Published in final edited form as:

Scand J Public Health Suppl. 2007 August ; 69: 45–51. doi:10.1080/14034950701355767.

Using health and demographic surveillance to understand the burden of disease in populations: The case of tuberculosis in rural South Africa¹

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Abstract

Aims: To utilize the Agincourt health and demographic surveillance system (HDSS) platform to assess the burden of pulmonary tuberculosis (PTB) in a rural South African sub-district.

Methods: During 1999, data from three sources were combined to estimate disease prevalence amongst a non-migrant adult population: (1) passive case-finding (PCF) through hospital register data; (2) active case finding (ACF) using a systematic household assessment of chronic coughers; and (3) verbal autopsy (VA) data on cause of death.

Results: Of 66,840 residents, 38,251 permanent adult residents were included in the analysis. A total of 102 cases of PTB were detected through PCF. ACF sweep detected 366 chronic coughers with 6 cases of confirmed PTB. Among 28 PTB deaths detected by VA, 13 (46%) were not previously identified by the health service. The total PTB prevalence was 157/100,000; 110/100,000 of prevalent cases were detected by PCF. Among undetected cases, 24/100,000 were identified through ACF, while 23/100,000 were detected by the VA process.

Conclusions: Amongst prevalent PTB cases in the permanent adult population, 70% were detected by the health service; 15% of cases were undiagnosed in the community, while an equal proportion died of PTB prior to diagnosis. The latter groups contributed disproportionately to infectiousness in the community through prolonged duration of symptoms. As most of these cases presented to the health service on a number of occasions, strengthening early case detection should remain the cornerstone of TB control efforts. Strategies to strengthen the application of health & demographic surveillance systems to disease surveillance are discussed.

¹This paper has been independently peer-reviewed according to the usual Scand J Public Health practice and accepted as an original article.

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Keywords

Active-case finding; demographic surveillance system; epidemiology; South Africa; tuberculosis; tuberculosis surveillance; verbal autopsy

Background

Estimates of the burden of disease in developing countries are generated primarily through routine surveillance activities within the health system. A minimum data set from district health information systems (DHIS) provides information on health service utilization, notifiable infectious diseases, and death certificate data on mortality. Where medical services are accessible and the quality of record keeping high, this information critically informs decisions around policy, resource allocation, and programme monitoring and development [1].

Data from established health and demographic surveillance systems (HDSS) have the potential to be an important adjunct to DHIS. HDSS data provide a profile of the burden of disease through a systematic and longitudinal collection of information from well-defined populations [2]. Within developing countries, HDSS sites are equipped to provide information on a range of health-related outcomes such as cause of death, health systems coverage (vaccination rates, health service utilization), or in some cases, growth and nutrition [3]. Such population-level data are especially important where the quality and accessibility of health services are poor; where record-keeping systems are underdeveloped; where deaths take place outside of the health system and go unrecorded; or where cultural interpretations of disease in more traditional societies present a competing array of alternative providers to communities.

Alongside routine data collection, HDSS platforms have the potential to contribute towards a more detailed understanding of the burden of disease through complementary strategies targeting specific public health priorities. This paper describes a portfolio of research activities housed within the Agincourt HDSS that attempt to explore the burden of pulmonary tuberculosis (PTB) at the sub-district level in South Africa's rural northeast.

The case of tuberculosis

Despite its importance as a public health problem, methods used to assess the burden of tuberculosis (TB) in high prevalence settings remain imprecise [4]. Historically, tuberculin surveys of non-BCG-vaccinated children have been used to determine the annual risk of tuberculosis infection (ARTI) [5]. This provides an estimate of the probability of an individual being infected by *Mycobacterium tuberculosis* in a given year.

Where countries have established surveillance systems, notification data based on passive case finding (PCF) are generally preferred and considered to be more reliable [6]. The World Health Organization (WHO) has set a global case-finding target of 70% for the proportion of new smear-positive TB cases that should be identified by the health service through PCF (the case detection rate) [7]. Despite TB being a notifiable disease, PCF estimates in many developing countries have the potential to seriously underestimate the burden of disease, as both the TB service and its recording and reporting system remain poorly developed [4].

South Africa is thought to have amongst the most reliable notification systems in sub-Saharan Africa, with the highest case detection rates in the region [8]. Current estimates suggest the annual incidence of TB is 495/100,000. Globally, the country ranks ninth in terms of the absolute number of cases identified each year [9].

Accurately assessing the burden of TB is challenging. The disease has a long asymptomatic period between infection and illness, and there is often a considerable delay between the onset of illness and the initiation of treatment – delays attributable to both late patient presentation and the failure of clinical services to investigate and treat appropriately [10]. Undiagnosed TB is of significant public health importance as it contributes to ongoing transmission in the community. Furthermore, whether undiagnosed TB cases are eventually detected by the health service, or instead progress to death or chronicity, is poorly understood [11,12].

The aim of this study was to utilize the Agincourt HDSS platform to accurately assess the burden of PTB. It brings together data from three sources: (1) PCF through an analysis of hospital register data; (2) active case finding (ACF) using a systematic household assessment of chronic coughers; and (3) verbal autopsy (VA) data to interrogate cause of death among individuals resident within the HDSS. Better understanding these relative proportions, and the degree to which WHO case finding targets are being met, can assist in developing effective strategies for reducing transmission – shaping the policy, planning, and management of TB programme activities.

Material and methods

Setting

This research took place during 1999 and presents data obtained from the Agincourt sub-district of the Limpopo Province of South Africa. A detailed description of the sub-district and the Agincourt HDSS can be found elsewhere [13].

Passive case finding – analysis of registered tuberculosis cases

The Agincourt sub-district refers to three public hospitals, and is served by six primary healthcare clinics and a limited number of private practitioners. All TB suspects and confirmed cases are referred to one of the three public hospitals. Cases are documented in TB registers held at these facilities, which hold data on the name, age, sex, address, and date of registration of TB cases, alongside clinical details including final diagnosis, AFB smear and culture results, and details of treatment and treatment outcome. PTB is defined as TB involving the lung parenchyma. At the time of the study, culture was not routinely done on smear-negative new TB suspects – where clinical history, X-ray, and absence of a response to broad-spectrum antibiotics were indications for initiation of TB therapy.

To obtain PCF estimates for TB incidence, two independent researchers familiar with the study site identified all patients registered for the calendar year 1999 that provided an address from the Agincourt field site. Village of residence was provided for over 99% of

registrations. Registers were cross-checked and evaluated thoroughly to ensure that individual new occurrences of TB had not been registered more than once. Relevant TB data for sub-district residents were transferred electronically to a separate database.

Active case finding – undiagnosed TB

During the annual Agincourt HDSS census update round, conducted from July to September 1999, heads of all households were visited and asked to identify individuals who had been experiencing a cough for more than three weeks. This screening question was posed during interviews lasting between 30 and 60 minutes. Training for census field workers consisted of a three-hour workshop on TB and chronic cough as a cardinal symptom. This was followed by weekly meetings with census managers at the time of census field activity.

Individuals identified as “chronic coughers” were revisited the following day by a specialized TB field worker. These individuals underwent two days of training in screening for active cases, inclusion criteria, sputum collection, and record keeping. Additional field support was provided by a medical team who accompanied the TB field worker on household visits on a weekly basis. Eligible TB suspects were those older than 10 years and not currently on TB treatment. This was the first time a TB module was included within the HDSS and we feel that the longitudinal presence of the census was unlikely to affect prior TB case detection.

After giving informed verbal consent, interviewees were asked to provide a sputum sample immediately and were then trained to collect two further early morning specimens the following day. Repeat visits were made to all households in order to collect sputum samples from potential cases. Two specimens were sent for microscopy and one for culture.

Laboratory methods

All specimens were transported on ice within 48 hours to the reference laboratory (National Health Laboratory Service). Microscopy was performed using conventional Ziehl–Neelsen staining on unconcentrated specimens. Positive smears were quantified using International Union Against Tuberculosis and Lung Disease (IUATLD) standards. Positive slides were confirmed by a second reader, and 10% of negative slides were reviewed by the reference laboratory. Culture specimens were decontaminated using 4% sodium hydroxide and then inoculated onto two Lowenstein Jensen slopes enriched with glycerol. Cultures were incubated at 37 degrees for 8 weeks. *Mycobacterium tuberculosis* was identified using the polymerase chain reaction with primers specific for *Mycobacterium tuberculosis* complex [14,15].

Verbal autopsy data – PTB deaths

A VA was administered as part of the same data-collection round of the Agincourt HDSS in all households where a death had occurred during the preceding year. The VA technique involves interviewing the household member most knowledgeable about the terminal illness, regarding the signs and symptoms noted or experienced by the deceased in the period leading up to death. Detailed information is collected in narrative form, followed by structured questions on the nature and duration of specific symptoms. In cases where a cough is felt to be a key symptom preceding death, the family is asked specifically “was this TB?” and if so, “was it being treated at a clinic or hospital?”. Information from death certificates is examined if available, and any other history of relevance is noted (such as health seeking behaviour, other sick individuals in the household). The interviews are conducted by a specially trained VA fieldworker, and take between 30 and 60 minutes to complete.

All VA information is reviewed by two physicians who arrive at an independent assessment of the most likely cause of death. In cases where there is disagreement physicians discuss the case. Where consensus is not achieved, a third physician undertakes an independent assessment. If this does not concur with one of the previous reviewers, the cause of death is listed as unknown. The Agincourt VA instrument has been locally validated using hospital records as the gold standard (including clinical notes, laboratory and radiological reports, autopsy and death certificate data where available) by a reviewer blinded to the VA diagnosis. This process demonstrated a sensitivity of 92%, a specificity of 99%, and a positive predictive value of 92% for detecting PTB deaths among adults [16]. Tuberculosis cases identified through the VA were categorized as “recognized” if there was evidence that they had been previously detected by the health service, and “unrecognized” if the evidence suggested death occurred prior to case detection.

Statistical analysis

Three independent data sets were generated from TB register information, ACF, and the VA process. These were combined with denominator data from the HDSS platform to estimate the incidence and prevalence of PTB amongst the Agincourt sub-district population during 1999. To facilitate comparison between them, analysis concentrated on cases of PTB amongst individuals aged greater than 10 years who are permanent (non-migrant) household members of the HDSS. As ACF can only provide an estimate of who has PTB at one point in time, all figures are expressed in terms of prevalence, which was estimated using data on mean duration of symptoms in the case of PTB deaths, and mean duration of treatment for registered cases (PCF) ($\text{prevalence} = \text{incidence} \times \text{mean duration of symptoms or treatment}$).

Results

An overview of the results is provided in Table I. In estimating the levels of prevalent PTB cases in the population, through PCF, ACF and VA, the denominator used included the permanent population aged greater than 10 years ($n=38,251$).

Passive case finding

During 1999 there were 1,107 registered hospitalizations for TB in the three hospitals, which serve a total regional population of c.500,000. Of these, 120 (10.8%) were among individuals from the Agincourt sub-district – of which 102 were from the permanent adult population. Hospitalizations for TB were distributed evenly throughout the year, with a slight excess of males. Among the population older than 10 years 93% of cases were of PTB, and among those PTB cases with sputum results the smear positivity rate was 66%.

Active case finding

There were 366 confirmed TB suspects amongst those older than 10 years and not currently on TB treatment. Sputum smear results were available for 340 individuals (92.9%). Six cases (five males, one female) of sputum-positive disease were identified among chronic coughers identified through the ACF process. In three cases sputum samples were collected directly in the field, while in the other three cases sputum samples were collected in hospital after repeated visits by the ACF team to the home of a chronic cougher. Patients identified by ACF had a mean delay of 28 weeks between recognition of symptoms (cough) and diagnosis. Five had sought attention at the health service prior to being identified by the ACF study but their condition had not been diagnosed as TB.

Verbal autopsy data

Tuberculosis was identified as a primary cause of death for 38 individuals from among the de facto adult population of 38,251 in 1999. In all cases there was independent consensus between reviewers. Eight deaths were identified among labour migrants and excluded from analysis. An additional excluded death was in a child younger than 10 years. In one case the VA file could not be located and this case was excluded from further analysis.

All of the remaining 28 cases presented with cough as the cardinal symptom and 27/28 (96%) had sought treatment in the health service at some time leading up to death. Associated symptoms were similar between groups. In all, 13/28 cases of PTB were regarded as previously undetected by the health service (unrecognized). The mean duration of cough was 39 weeks among recognized cases and 35.4 weeks among unrecognized cases. Among 14/15 recognized cases, the family member being interviewed answered affirmatively to both questions “was it TB?” and “was it being treated at a hospital?”. In one case, the clinical history alone suggested TB as the most likely cause of death. Death certificate confirmation of the diagnosis was available in three recognized cases, while six further cases were confirmed by hospital TB register data. For most deaths occurring in the area, death certificate confirmation is unavailable.

Estimating the burden of PTB

All estimates of TB incidence are derived from the permanent adult population. The incidence of TB (all cases) detected through PCF among the permanent Agincourt sub-district population was 212/100,000 person-years at risk during 1999 (95% CI 176–254). For PTB among the permanent population older than 10 years the incidence was 248/100,000 (95% CI 201–304). The prevalence of PTB in this latter group, where the average duration of treatment was measured to be 5.3 months, was 110/100,000 (95% CI 79–148).

Active case finding revealed a prevalence of 16/100,000 (95% CI 6–34) cases of sputum-positive PTB in the community among those older than 10 years. Information is not available on TB in younger individuals, and the current methodology did not aim to identify non-pulmonary or sputum-negative TB. Using the ratios of 66% sputum positivity found for hospitalized patients, the estimated prevalence of PTB in this group was 24/100,000.

Among 13/28 (46%) TB deaths there was no evidence of TB diagnosis prior to death based on hospital register data, death certificate data, patterns of health-seeking behaviour, a household member's narrative description of the time leading up to the death, or their response to the question “was it TB?”. The incidence of unrecognized PTB deaths was 34/100,000. The mean duration of coughing according to the VA data was 35.4 weeks. The average point prevalence of unrecognized TB in this group was 23/100,000.

In 1999, the total prevalence of PTB among permanent adult members of the Agincourt HDSS population ($n=38,251$) was 157/100,000; 110/100,000 of these prevalent cases were on treatment in the health service. Among undetected cases, 24/100,000 were identified through active case finding, while 23/100,000 died of TB prior to diagnosis.

Discussion

This study employed multiple methodologies to better understand the burden of PTB in a well-defined population under longitudinal health and demographic surveillance. These data suggest that among prevalent PTB cases in the adult population during 1999, 70% of cases are detected through the health service. Among prevalent cases as yet undiagnosed, 15% are

symptomatic in the community and were detected through a single-pass ACF sweep, while an additional 15% die of their disease prior to diagnosis.

In the South African context, national estimates of the burden of TB are derived from PCF data and reported as an incident figure, or numbers of new cases per 100,000 population. In the province where this research was conducted, the annual incidence of TB was reported to be 106/100,000 in 1999 [17]. Our data suggest that the incidence in the sub-district under study was closer to 212/100,000. While our work primarily describes PTB in terms of prevalent cases, VA data in particular can contribute to a better understanding of incidence. These data suggest that the numbers of new PTB cases is at least 10% higher than current PCF estimates. During 1999 the incidence of PTB detected by the health service for the sub-district population was 248/100,000 per year, while the VA highlighted unrecognized cases resulting in death at a rate of 34/100,000 per year.

There are additional public health implications of these findings. TB transmission relates primarily to exposure of unexposed individuals to active cases of pulmonary disease. While the burden of cases detected through ACF or the VA tool may appear modest, our data suggest that these cases contribute disproportionately to ongoing transmission. While the fate of cases detected by the ACF process is ultimately unknown, the VA data supports the premise that a substantial burden of PTB remains undiagnosed by the health service until death. In fact, 46% of PTB deaths identified during the VA process remain undiagnosed [18]. Furthermore, the duration of infectiousness from cases detected through the ACF and VA process is prolonged. Previous work in the area suggests that the median time between the onset of symptoms and diagnosis is 12 weeks for those presenting initially to a clinic or private practitioner and 8 weeks for those presenting initially to hospital [10]. This compares with a mean duration of symptoms of 35 weeks (median 16 weeks) for undiagnosed cases resulting in death as detected through the VA process, and 28 weeks (median 20 weeks) for those identified by ACF.

This work also has clear policy and programme implications. Among cases of PTB detected through ACF and VA process, nearly 90% had sought prior treatment at the health service – most on a number of occasions. As such, while issues of distance and transport, cultural interpretations of disease, and the use of non-Western healthcare providers might all surface as important barriers to care in this rural area of South Africa, interventions to improve the quality of the health system to facilitate early TB diagnosis remain paramount. Principle intervention opportunities include improving the quality and quantity of health workers, improved diagnostic services, and strengthened referral networks to name but a few.

There are also limitations to our data. Clearly, in the context of HIV/AIDS with its high proportion of non-productive, non-pulmonary TB and higher frequency of atypical presentations, the sensitivity of chronic cough as a cardinal symptom, and sputum for diagnoses, are substantially reduced. As such, cases detected by ACF and deaths reported by VA provide only a minimum estimate. Work is ongoing within the Agincourt HDSS to strengthen and validate the VA tool in light of AIDS-related diagnoses. HIV surveillance activities, though not conducted in the site to date, are planned and will draw on advances in accurate non-invasive screening technologies.

Issues of migration were also difficult to fully account for in our work. Within the area, nearly 60% of adult men and 25% of adult women are economic migrants, generally relocating to the cities for work, and away for up to 11 months of the year. Nonetheless, they are still considered household members by those interviewed. It has been previously noted that migrant household members do return to the study site in the event of illness and death. Because of this, the analysis took place on the de facto population, and cases of PTB found

in known migrants were excluded from the analysis. However, these dynamics are clearly complex and further research into their role and contribution to HIV and TB is clearly warranted.

The methods employed in this work are also limited in their ability to depict burden of disease accurately owing to inconsistency between hospital records and HDSS identifiers. In our study, health-sector patients identified as HDSS residents were not matched by HDSS identifier as the latter was unknown to the patient. Matching individuals to the HDSS is complex due to shared surnames, the common usage of different first names, a lack of knowledge of date of birth by patients (or inaccurate recording of date of birth by health workers), and an absence of standardized ways of reporting place of residence. Efforts to better integrate HDSS (population) data with health-sector utilization (clinic data) would undoubtedly enhance the capacity of such sites to contribute to profiling disease patterns and their determinants in populations. Furthermore, as GIS-based mapping becomes more commonplace within HDSS sites, linking disease patterns to geographic profiles can generate hypotheses around transmission (such as hotspots for TB), and provide opportunities for targeted interventions – such as intensified case-finding for HIV-related TB or directly observed therapy for TB treatment or antiretroviral therapy.

Despite these limitations, this is the first study to utilize multiple methodologies to paint a comprehensive picture of the burden of PTB at the population level. This could only have been done as complementary research within the context of a well-established HDSS platform. Such sub-studies have the potential to add substantial depth to routine health-sector surveillance data in relation to both infectious and non-communicable disease. The strength of our estimates lies in the accurate denominator provided by the HDSS, and its location within a well-circumscribed geographic area. The VA process, in its systematic recording of all household deaths, provides a unique opportunity to explore burden of disease in an area where hospital records and death certification remain suboptimal [16,19]. The ACF survey was carried out through employing a single additional question within the routine HDSS census – followed by the employment of a limited and specialized field team to further interrogate potential PTB cases. Taken together, and in the case of PTB, this allowed for a robust assessment of the disease profile, providing insights and opportunities for intervention strategies in the context of a country undergoing profound shifts in population, policies and program development.

Acknowledgments

This work was supported by the World Health Organization and the Department for International Development (U.K.), the Andrew W. Mellon Foundation (USA), the Wellcome Trust (058893/ Z/99/A) (UK), the University of the Witwatersrand (South Africa), and the Anglo American and De Beers Chairman's Fund (South Africa).

The authors would like to acknowledge the contribution of the study communities and field workers without whom such research could not be conducted. Ethical clearance was granted by the University of the Witwatersrand's Committee for Research on Human Subjects (Medical), No. M960720.

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Table I

Characteristics of pulmonary tuberculosis cases for the Agincourt sub-district, 1999.

Population	Total	66,840	
	Permanent > 10 years old ^a	38,251	
Passive case finding (PCF)^b	Number of hospitalizations	102	
	Male patients	60 (59%)	
	Pulmonary TB	95 (93%)	
	Sputum positive ^c	48 (66%)	
	Mean duration of treatment	5.3 months	
	Incidence (all PTB)	248/100,000	
	Prevalence (all PTB)	110 /100,000	
Active case finding (ACF)^b	Confirmed chronic coughers	366	
	Sputum specimens collected	366 (100%)	
	Sputum results available	340 (92%)	
	Positive smear and/or culture	6 (1.8%)	
	Sought treatment in the health system	5	
	Prevalence (sputum+PTB)	16/100,000	
	Prevalence (all PTB)	24/100,000	
Verbal autopsy (VA)^b			
		Recognized cases (n=15)	Unrecognized cases (n=13)
	Average age (years)	36	46
	Place of death		
	Hospital	9 (60%)	4 (31%)
	Home	6 (40%)	9 (69%)
	Sought treatment in the formal health system	15 (100%)	12 (92%)
	Mean weeks duration of chronic coughing	39 (median 20)	35 (median 16)
	Response to VA questions:		
	Was it TB?	14 (93%)	0
	Is it being treated at a hospital?	14 (93%)	0
	Confirm TB on hospital register	6 (40%)	0
	Incidence (all PTB)	39/100,000	34/100,000
	Prevalence (all PTB)	29/100,000	23/100,000

^aUsed for calculations of TB incidence and prevalence.^bPermanent population older than 10 years.^cPercentage of those where sputum results were available.