HIGH SENSITIVITY FOR TUBERCULOSIS IN A NATIONAL INTEGRATED SURVEILLANCE SYSTEM IN FINLAND

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Little is known about the sensitivity of surveillance for tuberculosis after integration of formerly dedicated tuberculosis surveillance and control into the general health care system, an integration which took place in Finland in 1987. We compared routine laboratory notifications to the National Infectious Disease Register (NIDR) for *Mycobacterium tuberculosis* from January 1, 1995, to December 31, 1996, with data collected independently from all laboratories offering *M. tuberculosis* culture, and with data from patient records. 1059 culture-positive cases were found. The overall sensitivity of the NIDR was 93% (984/1059). The positive predictive value of a culture-positive case in the NIDR to be a true culture-confirmed case was 99%. For the culture-confirmed cases in the NIDR, one or more physician notification forms had been submitted for 89%. A highly sensitive notification system for culture-positive tuberculosis can be achieved in an integrated national infectious disease surveillance system based on laboratory notification.

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Introduction

Each year eight million people worldwide develop tuberculosis and at least three million die from the disease [1]. Tuberculosis has re-emerged in countries from Eastern Europe to the United States [2,3]. Emergence of multidrug resistance [4,5] poses a threat even for those developed countries in which the incidence of tuberculosis has been constantly declining. Consequently, high quality surveillance with good sensitivity is needed also in countries with low incidence.

In countries endemic for tuberculosis, tuberculosis case finding, treatment, and outcome monitoring are commonly implemented by a vertical organisation dedicated to tuberculosis. The surveillance data thus collected are considered to be of high coverage, in contrast to low sensitivities reported from passive systems for the surveillance of other infectious diseases based on notification by physicians [6,7]. Little information is available on the sensitivity for tuberculosis in national systems where surveillance for tuberculosis has been integrated with surveillance for a wide range of infectious diseases.

In Finland, a dedicated, vertical national tuberculosis surveillance and control organisation was dissolved in 1986, and the surveillance for tuberculosis was incorporated into an integrated national system for infectious diseases. This system was revised in 1994 to incorporate a mandatory, laboratory based notification system for a wide range of microbes, including Mycobacterium tuberculosis, and complementing mandatory physician notification for a limited number of diseases (National Infectious Diseases Register, NIDR).

We investigated the sensitivity of the surveillance system in a two-year national cohort of culture-positive tuberculosis cases. We compared notifications to the NIDR with a reference dataset collected independently from all laboratories performing culture for Mycobacterium tuberculosis.

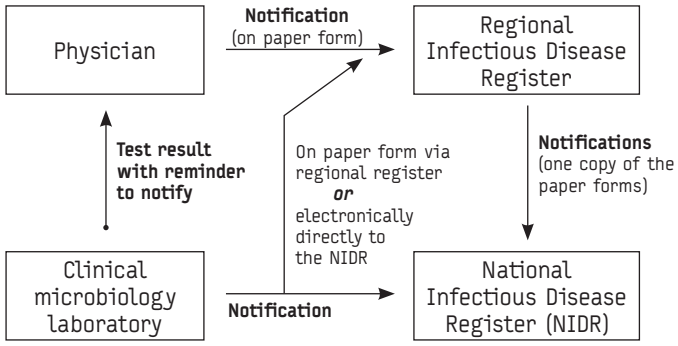
Material and methods

Integrated national surveillance system

Since 1994, the clinical microbiology laboratories in Finland have a mandatory duty to notify diagnostic findings for approximately 70 specified microbes or microbe groups, including *M. tuberculosis* [FIGURE 1], as well as all microbiological findings from blood and cerebrospinal fluid (CSF). In addition, the laboratory reminds in its report to the treating physician about the obligation to notify 32 diseases, which are mandatorily notifiable also by physicians. The data for NIDR are collected using one integrated laboratory notification form and one integrated physician notification form for all infections [TABLE].

FIGURE 1

Flow of information in the surveillance system for infectious diseases in Finland, 1995-1996



Notifications are sent to the NIDR via regional registers located in 22 hospital districts. During the study period 1995 to 1996, 20% of the laboratory notifications were sent electronically in encrypted format through the internet from the laboratories to the NIDR, and the remaining 80% on paper forms. Paper notifications are checked manually in regional registers and at the NIDR for missing or inconsistent information, and corrections are requested before data are entered into the NIDR database. For the infections notifiable by both laboratory and physician, notifications on an individual case are received and entered at different times. These notifications are linked automatically in the NIDR database using the national personal identity code or, in case this is missing, using date of birth, name, sex, and the municipality in which the case is treated. Country of birth, most recent nationality, and the place of residence are automatically extracted from the population information system using the national personal identity code. The earliest date of a diagnostic laboratory sample among the notifications of a case is recorded as the epidemiological date for a case.

TABLE

Data from laboratory and physician notifications of tuberculosis cases to the NIDR, and data retrieved from the population information system, Finland

Variable	Notifications to NIDR from		Retrieved from the population information system
	Laboratory	Physician	
Name	X	X	
National Personal Identity Code	X	X	X
Date of birth[1]	X	X	X
Gender	X	X	X
Place of residence		X	X
Current nationality		X	X
Country of birth			X
Date of death			X
Clinical unit treating patient	X	X	
International Classification of Diseases (ICD)		X	
Method of confirming diagnosis (clinical, microbiological, histological)		X	
Date of diagnostic sample	X		
Classification of TB (new, relapse, failure)		X	
Sputum smear result for AFB[2]		X	
Full TB treatment to be given		X	
Code for microbial species	X		
Laboratory method (culture, DNA/RNA)	X		
Sample type	X		
Resistance to INH or rifampicin	X		

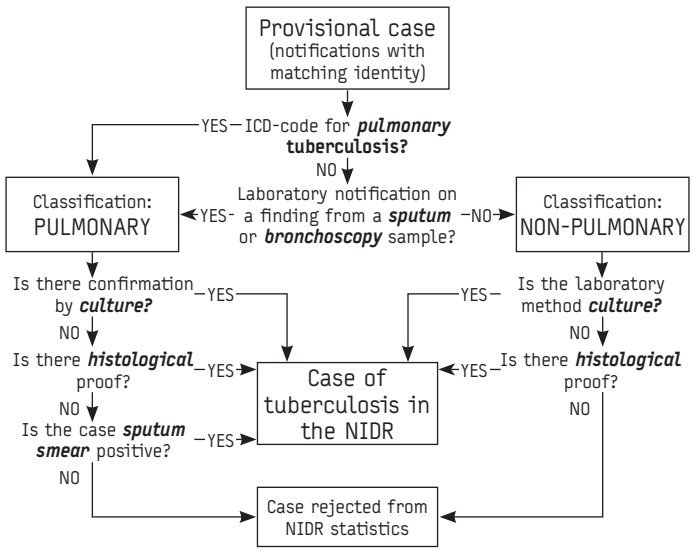
1. Incorporated in the national personal identity code.
2. Acid fast bacilli.

Tuberculosis surveillance data collection and processing

A clinically suspected case of tuberculosis with a decision to give full treatment is notifiable by a physician. Tuberculosis is the only infection in the NIDR for which a case does not have to be microbiologically confirmed to be notifiable. The algorithm for the fully computerised categorisation of TB cases, as well as the criteria for inclusion or rejection of a provisional case, automatically reassessed if a new notification on a pre-existing case is entered, are depicted in Figure 2. Cases included in the statistics, i.e. the case definition for a registered case, consist of (a) culture-confirmed cases notified by laboratories, (b) cases notified only by a physician and for which histological confirmation is reported, (c) cases of clinically suspected pulmonary tuberculosis for which the physician reports a sputum stain positive for acid fast bacilli. Because of the dynamic process where notifications on an individual case may accumulate over a period of several months, the categorisation of a case may change over time. Tuberculosis cases for which sample dates in further notifications are later than six months from the first date are assessed separately for their case status as a possible failure or relapse.

FIGURE 2

Automated computer algorithm for processing notifications of tuberculosis cases in the NIDR, Finland



All the physician notifications on tuberculosis without a link to a laboratory notification of *M. tuberculosis* are checked electronically for linkage to laboratory notifications on culture findings of non-tuberculous mycobacteria. All provisional cases under 15 years of age are checked in detail. Cases not fulfilling the case definition for registering remain in the database, but are not used for statistical purposes. During the study period no requests were sent for missing notifications in cases where either a laboratory notification, or a physician notification reporting microbiological confirmation, was registered without a corresponding notification from the other source.

Study population

For the evaluation of the coverage of the NIDR, a comparison was made between all cases notified by laboratories as positive for *M. tuberculosis* by culture and a reference dataset. The NIDR -derived set of cases included all the tuberculosis cases with a laboratory notification on a first specimen positive for *M. tuberculosis* by culture collected between 1 January 1995 and 31 December 1996.

For collection of the reference dataset, all the laboratories that had ever sent *M. tuberculosis* notifications to the NIDR or licensed to perform clinical microbiology testing for *M. tuberculosis* were contacted. Eighteen laboratories were found to have performed *M. tuberculosis* cultures during 1995-1996. One of the laboratories was private and the remaining ones, associated with university hospitals or other specialised care, were in publicly funded hospitals. A request was sent to the identified laboratories to provide a list of all samples culture-positive for *M. tuberculosis* between 1 October 1994, and 31 December 1996, with personal identifying information.

For the reference dataset the laboratories provided data as: (a) a print-out of laboratory computer files on culture-positive results of *M. tuberculosis* (five laboratories), (b) a manually-generated list from the laboratory database (six laboratories), (c) a photocopy of each confirmed identification and susceptibility test result returned from the national reference laboratory (three laboratories) and (d) a mixture of (b) and (c) (four laboratories). The laboratories were discouraged from using the previously sent notifications on *M. tuberculosis* findings as a base for the reference data. The data from the lists sent by the laboratories were entered as a reference dataset. Each case in this dataset was linked with cases in the NIDR database using the national personal identity code. Cases in either dataset without an electronic linkage initially to a case in the other dataset were carefully checked manually for spelling or digit mistakes in the name, date of birth, and national personal identity code for a final culture-confirmed cohort. For all the cases in this cohort, a chart review was performed for collecting further detailed microbiological, clinical, treatment and outcome data.

Statistical analysis

To estimate the sensitivity of the laboratory notifications to the NIDR as a proportion of all culture-confirmed cases, the number of laboratory-notified culture-positive cases in the NIDR was divided by the total number of culture-confirmed in the study cohort. To estimate the sensitivity of physician notifications of culture-positive tuberculosis cases in the NIDR, the number of physician notifications on culture-positive cases found in the NIDR was divided by the number of culture-positive cases notified by a laboratory to the NIDR. Positive predictive value was calculated by standard method.

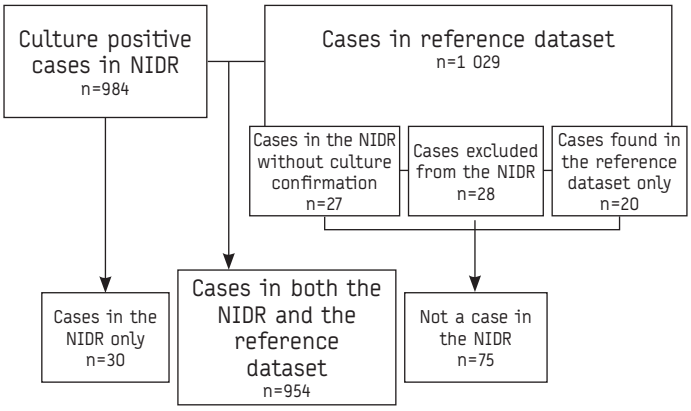
Results

During the 24 month study period in 1995-1996, 991 cases were notified as culture-confirmed to the national surveillance system NIDR. The retrospective, separate collection of culture findings for the reference dataset from each laboratory licensed to implement mycobacterial cultures yielded 1054 culture-confirmed cases. Linking these two datasets with the national personal identity code identified a total of 1088 culture-confirmed cases present in both or either of the datasets. Patient records were available and reviewed for 1057 of these 1088 cases.

Chart review revealed that a total of 29 of the 1088 cases had not actually fulfilled the case definition of the NIDR: in 14 the diagnosis was based only on PCR, three cases were caused by non-tuberculous mycobacteria, and a further five were excluded for varying reasons. A further seven cases had been registered in the wrong calendar year. After the exclusion of these 29 cases, a total of 1059 cases remained in the study cohort; 984 having been notified to NIDR as culture-verified, and 1029 present in the reference dataset [FIGURE 3].

FIGURE 3

Culture confirmed tuberculosis cases in the NIDR and reference dataset between 1 January 1995-31 December 1996, Finland



The sensitivity of the NIDR for culture-positive cases of tuberculosis was 93% (984/1059). The positive predictive value of a case recorded in the NIDR as culture-positive to be a verified culture-positive case was 99% (984/991).

Twenty (2%) of the 1029 culture-positive cases in the reference dataset, and also verified in the chart review process, did not have any notification to the NIDR [FIGURE 3]. Another 55 cases had one or more notifications in the NIDR, which did not, with the data included in the original notification(s), meet the NIDR definition for a culture-positive case. Twenty seven of these had been included in the NIDR statistics based solely on a physician notification fulfilling the case criteria, another twenty eight provisional cases had not fulfilled the case definition for registration as a case.

Thirty cases not found in the reference dataset were found in the NIDR as laboratory notified, culture-positive cases. Patient records or additional checks in the clinical microbiology laboratories verified that these cases had been positive for *M. tuberculosis* by culture, but had been omitted from the laboratory list for reference dataset, half of them from a single laboratory.

For the culture-confirmed cases in the NIDR (N=984), which were verified by the checking procedure, one or more physician notification forms were found for 876, for a sensitivity of 89% for physician notifications.

Discussion

We assessed the sensitivity for culture-confirmed tuberculosis of a recently introduced national integrated infectious diseases surveillance system based on mandatory laboratory and physician notification. By comparing data from the national surveillance system with a reference dataset collected separately from all laboratories performing *M. tuberculosis* culture, we found a sensitivity exceeding 90% for culture-confirmed cases of tuberculosis.

The sensitivity of the surveillance system was assessed using a nation wide population-based cohort of all cases positive for *M. tuberculosis* in culture over a two-year period. The laboratories performing *M. tuberculosis* culture were identified from two different sources. Subsequently, the reference dataset from each laboratory was collected by a mechanism unrelated to previous laboratory notifications to NIDR, confirmed by in-depth interview of procedures used in collecting the data at each laboratory. The overall high-degree match of the cases in the reference data with those in the NIDR and the additional validation procedure using patient records ensure that the cohort obtained by merging cases from these two sources is valid for assessing the sensitivity of the NIDR for culture-positive *M. tuberculosis* infection. A limitation of the study design is that it does not allow estimations on the sensitivity of the surveillance systems for tuberculosis cases, which have not been confirmed by culture.

Laboratory notification has been proposed to improve the sensitivity of passive surveillance systems based on physician notification [8,9]. We are not aware of previous reports on evaluating national large-scale laboratory-based surveillance of infectious diseases. The sensitivity of the NIDR for culture-positive *M. tuberculosis* cases observed in this study is considerably higher than those published previously in high or low incidence countries for tuberculosis. Using a combination of data sources such as hospital discharge registers, pharmacy listings of patients receiving antituberculosis medications, laboratory registries and special clinics treating tuberculosis patients for identifying cases a study from the United States [6] estimated in the 1970s that the reporting rate for tuberculosis was 63%. In Scotland, 60% of cases with a combined clinical and pathological diagnosis were notified [10]. In a five-year survey in London, 27% of tuberculosis cases were notified [11].

The new surveillance system, introduced in Finland in 1994, with mandatory laboratory-based notification, has some distinct advantages. To save manpower resources, automated computer algorithms are used in the NIDR without preceding manual synthesis of multiple notifications from a case. In a state wide pilot study in a limited geographic area in the United States, electronic laboratory reporting more than doubled the total number of reports as compared with reporting based on form [12]. In Finland, currently over 85% of all laboratory notifications are made electronically to NIDR with data automatically extracted from laboratory databases, in contrast to 20 percent at the time of the studied cohort. The data, including nominal identifiers, are transmitted in an encrypted format using public lines and internet technology. Using the national personal identity code, all the notifications for one person, sometimes exceeding 10 for one episode from several sources, distributed over a wide geographic spread due to referrals, can be linked. The system also supports easy electronic linkage of provisional tuberculosis cases to laboratory notifications of non-tuberculous mycobacteria as a checking procedure, as well as linkage between notifications of tuberculosis and HIV infection.

In the Finnish notification system the laboratory should also remind the physician to send a notification to the NIDR when a positive result of a pathogen causing disease also notifiable by a physician is reported to the clinic from the laboratory. With limited resources for surveillance of a large number of infectious diseases, physicians were not sent requests during the study period from the surveillance system to supply a notification on a patient for whom a

laboratory notification without a linking physician notification has been received. On this background, 89% sensitivity for physician notification, providing complementary clinical-epidemiologic data, in culture-positive cases seems high compared with previous reports on the evaluation of notification systems based on physician notification only. The sensitivity and efficiency of the surveillance system can still be improved with limited resources by combining computerised flagging systems for missing information in an individual case with the recently introduced remote access from all the regional registers to the NIDR database using encrypted internet technology.

In conclusion, high sensitivity for culture-confirmed tuberculosis cases can be achieved in an integrated system for infectious disease surveillance by incorporating mandatory laboratory notification. This will strengthen the understanding on the burden of disease caused by tuberculosis, as well as facilitate the detection of clusters of recent transmission when submission of strains for molecular typing is associated with laboratory notification.

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ORIGINAL ARTICLES

Surveillance report

PULMONARY TUBERCULOSIS IN TWO REMAND PRISONS (SIZOs) IN ST PETERSBURG, RUSSIA

T Lobacheva [1], V Sazhin [2], E Vdovichenko [2], J Giesecke [1]

The tuberculosis (TB) situation in the Russian penitentiary system has received much attention. We performed a descriptive epidemiological study of TB in two St Petersburg remand prisons (SIZOs). The medical databases of the TB divisions in these prisons were searched for all diagnosed cases of TB from 1 January 2000 to 31 December 2002. The main diagnostic method was chest x ray.

The total number of reported TB cases in these two remand prisons during this three-year period was 876. Out of these, 432 were diagnosed at entry to prison, and 444 developed the disease during incarceration, with the proportion diagnosed during incarceration increasing over time. The majority of cases were aged under 30 years.

TB incidence in Russian remand prisons is still very high and needs to be monitored closely.

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Introduction

Reliable data on tuberculosis (TB) incidence in the Soviet Union are lacking. There is, however, strong reason to believe that the incidence has increased considerably since 1991. According to official national figures, the incidence was 34/100 000 in 1991 and 90/100 000 in 2000 [1]. The TB problem has received much attention both in Russia and western countries [2,3]. The high incidence of TB in Russian prisons is of particular concern [4-6]: a search of the databases MEDLINE and CAplus yielded 45 publications since 1980 on TB in Russian prisons. However, 25 of these were published in Russian only. There have been several initiatives from international organisations to assist national authorities in their control efforts among prisoners [7]. TB in prison is not an isolated problem – especially not in a remand prison – since incompletely treated patients may well spread the disease in the general population after release [8-10].