Tuberculosis case finding in a population with high HIV prevalence in western Kenya
van 't Hoog, A.H.

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Summary
In this thesis, studies are presented on the epidemiology of tuberculosis (TB) in a rural population in western Kenya, with a high prevalence of HIV. The main aim of the studies was to evaluate TB case finding in the study population. Tuberculosis is an important cause of illness and death in Africa. Case finding of persons with infectious TB, followed by effective treatment, is a major pillar of TB control, and generally considered insufficient in Africa. Population studies addressing the prevalence of TB and the adequacy of case finding in African populations with high rates of HIV are few. Chapter 1 provides an overview of the TB burden and the disease, and the relationship between TB and HIV. Concepts that are relevant for TB control and for the measurement of TB burden and case detection are described, as is the study site. The studies were conducted among adults residing in an area that is monitored by a health and demographic surveillance system (HDSS), and includes a total population of approximately 225,000 in three areas: Asembo (Rarieda District), Gem and Karemo (Siaya District).

Chapter 2 describes a survey to measure the prevalence of bacteriologically confirmed pulmonary tuberculosis (PTB) in the population of Asembo and Gem. All persons of 15 and older residing in 40 randomly sampled clusters were eligible to participate. During household visits, 20,566 participants were screened with a symptoms questionnaire, 20,409 (99%) provided sputum samples for smear microscopy, 19,216 (93%) had a chest radiograph taken at a nearby mobile unit, and 7,342 participants were eligible to provide one additional sputum sample for mycobacterial culture. 123 had PTB, defined by a culture positive for *Mycobacterium tuberculosis* or two positive smears. The prevalence was high: 6.0 per 1000 for all bacteriologically confirmed PTB and 2.5 per 1000 for smear-positive PTB. Of 101 prevalent TB cases tested for HIV, 52 (51%) were HIV-infected. We estimated, using provincial surveillance reports and data on home based HIV testing in the HDSS, that 48% of prevalent and 65% of notified PTB cases were attributable to HIV. HIV-infected TB patients were detected at a higher rate (1.4 cases detected per person-year) compared to HIV-uninfected (0.6 cases per person-year), but the proportion, expressed as the case detection rate, was lower: 56% of HIV-infected and 65% of HIV-uninfected TB patients were detected, below the Kenya national estimate and the World Health Organization (WHO) target at the time. The study findings suggest that undiagnosed infectious TB is common in this population and that case finding needs improvement, both in the HIV-infected and HIV-uninfected population. Most of the identified prevalent cases would not have been identified by the current case detection approach based on smear microscopy in self-reporting patients with prolonged cough. One quarter of them had not sought care.
To identify factors affecting case finding, the study in Chapter 3 compared characteristics of 194 patients diagnosed with PTB in a health facility following patient self-report, to 88 patients who were identified through the prevalence survey, who were not on TB treatment at the time of survey and were interviewed on care seeking. HIV-infected PTB patients were detected faster than HIV-uninfected patients, which was largely explained by the presence of cough, illness and clinically diagnosed smear-negative PTB. HIV-uninfected patients with PTB who were older, female, less ill or coughed for a shorter duration were less likely detected through self-report. Reported current or past alcohol use was associated with slower case detection in both groups. Among smear-positive patients, the median reported duration of cough was significantly longer (6.9 months) in HIV-uninfected patients than in HIV-infected patients (4.0 months). Health provider consultation was lower among the elderly prevalent patients, but did not differ by sex. To improve case detection in this population, increasing the suspicion of PTB among HIV-uninfected women and the elderly is needed, in addition to already recommended intensified case finding in HIV-infected persons.

In most populations with high burdens of TB and HIV, TB mortality cannot be measured directly from vital registrations. Chapter 4 describes mortality in a cohort of TB patients registered for treatment in the former Bondo and Siaya Districts between 2006 and 2008 in excess of all-cause mortality in the HDSS population, and risk factors for mortality during treatment. The crude mortality rate during TB treatment was 18.0 (95% CI 16.8-19.2) per 100 person years, 8.8 times higher than in the general population when standardized for age and sex. Adjusted for other risk factors, mortality in excess of the general population was increased in TB patients who were co-infected with HIV (excess hazard ratio 2.1, 95%CI 1.5-3.1), and lower in patients who were female or started treatment in a later year. TB mortality during treatment was high in patients with unknown HIV-status, or if HIV-infected not on, or not known to be on, antiretroviral therapy (ART). Maximizing the uptake of existing TB-HIV interventions would accelerate the observed decline in TB mortality, and among HIV-infected TB patients further reduce mortality during treatment by at least one third.

Tuberculosis prevalence surveys require large sample sizes. Screening is applied to select participants for bacteriological examination (‘suspects’) who have a greater probability of TB, to reduce the laboratory burden and cost. In Chapter 5 and 6, we evaluate the screening methods used in the TB prevalence survey. To assess to what extent CXR-abnormalities that were missed during field reading may have affected our TB prevalence
estimate, we compared the chest radiograph field reading by clinical officers with the classifications of two expert readers, on a randomly selected sample of 1031 survey chest radiographs mixed with films of confirmed TB cases (Chapter 5). CXR reading for any abnormality by clinical officers had higher sensitivity (95%) than expert reading (83% and 81%) for the identification of bacteriologically confirmed TB cases. TB prevalence was underestimated by 1.5%-5.0%. We conclude that acceptable CXR screening for any abnormality can be achieved with clinical officers, reducing the need for expert readers, who are rare in most African countries.

In Chapter 6, we assess whether modifications of the screening approach used in our survey could be more efficient and would substantially reduce the number of participants requiring CXR and/or sputum culture. We calculated the accuracy of modified screening strategies with bacteriologically confirmed TB as the gold standard, and compared those with the methods applied in other surveys. CXR screening for any abnormality had higher accuracy compared to symptom screening alone. The sensitivity of CXR screening was 94% (95% CI 88-98%), and specificity was 73% (95%CI 68-77). The sensitivity was slightly lower in HIV-infected (92%). Symptom screening combinations had significantly lower sensitivity than CXR, except for ‘any TB symptom’ which had 90% (95%CI 84-95) sensitivity (96% in HIV-infected and 82% in HIV-uninfected), but low specificity (32%; 95% CI 30-34). Smear microscopy did not yield additional suspects. Sequential rather than parallel application of a symptom screen for ‘any symptom’, followed by CXR evaluation and different suspect criteria depending on HIV status would result in the largest reduction of the need for CXR and sputum culture, approximately 36%, but would underestimate prevalence by 11%. Combined CXR and symptom screening had the highest sensitivity and remains important for suspect identification in TB prevalence surveys in settings where bacteriological sputum examination of all participants is not feasible. Symptom screening alone has value for TB case finding, especially in HIV-infected populations.

Chapter 7 provides a general discussion of the study findings, and suggestions made with respect to improving TB case finding and the evaluation of the impact on TB transmission and mortality.