SURVEILLANCE OF TUBERCULOSIS

IN NORTHERN IRELAND

FROM 1992 TO 1998

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Summary

From 1992 to 1998 as part of the clinical tuberculosis notification system, DHSS received 690 notification forms. Ninety-four of these were reports of patients receiving chemoprophylaxis only, and 115 were subsequently identified as having non-tuberculous disease, giving a total of 481 cases of tuberculosis and an average annual prevalence of 4.2 cases per 100,000 population.

The annual prevalence of notified tuberculosis increased from 1992 to 1994 from 4.3 to 4.9 cases per 100,000 population and went down since then to 3.6 cases per 100,000 in 1998. The age and sex distribution did not show any particular trend over time and 93% of cases were born in the British Isles.
Of the 481 cases, 337 (70%) had pulmonary disease of whom 20 also had non-pulmonary involvement and 144 (30%) had non-pulmonary disease. The annual proportion of pulmonary cases did not change during the studied period and was always over 64%. Apart from pulmonary infection, the main sites of disease were lymph nodes and pleura.

The percentage of definite cases did not vary over time and was 66%. Out of the 337 cases of pulmonary tuberculosis, 57% were smear positive cases and 72% were confirmed by culture.

Details of initial treatment were recorded for 350 (73%) cases, of whom 56% received a combination of Rifampicin, Isoniazid and Pyrazinamide. Information on continuation therapy from follow-up forms was stated for 294 (61%) cases of whom 81% received a combination of Rifampicin and Isoniazid.

Sixty-eight deaths occurred among notified cases, of which 22 were stated to be caused by tuberculosis, were reported.

On the 301 isolates tested during the study period, 96% were fully sensitive, 3% were resistant to one drug, 0.3% to more than one drug and none was multi-drug resistant.

1. Introduction

This report presents the epidemiological data for tuberculosis cases reported in Northern Ireland (NI) from 1992 to 1998.

Northern Ireland has 1.7 million population (Registrar General Northern Ireland 1998 Estimate). The region is divided in four Health and Social Services Boards (Easter, Northern, Southern and Western) with responsibility for control of communicable disease in the area. Doctors are required to notify all clinically suspect cases of tuberculosis to the Director of Public Health of the appropriate Health and Social Services Board. Since 1992 there has been enhanced tuberculosis surveillance with specially designed forms to collect clinical on-going, demographic and microbiological information at the time of notification (TBS1). Approximately nine months after notification, in each Board, the Consultant in Communicable Disease Control (CCDC) forwards a follow-up form (TBS2) to the notifying clinician seeking details on confirmation of diagnosis, method and duration of treatment. Then, the CCDC sends to the Department of Health and Special Services (DHSS) completed TBS1 and TBS2 forms.

During the study period, all laboratories report a comprehensive list of microbiological data to the DHSS, including mycobacterium isolates.
Since 1993, the Northern Ireland Mycobacterial Reference Laboratory, based at the Northern Ireland Public Health Laboratory, at Belfast City Hospital, has participated in a national scheme for the surveillance of resistant strains of mycobacteria, the UK Mycobacterial Resistance Network or MYCOBNET.

2. Method

2.1. Source of information

Sources of information include Health and Social Services Board notification forms, the NI laboratory surveillance system and the information provided by MYCOBNET. The isolates sensitivity were tested for isionazid, rifampicin and ethambutol. *Mycobacterium tuberculosis* and *M.africanun* were also tested for pyrazinamide.

2.2. Case definitions

Case definitions are those recommended by the WHO/International Union Against Tuberculosis and approved by European country representatives[1].

A definite case was defined as one in which infection due to *Mycobacterium tuberculosis, M.bovis or M. africanum* is confirmed by culture (or an equivalent method e.g. DNA technology).

An **other than definite case** was defined as one, in the absence of confirmation by culture, in which:

i. A clinical judgement that the patient's clinical and/or radiological signs and/or symptoms are compatible with tuberculosis; **and**

ii. A clinicians' decision to treat the patient with a full course of anti-tuberculous treatment.

Pulmonary TB was defined as disease involving the lung parenchyma and/or bronchial tree; it includes all disease diagnosed by examination of sputum, broncho-alveolar lavage, bronchial washings, gastric washings, lung biopsy, etc.
It excludes pleural and intra-thoracic lymph node disease unless lung parenchyma and/or bronchial tree are also involved.
Non-pulmonary TB case included all cases not in the above definition.

2.3. Data analysis

Data were entered onto computer and analysed using the Epi-Info software package, version 6.04. The mid-year population estimates (Registrar General Northern Ireland, NISRA) were used for calculating rates.
Means were compared using parametric test (ANOVA, Student's test) or non-parametric test (Kruskall-Wallis one-way analysis for variance) according to the variances distribution. Trends were analysed using chi-square tests for rate.

2. Results

3.1. TB cases notified from 1992 to 1998

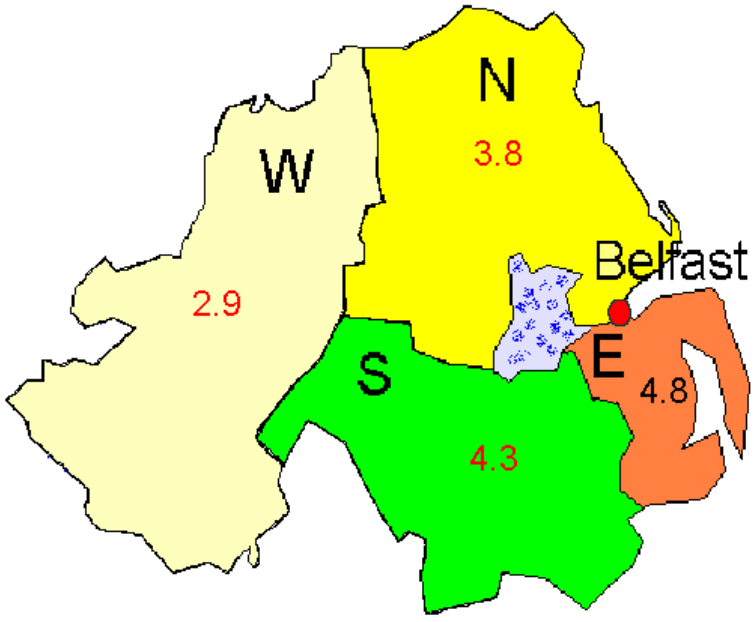
A total of 690 TBS1 forms and 471 TBS2 forms were received from Boards from 1992 to 1998.
Among the 690 notifications, 94 were reports of chemoprophylaxis, 88 were atypical mycobacteria, 20 were not tuberculosis and 7 could not be classified, giving a total of 481 tuberculosis cases notified to Boards and an annual prevalence of 4.2 cases per 100,000 population.

The distribution per year shows an increase of reported cases and prevalence from 1992 to 1994 (p for trend: 0.37), followed by a decline since then (p for trend: 0.01).

Table 1: Reported Tuberculosis cases, Northern Ireland, 1992-1998

Year	Cases	Prevalence per 100,000 population
1992	69	4.3
1993	75	4.6
1994	81	4.9
1995	75	4.5
1996	66	4.0
1997	55	3.3
1998	60	3.6
Total	481	4.2

The overall prevalence for the study period by Boards showed that the Eastern Board has the highest prevalence (map 1).



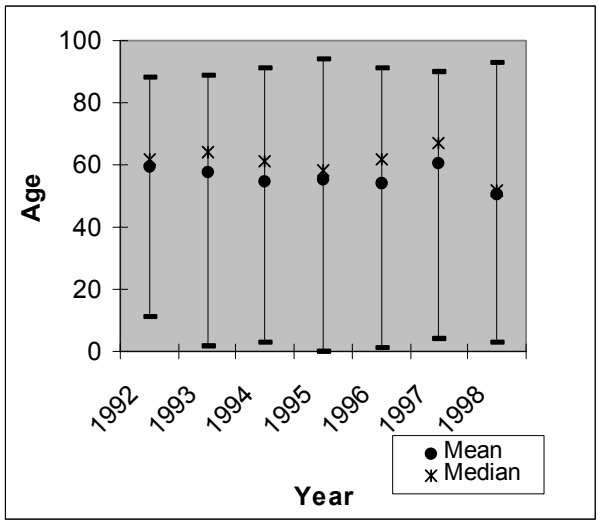
Map 1: Overall annual TB prevalence per Boards , 1992-1998, NI

3.2. Age and sex

The M/F sex ratio for the seven years was 1.3. Except in 1996, the number of males was always higher than the number of females.

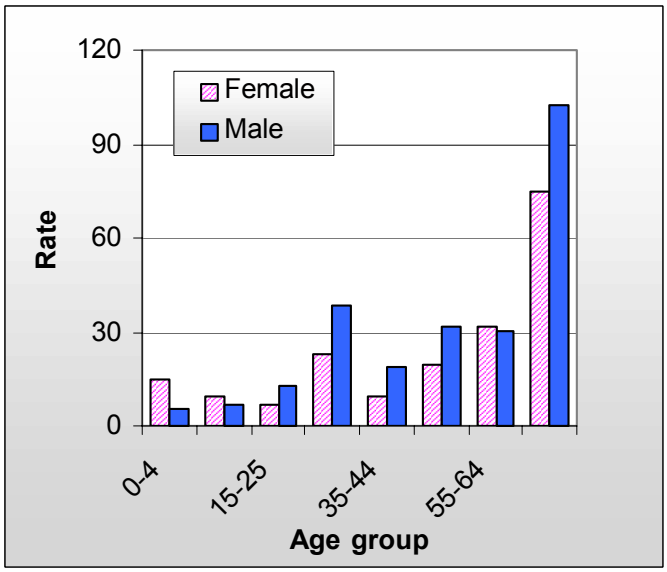
The ages ranged from 4 months to 94 year old with a mean of 56 years and a median of 61years during the studied period. The mean age distribution was the same over the 7 years (p =0.38).

Figure 1: TB cases: age distribution (mean, median, range), 1992-1998, NI



The age specific rate for the entire period was highest among the oldest age group. Except for children under 15 years, the prevalence was higher among males whatever the age group.

Figure 2: TB cases: sex and age-specific rate per 100,000 population for the period 1992-98, NI



3.3. Geographic origin and occupation

The country of birth was known for 469 (97.5%) patients. Four hundred and thirty six (93%) were born in the British Isles (UK and Ireland), 26 (6%) in Asia, 3 (<1%) in other European countries, 3 (<1%) in Africa and 1 in America.
The proportion born outside the British Isles has fluctuated from 1% in 1993 to 17% in the following year but with no particular trend over the studied period.

Table 2: TB cases: country of birth, 1992-1998, NI

YEAR	UK and Ireland	Others	
	N	N	*%*
1992	66	3	*5*
1993	74	1	*1*
1994	73	5	*7*
1995	60	10	*17*
1996	60	4	*7*
1997	53	2	*4*
1998	50	8	*16*
Total	436	33	*8*

The occupational status was recorded for 428 (89%) people of whom 179 (42%) were retired. Eleven patients (2%) had a profession related to health care and 10 (2%) related to farming. None of the latter was affected by *M. bovis*. Forty-five (11%) were unemployed.

3.4. Site of disease

Of the 481 TB cases, 337 (70%) had pulmonary disease of whom 20 had non-pulmonary involvement; 144 (30%) had non-pulmonary tuberculosis.
The proportion of cases with pulmonary involvement was 69% for the entire period and ranged from 62% in 1996 to 75% in 1992.

Table 3: TB cases and pulmonary involvement, 1992-1998, NI

YEAR	Pulmonary only	Pulmonary & non pulmonary	Non pulmonary only	*% with pulmonary involvement*
1992	49	3	17	*75*
1993	53	1	21	*72*
1994	48	6	27	*67*
1995	50	3	22	*71*
1996	39	3	24	*64*
1997	37	3	15	*73*
1998	41	1	18	*70*
Total	317	20	144	*70*

The major site of disease was pulmonary (70%), followed by the lymphatic system (11%) and the pleura (5%).

Table 4: Site of disease of TB cases, 1992-98, NI

	Major sites		Minor sites With pulmonary involvement	
	N	%	N	%
Pulmonary	337	*70*		*0*
Lymph node (Intra-thoracic)	52 (0)	*11*	3	*15*
Central nervous system (meningitis)	3 (0)	*1*	1	*5*
Genitourinary system	18	*4*	3	*15*
Bone/joint (spine)	16 (6)	*3*		*0*
Peritoneal/digestive tract	7	*1*	1	*5*
Pleura	26	*5*	1	*5*
Other	20	*4*	2	*10*
Disseminated	2	*0*	9	*45*
Total	481	*100*	20	*100*

3.5. Bacteriology

Sputum smear results

Among the 337 cases with pulmonary involvement, sputum smear results were available for 291 (86%), of which 166 (57%) were positive for acid-fast bacilli on microscopy.

Bacteriological confirmation

Of the 481 notified cases, 316 (68%) were bacteriological confirmed or definite cases**.** The proportion of definite cases per year did not differ significatively (p=0.7).
There were 303 (96%) *M.tuberculosis* and 9 (3%) *M.bovis* cultures isolated. The type of mycobacterium is unknown for 4 patients.

Table 5: TB cases by case definition, 1992-1998, NI

YEAR	Definite	Other than definite	Total	*% definite case*
1992	46	23	69	*67*
1993	46	29	75	*61*
1994	49	32	81	*60*
1995	52	23	75	*69*
1996	42	24	66	*64*
1997	37	18	55	*67*
1998	44	16	60	*73*
Total	316	165	481	*66*

The culture was positive for 242 (72%) of the pulmonary and 74 (51%) of the non-pulmonary tuberculosis cases.
Direct microscopic or histological examination showed evidence of mycobacterial infection for 80 not definite cases.

3.6. Contact tracing and clusters

Among the 481 cases, 20 (4%) were identified by contact tracing. The proportion varied from 0% in 1993 to 9% in 1995.
Information on the index case was available for 17 patients. All the index cases had pulmonary infection and were sputum positive except for one who was sputum negative and another with no information.
There were three clusters with one index case and two infected people.
One patient was first traced but not treated when the index case was notified. Two years later, he started chemotherapy and was notified. After exclusion of this patient, the time between the notification of the index case and the secondary cases ranged from 0 to 327 days with a median of 112 days and a means of 136 days.
In one of the Board, a cluster involved nine cases with 2 deaths in two extended families. The index case was diagnosed in June 1993, the first secondary case developed pulmonary tuberculosis seven months later and the last case was diagnosed on January 1995.

3.7. Previous treatment

Among the 481 patients, information regarding previous TB treatment was available for 462 (96%) of whom 71(15%) patients reported having been treated. The year of treatment was available for 61(86%) people of whom 46 (75%) reported treatment after 1949. The treatment given (surgery or chemotherapy) was not recorded except for two patients initially treated during the study period. One received a full treatment in 1994 and relapsed the following year. One was treated 10 month before in England but did not take the drugs properly.

Table 6: Previous TB treatment, 1992-1998, NI

YEAR	Yes	No	Total	*% treated*	*% treated after 1949*
1992	9	60	69	*13*	*8*
1993	14	61	75	*19*	*15*
1994	11	65	76	*14*	*13*
1995	13	60	73	*18*	*14*
1996	10	49	59	*17*	*12*
1997	11	42	53	*21*	*19*
1998	3	54	57	*5*	*5*
Total	71	391	462	*15*	*12*

3.8. Outcome

On the 481 cases, 374 follow-up forms (TBS2) were collected. Over time, the ratio TBS2/TBS1 went from 88% in 1992 to 67% the following year and is now stabilised around 80% since 1996.
Among the 107 patients with no follow-up form, 19 (18%) died.

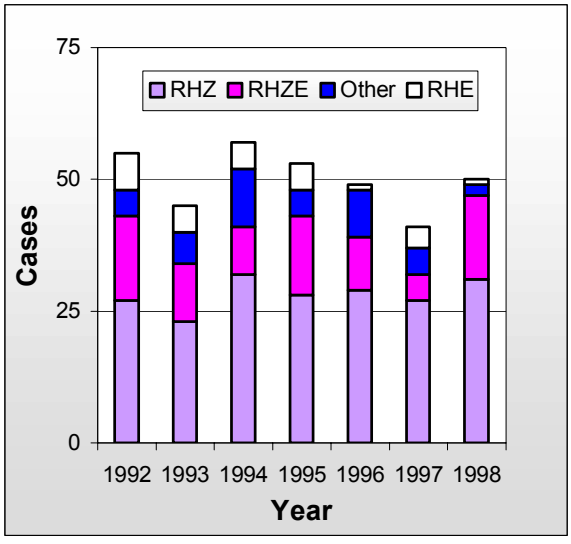
Sixty-eight deaths, of which 22 were stated to be caused by tuberculosis, were reported. The case fatality ratio for TB cases went from 0% in 1998 to 9% in 1992 with a global TB case fatality ratio at 5% for the entire study period.

3.9. Treatment

Initial therapy

Initial therapy was recorded for 350 (73%) cases. The most commonly reported treatment regimen was a combination of rifampicin, isoniazid and pyrazinamide (RHZ)**.** RHZ was recorded in 197 (56%) cases, 82 (23%) received rifampicin, isoniazid, ethambutol and pyrazinamide (RHZE), 28 (8%) were treated with rifampicin, isoniazid and ethambutol (RHE) and 43 (12%) with other drug regimens.
The proportion of people treated with the tri-therapy RHZ increased from 49% in 1992 to 62% in 1998.

Figure 3: Drug regimens for initial therapy of reported TB cases, NI, 1992-98



Among the 481 TB cases, 71 had already been diagnosed with TB in the past. The information on initial treatment was available for 47 of them, of whom 11 were treated with the four drugs RHZE, 24 with RHZ, 5 with RHE and 7 with other regimens. Among the 47 people, the year of previous diagnosis was available for 40, of whom 31 were diagnosed after 1949 and have probably received antituberculous drug treatment. Only 7 of them received a four-therapy regimen during the study period.
Twelve of the 20 non-white patients for whom the information was available received four drug regimen.

The duration of initial therapy (excluding cases who died) was stated for 300 cases of whom 213 (71%) were treated for 2 months.

Continuation therapy

Continuation therapy was recorded for 294 (61%) cases. The most commonly reported treatment regimen was a combination of rifampicin and isoniazid (RH) recorded in 237 (81%) cases, and 57 (19%) received other drugs regimens.
Except in 1990 where 90% of people received RH, the proportion was stable over the years and around 79%.

The duration of continuation therapy (excluding cases who died) was stated for 282 cases and went from 1 to 18 months with a median of 5 months.

Adverse effects

Adverse effects were reported for 55 people. Details were included for 38 people:

- Hepatic toxicity: 12 cases (2 linked to Isoniazid , 2 with Rifampicin and 1 with both)
- Rash/allergy: 7 cases (3 linked to Isoniazid , 3 to Rifampicin and 1 with both)
- Diarrhoea with Rifater : 1 case
- Oculo-toxicitry: 2 cases (1 linked to Ethambutol)
- Neuro-toxicity: 3 (2 linked to Isoniazid)
- Unspecified adverse events: 13 (4 due to Pyrazinamide)

3.10. Drugs resistance

The fully sensitive was recorded for 96% of the 301 *M.tuberculosis* complex isolates between 1993 to 1998. The annual proportion went from 92% in 1994 to 100% in 1998.
There were 9 (3.0%) isolates resistant to one drug of which 7 were resistant to Isoniazid, one to streptomycin and one to pyrazinamide.
Two (0.7%) isolates were resistant to two drugs. One isolate was resistant to isoniazide and ethambutol and one to isoniazide and Rifampicin.
Since 1993, multi-drug resistance has never been reported in Northern Ireland.

Table 7: Drug sensitivity in *M.tuberculosis* complex isolates in Northern Ireland from 1993 to 1998

	Isolates tested	Fully sensitive		Resistant*		
		N	%	One drug	More than one drug	Multi-drug resistant
1993	43	42	*98*	1		
1994	49	45	*92*	3	1	
1995	61	58	*95*	2	1	
1996	59	57	*97*	2		
1997	41	39	*95*	1		
1998	48	48	*100*			
Total	301	289	96	9	2	0

* Excludes pyrazinamide for *M.bovis* Source: MYCOBNET

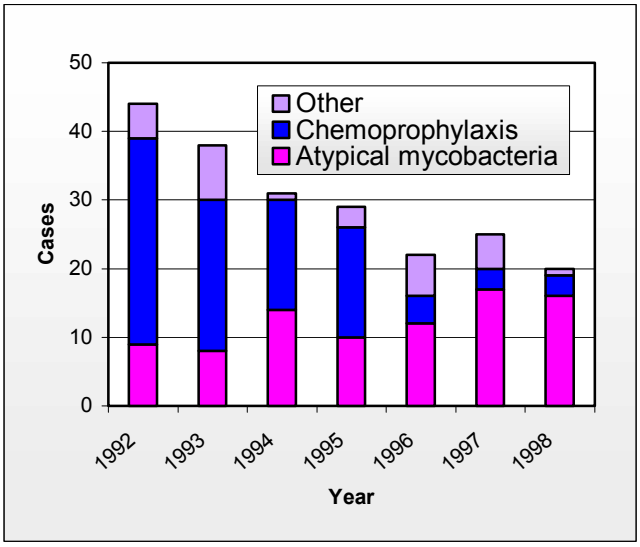
3.11. Over-notification

The proportion of over-notification was 30% for the study period. It decreased from 39% in 1992 to 25% in 1998.

Among the notifications received from Boards, 88 were excluded because there were later confirmed as atypical mycobacterium tuberculosis.
The most common types were *M.avium intracellulare* (27), *M.malmoense* (29) and *M.kansasii* (23). The atypical mycobacteria represented 8% of the notification in 1992 and 20% in 1998. During the study period, the laboratories reported 133 atypical mycobacteria. This number went up from 14 (11%) cases in 1992 to 34 (26%) in 1997 and then decreased to 25 (19%) in 1998.
The ages of the atypical mycobacterium tuberculosis patients ranged from 1.5 to 84 year old with a mean of 49.7 years and a median of 60.8years during the studied period The difference of age means with the mycobacterium tuberculosis patients was statically significant (p=0.01)

Ninety-four individuals were reported as receiving chemoprophylaxis: 58 males and 36 females. Among them, 37% (19/51) were identified by contact tracing. The age ranged from 3 months to 81 years with a median of 11 years and a mean of 13 years. The proportion of chemoprophylaxis among notifications went from 27% in 1992 to 4% in 1998.

Figure 4: Over notification per category, 1992-1998, NI



3.12. Under notification

During the study period, 42 cases of tuberculosis identified by the laboratory were not reported to Boards. The Board was only known for 20 of them. It is not known if the remaining 22 people were resident in Northern Ireland.

Table 8: Under notification, 1992-98, NI

	Laboratory cases not reported to Board	
Year	N	*%*
1992	2	*3*
1993	2	*3*
1994	6	*7*
1995	9	*11*
1996	12	*15*
1997	10	*15*
1998	1	*2*
Total	42	*8*

4. Discussion

The number of patients with tuberculosis has declined over the study period. This decline had been observed previously[2]. In the beginning of the seventies, the annual prevalence was around 20 cases per 100,000 population. Ten years later, the prevalence has dropped to 10 cases per 100,000 and is now under 5 cases per 100,000. This rate is lower that the prevalence registered in 1998 in England & Wales (10.9 overall and 7.7 excluding London) or in the Republic of Ireland (11.7) and ranks Northern Ireland in the group of European countries with the lowest prevalence[3,4,5.]

The prevalence has not levelled off in Northern Ireland in the recent years as it has been observed in the late 1980s in industrialised countries. One of the explanations is that tuberculosis is still a disease of the local population and not yet a disease affecting subgroups as people with AIDS or immigrants who are very few in the region. Most of cases were born in the UK or Ireland. Males and those aged over 65 remain the most affected by the disease. The age and sex distribution have not changed over time.

The major site of disease was pulmonary and the proportion of patients with pulmonary involvement was relatively stable (around 70%). Fifty seven percent of cases with pulmonary involvement were sputum positive. Most of the cases (68%) were laboratory confirmed and the annual proportion of definite cases did not change over time. This proportion is higher than the 54% observed in England & Wales in 1998. In Northern Ireland, 96% of the isolates were *M.tuberculosis*. The major sites of disease after pulmonary were lymph nodes (11%) and pleura (5%). There were also the 3 most common sites reported in the 1998 England and Wales survey.

Previous treatment was recorded for 71 patients (15%) compared to 66 (12%) for the previous study period 1982-86. This proportion of previously treated cases was rather high compared 8% in England and Wales in 1998. In Northern Ireland, "previous treatment" includes surgical and chemotherapy treatment and there is no information on the outcome. This large case definition could explain the difference. In England & Wales, in 1998, 56% of TB cases were born outside the UK and this may also account for this difference. In Northern Ireland, during the study period, less than 1% per year met the case definition of recurrent case used in the Republic of Ireland (TB in the previous calendar year treated at least one month with anti-tuberculous drugs). This figure was similar to the ratio observed in the Republic of Ireland in 1998 (3/424). In Northern Ireland, the case definition for recurrent cases is not used for surveillance. With the increase of multi-drug resistance in Europe, the case definition of recurrent cases should be used and would assist to identify those at risk.

The triple-therapy was the most commonly used during the initial treatment. Only 7 of the 31 people previously treated after 1949 received a quadruple therapy. The previous treatment was not known but it will be important to ensure that clinicians are aware of the recommendations regarding quadruple therapy[6].
Sensitivity to antituberculous drugs is better in Northern Ireland than in the rest of the UK. The proportion of drug resistance to one drug or more was double in the UK compared to Northern Ireland for the study period and multi-drug resistance was 1.3% in the UK compared to 0% in NI.

The treatment outcome was not systematically reported and could not be analysed. Treatment outcome results should be a part of any TB report and data collection should include the 6 outcomes (cure, treatment completed, failure, death, treatment interrupted, transfer out) as recommended[7].
During the seven years, the TB case fatality ratio was 6%. In the Republic of Ireland in 1998, this ratio was 1.4% (6/424). A younger TB population in Ireland (median age of cases around 45 years) may explain the difference.

The proportion of over-notification decreased from 1992 to 1998 mainly because of a reduction of chemoprophylaxis reports. Since 1992, clinicians have become increasingly aware that these patients do not need to be reported or notified. In contrast, the number of atypical mycobacteria reports was increasing. The age of the atypical mycobacterium cases was younger that the tuberculosis patient but it is not enough to assume that HIV/AIDS could explain the augmentation, especially because the prevalence of the disease is rather low in Northern Ireland. The increase has already been reported in England and Wales[8] and one of the explanation could be the improvement of laboratories technique.

The overall under-notification was 8% for the seven years. Effort must be maintained to keep this proportion has low as possible. Northern Ireland has joined England and Wales for enhanced surveillance of tuberculosis in January 2000. This should help to trace cases reported by laboratories and not notified to Boards.

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