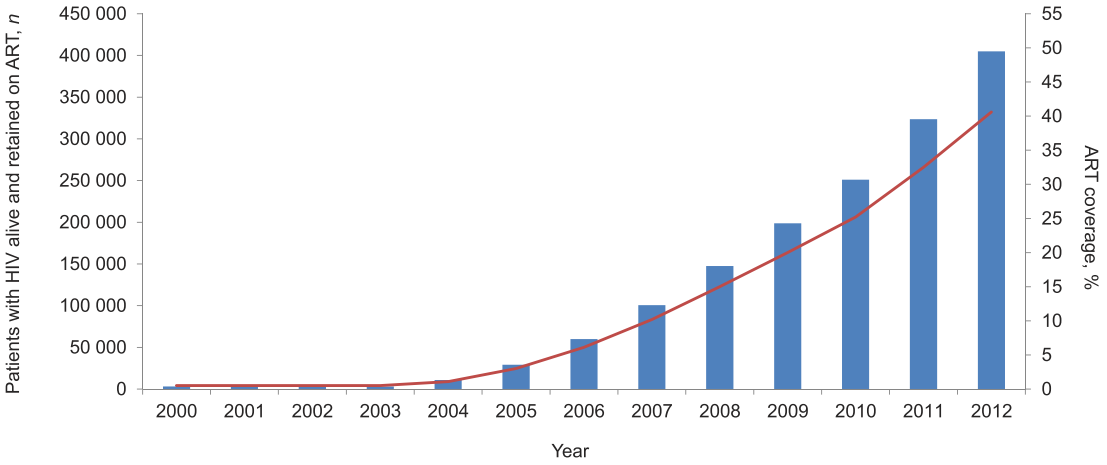

FIGURE 1 Numbers and coverage of patients with HIV infection alive and retained on ART in Malawi, 2000–2012. ART coverage was calculated using the total HIV population as the denominator from national epidemiological projections using Spectrum. HIV = human immunodeficiency virus; ART = antiretroviral therapy.

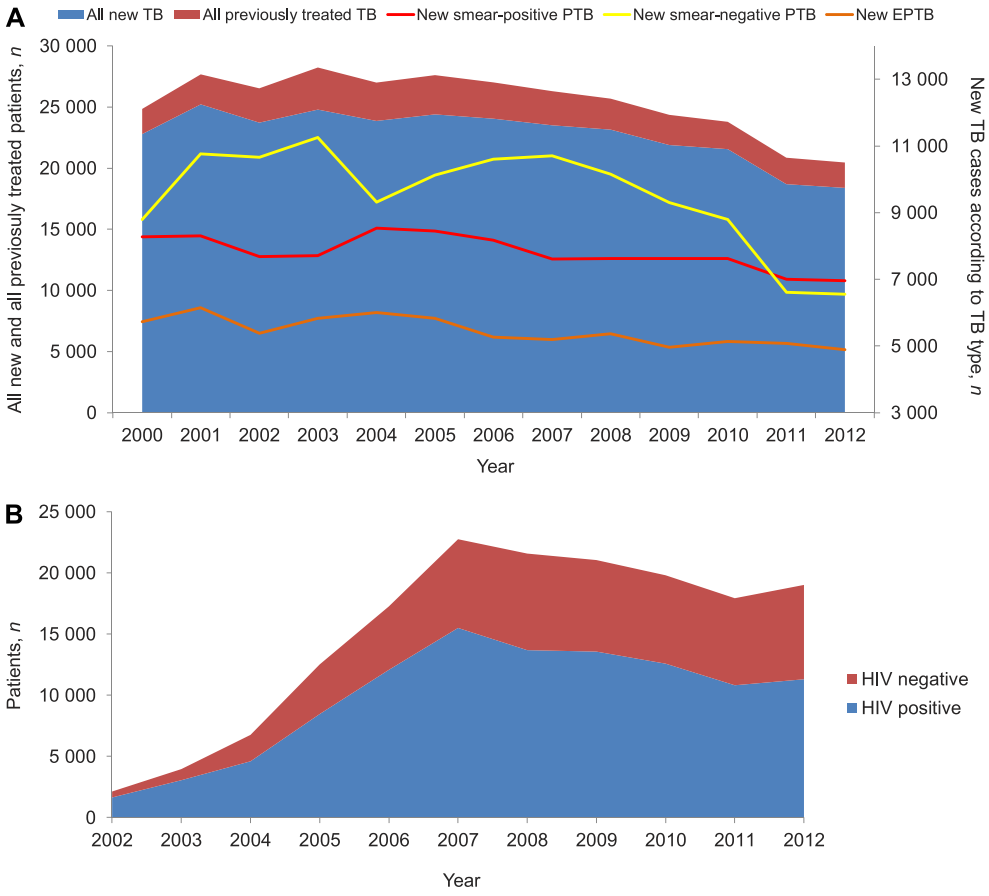

FIGURE 2 TB notifications in Malawi, 2000–2012. A) TB notifications stratified by category and type of TB. B) TB notifications stratified by known HIV status. TB = tuberculosis; PTB = pulmonary TB; EPTB = extra-pulmonary TB; HIV = human immunodeficiency virus.

follows: all types of TB (28%); new TB (26%), previously treated TB (40%) (OR 1.9, 95%CI 1.8–2.0, $P < 0.001$); new smear-positive PTB (19%), new smear-negative PTB (42%) and EPTB (19%) (smear-positive PTB vs. smear-negative PTB, OR 3.1, 95%CI 2.9–3.4, $P < 0.001$); HIV-positive TB (30%), HIV-negative TB (10%) (OR 1.3, 95%CI 1.2–1.4, $P < 0.001$).

DISCUSSION

This study shows pronounced inverse trends between the national scale-up of ART and national TB case notifications, particularly in the last 6 years when ⩾10% of PLHIV were estimated to be receiving treatment. The decline was noted for all types and

categories of TB, particularly patients with previously treated disease, smear-negative PTB and HIV-associated TB. These trends are not unexpected. ART is associated with a decline in recurrent or relapse TB as a result of the increased CD4 lymphocyte counts and improved cell-mediated immunity that accompany treatment.[3,5] The marked declines in smear-negative PTB reflect the fact that this type of TB is strongly associated with HIV infection.[8] Finally, the reduction in HIV-negative TB may be due to the overall decrease in HIV-associated TB in the community, which in turn would have led to reduced community transmission and thus fewer TB cases in the HIV-negative population.

The strengths of this study are the comprehensive national reports and excellent quality of Malawi's ART data.[6] There are several limitations. First, the diagnosis of smear-negative PTB and EPTB, particularly in high HIV prevalence, low-income countries, is difficult,[8] and this may have resulted in inaccurate notifications. Second, Malawi's ART programme includes Malawians and other nationals living in Malawi, while the NTP includes only Malawians living in the country (foreigners are recorded in separate TB registers and are not reported: in one study, however, foreigners accounted for only 1% of all cases).[9] Third, the decrease in TB notifications might have occurred as a result of other changes in the last 12 years, such as the socio-economic status of the population, changes in the coverage or quality of TB diagnosis or implementation of isoniazid preventive therapy (IPT). However, we have no evidence of any marked improvement in socio-economic conditions of the rural population, there has been no changes in coverage or quality of TB diagnosis and there has been no significant scale-up of IPT in the last 12 years.

Although this study is based on the interpretation of inverse trends rather than causality, the progressive decline in annual TB notifications in the last 6 years suggests a real change in TB epidemiology. This decline has also been noted in several neighbouring countries such as Tanzania, Zambia, Zimbabwe, Botswana and Namibia, which have similar high HIV prevalence and good national scale-up of ART.[1,10] This is encouraging, and supports the continuation of ART scale-up to PLHIV in need as a means of controlling not only the HIV/AIDS epidemic, but also the TB epidemic.

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De 2000 à 2012, le Malawi a étendu la thérapie antirétrovirale (ART) de <3000 à 404 905 personnes vivant avec le VIH/SIDA (virus de l'immunodéficience humaine/syndrome de l'immunodéficience acquise), aboutissant à une couverture par antirétroviraux de 40,6% parmi les personnes vivant avec le VIH. Durant cette période, la déclaration annuelle de la tuberculose (TB) a chuté de 28%, de 28 234 à 20 463. Les pourcentages de diminution annuelle des déclarations de cas de TB se répartissaient comme suit : nouveaux cas de TB (26%), rechute de TB (40%), nouvelle TB pulmonaire à frottis positif (19%), nouvelle TB pulmonaire à frottis négatif (42%), TB extra-pulmonaire (19%), TB chez un patient VIH positif (30%), TB chez un patient VIH négatif (10%). Un déclin dans la déclaration de la TB est associé à une expansion de l'ART, ce qui témoigne de sa valeur dans la lutte contre la TB dans les zones à prévalence élevée de VIH en Afrique sub-saharienne.

Entre el año 2000 y el 2012, se amplió en Malawi la escala de aplicación del tratamiento antirretrovírico (ART), de menos de 3000 a 404 905 personas con infección por el virus de la inmunodeficiencia humana (VIH) y síndrome de inmunodeficiencia adquirida, con lo cual se alcanzó una cobertura de 40,6% de las personas seropositivas. Durante este tiempo, disminuyó un 28% la tasa anual de notificación de tuberculosis (TB), de 28 234 a 20 463 casos. Se observaron las siguientes proporciones en la disminución de la notificación de casos: 26% en casos nuevos de TB, 40% en recaídas de TB, 19% en casos nuevos de TB pulmonar con baciloscopia positiva; 42% en casos nuevos de TB pulmonar con baciloscopia negativa, 19% en casos de TB extrapulmonar, 30% en casos de TB y seropositividad frente al VIH, y 10% en los casos de TB y seronegatividad frente al VIH. La observación de una disminución de la notificación de casos de TB asociada con la ampliación de escala del ART confirma la utilidad de esta estrategia en el control de la TB en las regiones con alta prevalencia de infección por el VIH en África subsahariana.

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