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Validation of the surveillance system for new cases of tuberculosis in a province of Northern Italy

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ABSTRACT: In Italy tuberculosis (TB) surveillance is hampered by several problems (inconsistency of data and underreporting). A tuberculosis surveillance system was established in Varese Province (VSS) in 1992. The aim of the present study was, using VSS, to estimate: 1) coverage and validity of data collected by the national Compulsory Surveillance System (CSS); 2) validity of diagnosis and risk factors for tuberculosis; 3) tuberculosis incidence.

A specifically designed form, including the same items as the CSS form and 10 more questions on risk factors and diagnostic issue, was completed in all the existing health facilities in the province for each new tuberculosis case diagnosed, collected by the study co-ordinator during monthly supervision after a review of clinical records, and stored in a database at the co-ordinating centre. Routine notifications collected at national level by CSS for the province were nominally linked with VSS data. To evaluate coverage and data validity, a comparison was made between VSS and CSS data after removal of duplicates. Quality of data, risk factors and incidence were evaluated on VSS data (gold standard).

CSS coverage was 63%with a significant underreporting of extrapulmonary cases. Within CSS, 20% of data were missing (particularly diagnostic information: 42–72%). According to VSS, smear was performed on 88% of cases and culture on 66%. Half of the cases had no risk factors. The overall incidence of tuberculosis in Varese Province was 15 per 100,000.

We estimated the coverage and validity of the data collected by CSS, validity of diagnosis, risk factors for and incidence of tuberculosis and proposed several suggestions to improve CSS nationwide.

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For decades, case notification rates of tuberculosis (TB) declined steadily in most developed countries [1]. After a period of relevant neglect, interest in TB has been revived as the disease has again become a clinical and public health problem in industrialized countries [2]. In some industrialized countries a slowing or a reversal in the decline of case rates of TB was reported in the past few years, the reasons for these changes being mainly increased immigration, poverty, homelessness, intravenous drug abuse and human immunodeficiency virus (HIV) infection [3, 4].

Comparative analysis of the TB notification data in Western Europe is fraught with problems. Within each country, case definitions and reporting criteria have changed; and between countries, there are large differences in the quality of surveillance and reporting criteria [4–6]. Basic strategies to effectively counteract the resurgence of TB cases are direct government responsibility for supervision of diagnosis, treatment and prevention of TB, as well as the maintenance of properly designed surveillance systems [7].

The Italian TB surveillance system has several pitfalls: only infectious pulmonary TB cases and some extrapulmonary TB cases (bones, lymphatic, ulcerous skin) were notified until 1990, although inconsistency of data [8], and underreporting is a recognized problem [4, 9, 10]. Whilst officially 4,185 TB cases were reported in 1990 (corresponding to 73 cases per 100,000 population) [4], it was estimated that approximately 20,000 (*i.e.* up to 35 cases per 100,000 population) may have occurred annually around the same year [11]. The present study started in a model area of northern Italy (the province of Varese) as a co-ordinated effort of the Italian Study Group on Tuberculosis and the Europe Region of the International Union Against Tuberculosis and Lung Disease (IUATLD).

A surveillance system (Varese Study System=VSS) was established in the province of Varese in 1992. The

aim of the present study was, using the VSS, to estimate: 1) the coverage and validity of data collected by the National Compulsory Surveillance System (CSS); 2) the validity of diagnosis and risk factors for TB in the perspective of adequate TB control; and 3) the incidence of TB.

The ultimate goal of comparing data deriving from two different surveillance systems is to identify the possible weak points in order to improve CSS nationwide.

Materials and methods

Background

The province of Varese is located in the region of Lombardia, north-western Italy. In 1992, according to the Provincial Statistical Office, its average population was 807,345 inhabitants (29,000 of them estimated to be immigrants). The average number of inhabitants per square kilometre was 673, ranging 60–1,200. The Province included five municipalities with >20,000 population and 10 with 10,000–20,000 inhabitants. The proportion of the population working was 46%, and the mean annual income per inhabitant was estimated to be about 16,250 US$.

Structure and flow of information of the routine Compulsory Surveillance System (CSS)

Since 1934, infectious pulmonary and selected extrapulmonary TB cases have been compulsorily notified in Italy. Since 1990 (Ministry of Health Act on Communicable Disease Surveillance No. 36), TB notifications have become compulsory for all cases (infectious or not) within the class III, *i.e.* communicable diseases for which additional data are required. The physician is required to notify the case (demographic characteristics, diagnostic data, date of onset) to the local health authority (Public Health Service).

From this level, a form is mailed to the regional level (Regional Epidemiological Office) and another to the national level (Istituto Superiore di Sanità, Ministry of Health and National Institute of Statistics). The CSS form consists of four sections (A, and B class I–III). Section A (23 items) is devoted to demographic issues, including the patient's name, sex, age, profession, citizenship, residence, onset date, place of symptoms onset, vaccination status and kind of management (in- or out-patient). Section B (class III) consists of 12 items, including microorganism, responsible criteria used to diagnose the case (clinical picture, direct smear, culture, tuberculin test, chest radiograph), localization (pulmonary or extrapulmonary), and information concerning the notifying public health officer.

Structure and information flow of the Varese Surveillance System (VSS)

All the health-care facilities available in the area surveyed were contacted and agreed to participate in the surveillance assessment. A specifically designed surveillance form was proposed by the study co-ordinator, discussed with the medical officers operating in the health-care facilities and approved. The form was distributed to the medical officers in charge of each health unit (9 public health services, 10 hospitals and 9 dispensaries). They were requested to fill the surveillance form for every new TB case diagnosed in 1992. Every month, the study co-ordinator visited each health-care facility, reviewed the clinical records for each TB case together with the officer in charge, and collected the notification form. The 10 laboratories available in the province were regularly surveyed to countercheck that at least all bacteriologically proven cases were enrolled into the study. Data forms were stored in a database at the co-ordinating centre, using Informix SE DBMS, running on Compaq 486/25 PC.

The form consisted of 55 items and was designed to compare information collected through the CSS system with the results of a 1988 published survey [8]. In addition to the items included in the CSS form, 10 more questions concerning risk factors and diagnostic issues were included in the VSS form.

We considered smokers both light and heavy smokers, according to recently published definitions [12]. An immigrant was defined as a foreigner legally admitted and expected to settle in the host country [13]. Any radiological abnormality typical of TB, identified on radiology reports, was considered as a positive radiological criterion for TB.

Notifications collected by CSS at national level at the Istituto Superiore di Sanità, Rome, were examined and nominally linked with VSS notifications.

In the one centre of VSS, where nominal information was not available, cases were identified by name/surname initials, age, sex and National Health System code number. In order to obtain the coverage and to evaluate the validity of data, a comparison was made between VSS and CSS. To evaluate CSS coverage and validity of data and to estimate the incidence of TB, VSS data were considered as gold standard. The additional information derived from VSS forms was used to evaluate validity of diagnosis and risk factors for TB (smoking, contact with TB case, alcohol consumption, immigration, HIV infection, *i.v.* drug use, use of steroids, professional exposure to TB cases and silicosis).

According to the World Health Organization (WHO) definitions, cases were classified as follows [13, 14]: definite cases (culture-confirmed TB); probable cases (in the absence of culture confirmation, all four of the following criteria had to be met: positive tuberculin test; treatment with multidrug therapy; response to treatment; positive direct smear or histology result); and possible cases (less than four of the criteria mentioned above).

Since bacteriological confirmation is a key point in surveillance, pulmonary TB was considered with particular attention.

Statistical analysis

Within each of the two systems, duplicated cases, reports with mention of previous anti-TB treatments, cases

due to Mycobacteria other than tuberculosis (MOTT), and cases receiving preventive therapy were excluded from analysis.

Notified cases were included if bacteriologically confirmed or when at least two diagnostic criteria were met.

The CSS coverage was determined in percentage as CSS data\VSS data. The type of information for which a disagreement between VSS and CSS was identified, was described. Cases detected through VSS and those notified to CSS were compared, according to the following variables: age, sex, clinical form, and microbiological status. The validity of CSS forms was evaluated from the proportion of missing data on the various items in comparison with VSS.

Incidence rates (per 100,000 population) were calculated by applying the number of cases detected by VSS (all cases, culture positives, *etc*.) to the average population of the area during mid-1992. Rates were determined for both native Italians and immigrants.

Statistical analysis was performed with SPSS and Statgraphics (version 6.0) statistical packages. Expected and observed frequencies (qualitative data) were compared by uncorrected Chi-squared test, or by Fisher exact test where appropriate. The mean values of two different distributions of quantitative variables were compared by Student's t-test for unpaired data. A p-value of less than 0.05 was considered statistically significant.

Ethical considerations

The VSS protocol was approved by the Ethics Committees of the participating centres. All but one centre approved the nominal notification on VSS forms to facilitate removal of duplicate reports. In the one centre where nominal notification was not allowed, only patients' initials were reported. In the co-ordinating centre database, after duplicate removal, only specific codes were left. In all feedback reports only aggregated data were presented.

Results

Information from VSS, and coverage and quality of CSS

In 1992, 143 cases were reported by VSS and 89 by CSS. A comparison between the notifications of the two systems is presented in table 1. Thirteen cases were removed from CSS because of duplication and 22 from VSS (8 duplicates, 6 mycobacterial infection other than TB, and 8 preventive therapy). After removal of duplicates, 121 cases of TB were notified by VSS and 76 by CSS. All cases notified by CSS were also notified by VSS. Forty five cases notified by VSS were not reported by CSS. Thus, the CSS coverage was 63%. Within CSS, undernotification was significantly higher in females and in the extrapulmonary group (table 2). Similarly, duplications occurred more frequently among extrapulmonary cases (p=0 00018, Fisher exact test).

Table 1. – Tuberculosis (TB) cases notified by the Compulsory Surveillance System (CSS) and the Varese Surveillance System (VSS), Varese Province, 1992.

	VSS	CSS	Difference
Total cases notified	143	89	54 (-38%)
Duplicates	8	13	
Not TB	14	0	
True cases	121	76	45 (-37%)

Table 2. – Tuberculosis cases (overall and not notified) by age, group, sex, clinical form and bacteriological status, Varese Province, 1992

	Variable n	Overall cases n	Cases not notified %	p-value
Age group				
0–12 yrs	5	0	0	0.19
13–65 yrs	83	31	37	
>65 yrs	33	14	42	
Sex				
Male	74	20	27	<0.001
Female	47	25	53	
Site				
Pulmonary	88	24	27	<0.0005
Extrapulmonary	33	21	64	
Smear				
Positive	60	23	38	0.17
Negative	47	14	30	
Not done	14	8	57	
Culture				
Positive	44	12	27	0.19
Negative	36	14	39	
Not done	41	19	46	

The validity of CSS data, in comparison with VSS data, is summarized in table 3. A significant difference was found between CSS and VSS data concerning 6 of the 13 variables examined, namely tuberculin test at diagnosis, culture, direct bacteriological examination, chest radiograph and hospitalization. No significant difference in the age distribution of notifications was found comparing CSS and VSS.

Validity of diagnosis and risk factors for TB

Among 121 VSS TB patients, culture was performed in 80 cases (44 positive and 36 negative), smear in 107 cases (60 positive and 47 negative), radiography in 118 cases (101 positive, and 17 negative), tuberculin test in 97 cases (72 positive and 25 negative) and histology on biopsy specimen in 18 cases (13 positive and 5 negative). Two cases were diagnosed following postmortem examination.

Table 3. – Missing information (absolute number and percentage value) from notified forms, Varese Surveillance System (VSS) (n=121) and Compulsory Surveillance System (CSS) (n=76), 1992

	VSS		CSS		p-value
	n	%	n	%	
Tuberculin test at diagnosis	24	20+	55	72++	<0.0001
Culture at diagnosis	14	12	39	51	<0.000
Direct smear at diagnosis	14	12	38	50	<0.0001
Date of onset	10	8	9	12	0.04
Chest radiograph	3	3	32	42	<0.0001*
Occupation	1	1	14	18	<0.0001
Hospitalization	0	0	7	9	<0.0006*
Age	0	0	3	4	<0.06*
Pulm/extrapulm. site	0	0	0	0	NS
Citizenship	0	0	2	3	<0.14*
Date report	0	0	1	1	0.4*
Sex	0	0	0	0	NS
Extrapulmonary site	0	0	0	0	NS
Total	66	4$	200	20$$	<0.0001

Statistical comparison was made by Chi-squared test; 2×2 contingency tables were as follows: VSS present; CSS present; VSS missing; CSS missing. Pulm: pulmonary; extrapulm: extrapulmonary; NS: nonsignificant. +: % out of 121 VSS forms; ++: % out of 76 CSS forms; $: % out of 1573 items; $$: % out of 988 items; *: Fisher exact test.

Table 4. – Distribution of 121 notified cases by risk factor and clinical form, Varese Surveillance System, 1992

Risk factor	Pulmonary		Extrapulmonary		Total		p-value
	n	%	n	%	n	%	
None	33	38	22	67	55	45	0.004**
Smoking	30	34	3	9	33	27	0.006*
Case contact	11	13	3	9	14	12	0.7*
Alcohol	11	13	1	3	12	10	0.17*
Immigration	8	9	1	3	9	7	0.44*
HIV	5	6	4	12	9	7	0.25*
i.v. drug use	4	5	3	9	7	6	0.38*
Steroids	4	5	0	0	4	3	0.57*
Health staff	3	3	2	6	5	4	0.6*
Silicosis	1	1	0	0	1	1	1.0*

*: Fisher exact test; **: uncorrected Chi-squared test. HIV: human immunodeficiency virus.

According to CSS, 25 definite, 40 probable and 11 possible cases were notified. The same patients were classified in VSS as follows: 32 definite, 25 probable and 19 possible. Considering 121 VSS patients, 44 definite, 44 probable and 33 possible cases were reported.

The risk factors for TB identified by VSS are summarized by form of disease in table 4. About half of the cases had no identifiable risk factors. A significant difference was found between pulmonary and extrapulmonary cases concerning absence of risk factors (more frequent in extrapulmonary cases) and smoking (more prevalent in pulmonary cases).

Estimates of TB incidence

VSS cases represented 3.3% of all cases reported nationwide in 1992 (2.7% of all pulmonary and 4.7% of all extrapulmonary cases). According to VSS, the overall incidence of TB cases was 15 per 100,000 population and the incidence of smear-positive cases 7.4 per 100,000. According to CSS, the overall incidence of TB cases was 9.4 per 100,000 population and the incidence of smear positive cases 4.6 per 100,000. A summary of the specific incidence rates is presented in table 5.

Table 5. – Summary of the specific incidence rates per 100,000 population (overall, native Italians, immigrants), Varese Province, 1992

	Overall	Native Italians	Immigrants
Population n	807345	778345	29000
Incidence per 100,000			
All cases	15.0	14.4	31.0
Pulmonary	10.9	10.3	27.6
Extrapulmonary	4.1	4.1	3.4
Smear positive	7.4	7.1	17.2
Culture positive	5.4	4.9	20.7
Known HIV positive	1.1	1.0	3.4

HIV: human immunodeficiency virus.

Discussion

Using VSS, we estimated coverage and validity of the data collected by CSS, validity of diagnosis, risk factors for TB, and incidence of TB.

Coverage and data validity of the national CSS

According to the results of our study, the national CSS detected 63% of TB cases identified by VSS. According to other studies, the Italian surveillance system is inefficient [4, 8]. However, traditionally good systems have also shown unexpected limitation, such as those described in England and Wales, Scotland and the United States [15–17]. A recent retrospective study performed in London [15], based on hospital registry, found that 27% of TB cases were not notified, including 14% of all smear-positive cases. As a consequence, in Britain the true incidence was probably one third higher than current notification figures suggest. To clarify the issue, two studies were performed in Italy as recommended by the national TB Study Group of the Associazione Italiana Pneumologi Ospedaleri (AIPO) [18]. The proportion of nonreported TB cases was found to be 37% in our study, including 38% of all smear-positive cases. In the second study, performed in Italy in 1992 [19], out of 462 notifications, 65 (14%) were duplicates, and 106 (27%) notifications issued by the dispensary of Torino, never reached the regional epidemiological office.

In our study nonreported cases were observed significantly more often in the extrapulmonary group, probably reflecting a lower attention towards noninfectious TB cases. CSS duplications were also more frequently observed among extrapulmonary cases. The analysis of CSS and VSS duplicate notifications, revealed that the vast majority belonged to different patients as a consequence of the different study design (only two cases were duplicated in both systems). Duplicates were frequently the result of movement of TB patients within the different health structures of the province. Within VSS, clinicians had frequent opportunities to meet and exchange information on patients. As a consequence, some duplications were avoided.

The main difference concerning data validity between CSS and VSS was on bacteriological status of the cases. This may result from the fact that the case was notified before the availability of smear and culture results. According to recent proposals by the Istituto Superiore di Sanità and the AIPO TB study group, the case should be reported in two steps: an immediate call to health authorities for preventive action (within 3 days), followed by a complete notification when all clinical data are available (within 60 days). During the Second European WHO IUATLD Workshop on TB Surveillance and Programme Monitoring in Europe (Wolfheze, 23–24 March 1994), a system based on individual case reports was still considered the best option, and the following variables were considered mandatory: date of diagnosis, site of the disease, bacteriological status (smear and culture), age, gender, citizenship (immigration), history of previous treatment.

In our study, more information concerning diagnostic issues was missing (from 42–72%, table 3) than additional information (occupation, hospitalization, data of onset), and demographic data (0–9%). Our findings are consistent with those of another study performed in Italy showing that the data missing from the routine system were 39% in Piemonte and 18% in Emilia-Romagna regions (ranging from 0–72%, particularly diagnostic issues) [19].

These findings suggest that public health officers filling notification forms were more accurate in reporting than physicians. As recently suggested, a standardized approach to physicians' training on TB is considered a public health priority in Italy [18]. Efficient feed-back of reports with aggregated data, from the national to the local level, may contribute to an improvement in the quality of reports.

Evaluation of diagnosis validity and risk factors

The quality of diagnosis in the VSS surveyed area may be further improved. CSS is based on the bacteriological evidence. Consistent international comparisons on cure rate and other programme indicators should be made only among bacteriologically (culture positive) confirmed cases. In this respect, a standardized approach to diagnosis and physicians training are priorities.

Smoking habits are significantly less prevalent in VSS TB patients (26%) in comparison with the previous study (36%) and the estimated national value (40%) [8, 20]. The low percentage of smokers may reflect the general welfare of the area surveyed. In our opinion, the importance of smoking as a risk factor for TB is overinterpreted. A simple message to be kept in mind in clinical practice is that a patient without the traditional risk factors can also be affected by TB.

Estimates of TB incidence

Our study showed that the incidence of all cases was 15 per 100,000 population (14.4 in native Italians and 31 in immigrants), and that of smear-positive cases 7.4 per 100,000. These figures, which are similar to those of several northern European countries, are significantly higher than the overall rate of TB cases notified in Italy from 1981 and 1991 (ranging 6.6–7.5 per 100,000) and in 1992 (8.2 per 100,000) [4, 21].

Surveillance and TB control

The objectives of a surveillance system are mainly guidance for health interventions, estimate of trends, identification of groups at risk, changes in patterns of transmission, evaluation of preventive strategies, and hypothesis for further research [6]. In Europe, mandatory notification systems are often completed by voluntary laboratory, physician or hospital-based systems [6]. In general, mandatory notification systems are not very reliable, their performances depending on the country and/or the disease.

In addition they need to be tailored to the public health objectives and health systems of each country [6], and they should also be evaluated regularly [22–24].

There are different possible approaches to evaluate a surveillance system. The outcome of a system should be compared with estimates obtained by alternative methods. For instance, the capture-recapture system, is based on the use of two or more sets of data potentially including the same individuals, in order to estimate the true number of cases in a given area [25]. An interesting approach was developed in Greece [24] and Italy [10] to estimate the number of TB cases from anti-TB drugs consumption. Another method of estimation is that based on the annual risk of infection model [26], though its use in industrialized countries is not recommended because of the distortion in case prediction when the risk is low or decreasing rapidly. These methods present disadvantages: estimates and not real data are produced; different biases (*e.g.* selection bias) may affect results; areas with the highest need for intervention may be identified with difficulty.

The method utilized in this study (to compare CSS data with those of a simple control system) may overcome some of the problems mentioned above: the results are calculated, the selection bias is avoided (no sampling), the local health units needing intervention may be easily detected. The main limitation of our study is that the study area was small and not representative of the general Italian situation (although the methodology may be applied easily to other areas).

Conclusions and proposals

The results of our study suggest that the routine surveillance system in Italy is hampered by problems: low coverage, limited validity of data and diagnosis, significant underreporting. The following conclusions are evident: 1) bacteriological and clinical data must be collected at the lowest possible level (local health unit); 2) smear positive cases should be notified immediately to public health officers; 3) public health officers should co-operate with physicians to collect all additional information (clinical data) as soon as the diagnostic procedures are completed; cases can be classified as confirmed (culture positives) or unconfirmed (possible and probable cases); 4) only a minimum set of essential variables should be included in the notification form (date of diagnosis, site of the disease, bacteriological status, age, gender, citizenship, recurrent or new case); 5) a surveillance unit should be implemented at regional and national level; and 6) a system to monitor treatment outcome should be implemented as soon as the surveillance system works.

To increase CSS sensitivity some interventions may be proposed: a prompt notification by diagnostic laboratories both to health-care providers and to public health authorities (who can request physicians to ensure a proper collection of information) will allow identification of infectious cases as suggested by a European Task Force [13]; the notification to public health authorities of the list of patients discharged from hospitals with diagnosis of TB will ensure that hospitalized cases are reported [6]; and 3) an additional measure, recently suggested in Italy [18] and successfully implemented in Norway (E. Heldal, personal communication, 1994) is based on a health system which allows treatment only in selected public health clinical units; in this situation, anti-TB drugs are not available in the private market, which would guarantee automatic notification following TB treatment prescription within the public health system.

Surveillance is "an essential requirement" of TB control. Since poor control engenders chronic cases, resulting in increased cost of cure and rehabilitation, improvement of surveillance in Italy is a public health priority.

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