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A cluster randomised trial to evaluate the effect of optimising TB/HIV integration on patient level outcomes: The "merge" trial protocol

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ABSTRACT

Introduction: We describe the design of the MERGE trial, a cluster randomised trial, to evaluate the effect of an intervention to optimise TB/HIV service integration on mortality, morbidity and retention in care among newly-diagnosed HIV-positive patients and newly-diagnosed TB patients.
Design: Eighteen primary care clinics were randomised to either intervention or standard of care arms. The intervention comprised activities designed to optimise TB and HIV service integration and supported by two new staff cadres—a TB/HIV integration officer and a TB screening officer—for 24 months. A process evaluation to understand how the intervention was perceived and implemented at the clinics was conducted as part of the trial. Newly-diagnosed HIV-positive patients and newly-diagnosed TB patients were enrolled into the study and followed up through telephonic interviews and case note abstractions at six monthly intervals for up to 18 months in order to measure outcomes. The primary outcomes were incidence of hospitalisations or death among newly diagnosed TB patients, incidence of hospitalisation or death among newly diagnosed HIV-positive patients and retention in care among HIV-positive TB patients. Secondary outcomes of the study included measures of cost-effectiveness.
Discussion: Methodological challenges of the trial such as implementation of a complex multi-faceted health systems intervention, the measurement of integration at baseline and at the end of the study and an evolving standard of care with respect to TB and HIV are discussed. The trial will contribute to understanding whether TB/HIV service integration affects patient outcomes.

1. Introduction

Tuberculosis is a major public health problem in South Africa. In 2012, there were an estimated 530 000 new TB cases reported in the country, equivalent to 1000 cases per 100 000 of the population [1]. An estimated 63% of these new cases were HIV positive [1]. The implementation of TB/HIV collaborative services with or without service integration is a recommended strategy to reduce joint burden of TB and HIV. These activities are described in the World Health Organisations (WHO) three I's policy of 2008 and in the revised policy of 2012 [2,3], and include activities to reduce morbidity and mortality from HIV among TB patients—HIV counselling and testing, initiation of cotrimoxazole preventive therapy (CPT) and earlier initiation of antiretroviral therapy (ART)—and those

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to reduce morbidity and mortality from TB among HIV positive people—intensified case finding, isoniazid preventive therapy, TB infection control and early initiation of ART.

TB and HIV service integration refers to the joining together of these two services in order to maximise outcomes [4]. A broader definition of integration proposed is "managerial or operational changes to bring together inputs, delivery, management, and the organisation of particular service functions as a means of improving access, quality, user satisfaction, equity and effectiveness" [5]. TB/HIV integration has been implemented at primary care level in a spectrum of models ranging from separate services with varying degrees of collaboration and referral between services to the one-stop-shop model where a single health care provider provides both TB and HIV services in one visit [5]. Proponents of TB/HIV service integration argue that it may improve TB and HIV programme efficiency through better use of space and human resources, reducing delays in accessing care by patients, patient visits and costs and may result in better continuity of care and retention in care [5,6]. Those opposed to service integration cite longer wait times for people who do not immediately benefit from integrated services [7,8], reduction in the quality of care—as care may be provided by less specialised providers [8,9]—and the potential for increased experience of stigma [10], which may deter patients from seeking care.

Most published studies on TB/HIV integration report outcomes relate to coverage of the TB/HIV collaborative activities, but not patient-relevant outcomes [5]. There is little evidence on the effect or impact of integrating TB/HIV services on patient-relevant outcomes such as mortality, morbidity, retention in care or costs. We describe the methods of a cluster-randomised controlled trial to evaluate the effect of a TB/HIV integration intervention on patient outcomes. The trial is registered on the South African Register of clinical trials, registration number DOH-27-1011-3846.

1.1. Rationale for and objectives of the trial

At the start of protocol development in 2010, primary care clinics in South Africa were required to provide TB and HIV services under one roof with referral for additional diagnostic tests or complications as needed. Although services were available under one roof in most clinics in the country, they were run separately with referrals between the two. The provision of integrated TB and HIV care was limited by shortages of human resources, limited training, poor referral between services and weak follow-up systems [9]. In addition the implementation of TB/HIV collaborative activities was not uniform within the clinics: better progress was made in the implementation of TB entry point activities (such as HIV counselling and testing for TB patients, cotrimoxazole prophylaxis and ART) compared to the HIV entry point ones (such as intensified case finding, isoniazid preventive therapy and TB infection control) [11].

The study was implemented at 18 primary care clinics in a sub-district of Ekurhuleni District in Gauteng Province of South Africa. The catchment areas of the clinics were urban with formal and informal housing. The TB case notification rate in the district was 334 per 100 000 population in 2011 [12], while the HIV prevalence in the general population was 14.3% (10.3–19.5%) in 2012 [13]. We hypothesised that implementation of an intervention to optimise TB/HIV service integration at primary care clinics would improve patient-relevant outcomes by promoting earlier diagnosis and treatment of both diseases, less morbidity or mortality, better coordination of care for patients and adherence to clinic visits. We also hypothesised that integrated care will be more efficient for health care providers because patients requiring care for both diseases will be seen by one provider instead of two. The cluster-randomised trial design was chosen and implemented because the intervention could only be implemented and evaluated at clinic level [14].

1.1.1. Objectives of the trial

The MERGE trial is a pragmatic cluster-randomised controlled trial designed to evaluate the effects of optimising TB/HIV integration at primary care level on morbidity, mortality and retention in care among newly-diagnosed HIV-positive patients and newly-diagnosed TB patients. The primary and secondary objectives of the trial are listed in Table 1.

1.2. Operational aspects of the trial

1.2.1. Design of the trial, clinic selection and process of randomisation

Fig. 1 shows the outline of the study from clinic selection to recruitment of evaluation cohorts and analysis of outcomes. In the trial, 18 out of 32 primary care clinics located in a sub-district in Ekurhuleni Metropolitan Municipality in Gauteng Province, were selected and randomised to either intervention or standard of care arms. The 18 participating clinics were selected in a way that ensured availability of TB diagnostic and treatment services, sufficient numbers of TB patients available for enrolment, geographical distribution in the sub-district and the absence of other completing research studies. Stratified randomisation was used to assign clinics to either arm, to help reduce between-cluster variation and help achieve balance of baseline patient characteristics. Facilities were stratified according to case-fatality rates among smear-positive TB patients diagnosed in 2010, with ten and eight clinics in the lower and higher TB case fatality rates strata, respectively. Following randomisation, all 18 clinics were assessed using a standardised facility assessment tool to collect data on clinic characteristics and the level of TB/HIV integration at baseline. These data were collected in order to adjust for clinic level imbalances in the analyses if necessary.

1.2.2. Recruitment of the evaluation cohorts

To measure the trial outcomes, a research assistant was assigned to each participating clinic in order to enrol a consecutive sample of i) newly diagnosed TB patients, defined as patients older than 18 years who initiated TB treatment in the preceding 60 days and ii) newly diagnosed HIV positive patients, defined as patients older than 18 years who tested HIV positive in the preceding 60 days. These target populations were selected as they would be the ones who would immediately benefit from the integrated care. Health care providers at each clinic referred consecutive newly diagnosed TB patients and newly diagnosed HIV-positive patients to the research assistants for eligibility assessment and enrolment. At enrolment, data on participant contact details,