International Journal of Mycobacteriology 5 (2016) 374–378

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO

Review

Passive case finding for tuberculosis is not enough

Jennifer Ho [a,b,c,*], *Greg J Fox* [a,c,d], *Ben J Marais* [c,d,e]

[a] *Woolcock Institute of Medical Research, University of Sydney, Sydney, Australia*
[b] *South Western Sydney Clinical School, University of New South Wales, Sydney, Australia*
[c] *Centre for Research Excellence in Tuberculosis (TB-CRE) and the Marie Bashir Institute for Infectious Diseases and Biosecurity (MBI), University of Sydney, Sydney, Australia*
[d] *Sydney Medical School, University of Sydney, Sydney, Australia*
[e] *The Children's Hospital at Westmead, University of Sydney, Sydney, Australia*

ARTICLE INFO

Article history:
Received 8 September 2016
Accepted 21 September 2016
Available online 28 October 2016

Keywords:
Active case finding
Screening
Diagnosis
TB elimination
End TB strategy

ABSTRACT

Current World Health Organisation targets calling for an end to the global tuberculosis (TB) epidemic by 2035 require a dramatic improvement in current case-detection strategies. A reliance on passive case finding (PCF) has resulted consistently, in over three million infectious TB cases per year, being missed by the health system, leading to ongoing transmission of infection within families and communities. Active case finding (ACF) for TB has been recognized as an important complementary strategy to PCF, in order to diagnose and treat patients earlier, reducing the period of infectiousness and therefore transmission. ACF may also achieve substantial population-level TB control. Local TB epidemiology and the resources available in each setting will influence which populations should be screened, and the types of ACF interventions to use for maximal impact. TB control programs should begin with the highest risk groups and broaden their activities as resources allow. Mathematical models can help to predict the population-level effects and the cost-effectiveness of a variety of ACF strategies on different risk populations.

Contents

* Corresponding author at: Woolcock Institute of Medical Research, 431 Glebe Point Road, Glebe, NSW 2037, Australia.
E-mail address: jennifer.ho@sydney.edu.au (J. Ho).

Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2016.09.023
2212-5531/

Introduction

In the past two decades, the Directly Observed Treatment Short-Course (DOTS) strategy and the subsequent Stop TB (DOTS expansion) strategy, recommended by the World Health Organisation (WHO), saved more than five million lives [1]. However, total case numbers continue to rise and tuberculosis (TB) remains the leading infectious cause of death worldwide [2]. The WHO launched the End TB Strategy in 2015 with the ambitious goal of ending the global TB epidemic [3]. Targets include a 90% reduction in TB incidence and 95% reduction in TB deaths by 2035, compared to 2015. "Bending the epidemiological curve" of TB incidence and mortality to meet these targets, will require improved case detection to ensure early disease diagnosis, improve individual patient outcomes, and limit ongoing transmission.

In the majority of TB endemic settings worldwide, the status quo for TB case finding is based on "passive case finding" (PCF). This relies upon a patient with active TB experiencing symptoms serious enough to seek health care and a healthcare system capable of correctly diagnosing the patient's condition. [4] However, this strategy, as shown consistently in prevalence surveys [5,6], is grossly inadequate to detect the substantial burden of undiagnosed TB in the community. It is estimated that in 2014, more than 3.5 million people who developed TB (one-third of all cases) were "missed" by the health system [2]. This massive case detection gap culminates in late disease presentation, with poor disease outcomes, and undiagnosed infectious cases continuing to spread infection within families and communities.

The term "active case finding" (ACF) includes any methods for TB identification that does not rely on patients presenting to the healthcare system of their own accord [7]. The objectives of ACF are to diagnose and treat patients earlier, thereby reducing negative treatment outcomes, sequelae, and socioeconomic consequences, as well as reducing the period of infectiousness and therefore transmission [4]. ACF has been increasingly recognised as an important complementary strategy to PCF in high-prevalence settings in order to overcome the gaps in TB detection and treatment. This need has also been recognized by international donors, with initiatives such as TB REACH established to support innovative approaches to increasing TB case detection [8]. Although two WHO guidelines, systematic screening [4] and household contact investigations [9], provide some guidance to ACF in resource limited settings, designing and implementing interventions that target the most appropriate populations, and utilise feasible and cost-effective strategies, may be difficult for national TB control programs (NTP) already struggling to manage the existing burden of known disease.

In this review, we compare the additional individual and population-level benefits of ACF with those of PCF, consider pragmatic and economic factors relevant to ACF implementation in resource-limited settings, and highlight future research needs and priorities.

Active case finding versus passive case finding

The principle objective of ACF is to find and treat cases of active TB that would otherwise not have been diagnosed at this time, using strategies that are in keeping with available resources. An important distinction between ACF and PCF is that the former is a screening intervention initiated by health services, as opposed to the latter, which is initiated by symptomatic individuals presenting to health-care. In general, ACF activities are additive to PCF. Consequently, the diagnostic algorithms and measures of success used in ACF may differ from those used for PCF. The population targeted for ACF is typically larger, and the prevalence of disease (or pretest probability) is lower. This results in a higher number needed to screen, to diagnose one TB patient, compared to the PCF context.

ACF for TB generally begins with an initial screening step followed by confirmatory testing. Initial screening may comprise of one or a combination of symptom reporting or chest radiography, and if either are positive, a confirmatory microbiological test, such as smear microscopy, or a molecular test e.g. Xpert MTB/RIF [4]. Ideally, the confirmatory test should be rapid, hence *Mycobacterium tuberculosis* (MTB) culture is a less feasible option, unless the health system in place has sufficient capacity to follow-up screened patients [4].

However, the use of symptoms or chest X-ray as the initial screening step has important limitations. Prevalence surveys have shown consistently that the majority of undiagnosed TB patients in the community lack typical symptoms of TB and a large proportion have no symptoms at all [10–12]. Furthermore, while chest radiography is more sensitive than using a symptom-based approach alone, this can be logistically difficult in many rural and remote settings. Xpert MTB/RIF used up-front as a primary screening tool (i.e., regardless of symptoms reported or chest X-ray findings), has been shown to be feasible and improve case detection in certain high risk populations, such as people living with HIV (PLHIV) [13,14], and also in ACF conducted in the general community [15]. While this approach may overcome some limitations of traditional TB screening, the feasibility and cost-effectiveness of this strategy in a programmatic setting is yet to be determined.

One argument against ACF it that it merely detects disease earlier, but does not substantially alter individual patient outcomes. However, diagnosing and treating TB disease earlier is likely to have a substantial impact on TB transmission, decreasing the long term trajectory of TB in a population, and subsequently reducing the cost of TB control overall [16]. It is important however, when evaluating the population-level effects and the cost-effectiveness of ACF, to consider its impact over a longer time frame (e.g., a 20-year time horizon), as short-term assessments can dramatically underestimate longer- term gains of ACF [16]. Table 1 lists outcome measures that should be considered when evaluating the benefit of ACF, as well as the other key characteristics of ACF compared to PCF for TB.