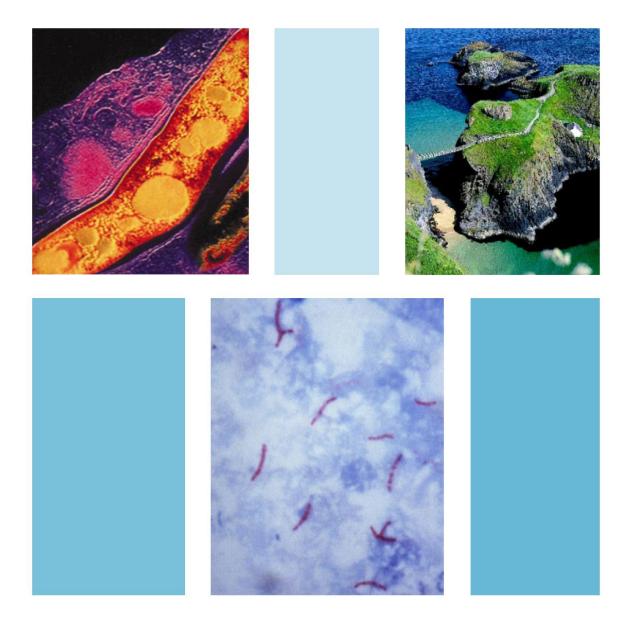


Epidemiology of Tuberculosis In Northern Ireland

Annual surveillance report 2013



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Key Points

- There were 74 notified cases of tuberculosis (TB) notified in Northern Ireland in 2013, giving a rate of 4.0 cases per 100,000 population. This represents a 15% decrease in cases and a slight decrease in rates from 2012 when the number of cases was 87 and the rate was 4.8/100,000.
- There are five Health and Social Care Trusts in Northern Ireland. Rates of TB remained highest in the Belfast and Southern Health and Social Care Trusts at 6.3 cases per 100,000 respectively. Rates of TB in both Trusts decreased compared with 2012, when rates were 8.6 and 8.0 cases per 100,000 respectively.
- The age of cases ranged from 24 to 96 years, with a median age of 45 years. The largest proportion of cases (49%) was in young adults aged between 15 and 44 years. Those aged 65 and over continue to have the highest rate of tuberculosis at 6.1 cases per 100,000 population; however this is a reduction from 8.43 cases per 100,000 in 2012.
- The proportion of TB cases that were born in countries with a high-burden of TB decreased from 55% of all reported cases in 2012 to 40% of cases reported in 2013.
- The proportion of cases with a pulmonary component in 2013 was 55%, a very slight increase on 2012 (54%).
- Rates of extra-pulmonary disease have been increasing annually in the region from 2011 when the rate was 0.8/100,000, to 4.0/100,000 in 2013.
- The proportion of cases confirmed by culture in 2013 was 61%, of which 91% were Mycobacterium Tuberculosis and 9% were Mycobacterium Bovis.
- In 2013, six of the 45 isolates cultured showed resistance to the first-line drug isoniazid, two of these isolates were also resistant to pyrazinamide.

Introduction

Northern Ireland is a low incidence region for TB. However, the epidemiology of TB has changed over the years, largely as a result of immigration. Subsequently almost half of the cases of TB reported annually in recent years have been individuals born outside the region.

The majority of TB cases in Northern Ireland are now in young adults with a year on year decrease in rates of TB in the elderly population.

This report presents the epidemiological data for TB cases reported in Northern Ireland from 1 January 2013 to 31 December 2013. For comparative purposes and to give indications of trends in TB epidemiology, this report will present data for a 10 year period, from 2004-2013.

Outcome of TB treatments are collected annually and reported in retrospect. The treatment outcomes reported in this report are therefore on individuals notified to the Public Health Agency in 2012.

Definitions

Notified case: Refers to clinically active disease caused, or thought to be caused, by infection with organisms of the *Mycobacterium tuberculosis* complex (*M. tuberculosis, M. bovis, M.africanum*).

Culture confirmed cases: Where the diagnosis has been confirmed by culture as *M. tuberculosis, M. bovis or M. africanum.*

Other than culture confirmed cases: In the absence of culture confirmation, a case with a clinician's judgement that the patient's clinical and/or radiological signs and/or symptoms are compatible with tuberculosis *and* a clinician's decision to treat the patient with a full course of anti-tuberculosis treatment"¹

Pulmonary tuberculosis: A disease involving the lung parenchyma and/or bronchial tree, with or without extra-pulmonary tuberculosis diagnosis.

Sputum smear result: Sputum smear positive tuberculosis is defined as a positive microscopy result on spontaneously produced or induced sputum.

Multi-drug resistance (MDR): Resistance to at least isoniazid and rifampicin.

Extensively-drug resistant (XDR): An MDR case with additional resistance to any fluoroquinolone and at least one of the second-line drugs (capreomycin, karamycin, amikacin) (see ref 6 ROI 2009 report).

Health and Social Care Trusts in Northern Ireland (HSCT): There are 5 HSCTs in Northern Ireland; Belfast (BHSCT), South East (SEHSCT), Northern (NHSCT), Southern (SHSCT) and Western (WHSCT).

Treatment outcome: A patient is defined as having completed treatment if; a) the case was reported, b) the patient completed a full course of treatment and c) was officially discharged by the attending physician.

Methodology

Data collection

Completed tuberculosis notification forms are forwarded to the Public Health Agency (PHA) in Northern Ireland where the information is entered onto a secure database. Treatment outcome forms are generated and forwarded, approximately twelve months after initial notification, to the patient's clinician, who then returns it to the PHA. This data is then appended to the initial notification details.

Information on *Mycobacterium tuberculosis* complex isolates are obtained from local hospital diagnostic laboratories and the mycobacterial reference laboratory. Collected data include species (*Mycobacterium tuberculosis*, *M. bovis* and *M. africanum*), specimen type, strain type and drug susceptibility.

Data on cause of death, including tuberculosis, are also collected from the Northern Ireland Statistics and Research Agency (NISRA).

Datasets are validated (using laboratory reports and anti-microbial susceptibility information), updated and analysed.

Data analysis

Data are entered onto the PHE National Enhanced TB Surveillance database and analysed using STATA. Tuberculosis rates per 100,000 of the population, stratified by age, sex and HSCT, were calculated using the mid-year estimates of the Northern Ireland population from NISRA.

Results

Overall number of cases and rates of infection

In 2013, a total of 74 cases of tuberculosis were reported in Northern Ireland giving a rate of 4.0 cases/100,000 population, a slight decrease from 4.8 cases per 100,000 population In 2012 (Figure 1).

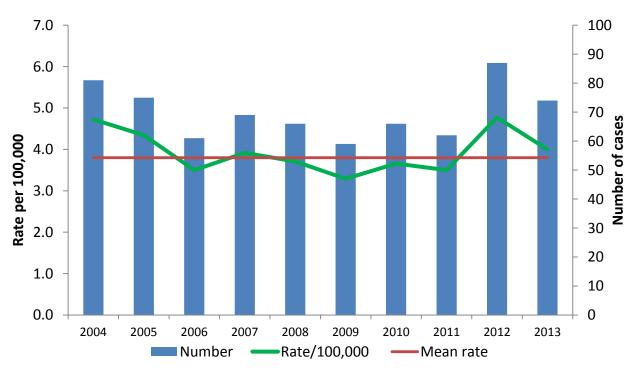


Figure 1: Tuberculosis case reports and rates, Northern Ireland, 2004-2013

From 2009 there has been on average a slight increase in both numbers of cases and rates of TB in the region. The three-year moving average numbers and rates of notified TB cases for 2004-2013 are shown in Figure 2.

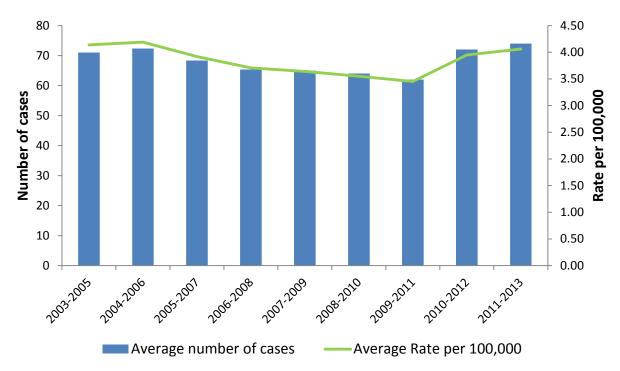


Figure 2: Three year moving average numbers and rates of Tuberculosis cases in Northern Ireland, 2003-2013

In 2013, TB rates remained highest in the Belfast Health and Social Care Trust (BHSCT) and the Southern Health and Social Care Trust (SHSCT) at 6.3 cases per 100,000, respectively. Average TB rates in both of these Trusts have generally showed trends of increasing annually. However, rates of TB decreased in both Trusts compared with 2012. TB rates also decreased slightly in the South Eastern Health and Social Care Trust (SEHSCT). Conversely, rates of TB increased from 2.7 to 4.4 cases per 100,000 in the Western Health and Social Care Trust (WHSCT), with a very slight increase from 2.2 to 2.6 cases per 100,000 in the Northern Health and Social Care Trust (NHSCT). Small numbers of cases in some of the Trusts will affect percentages (Figures 3 and 4).

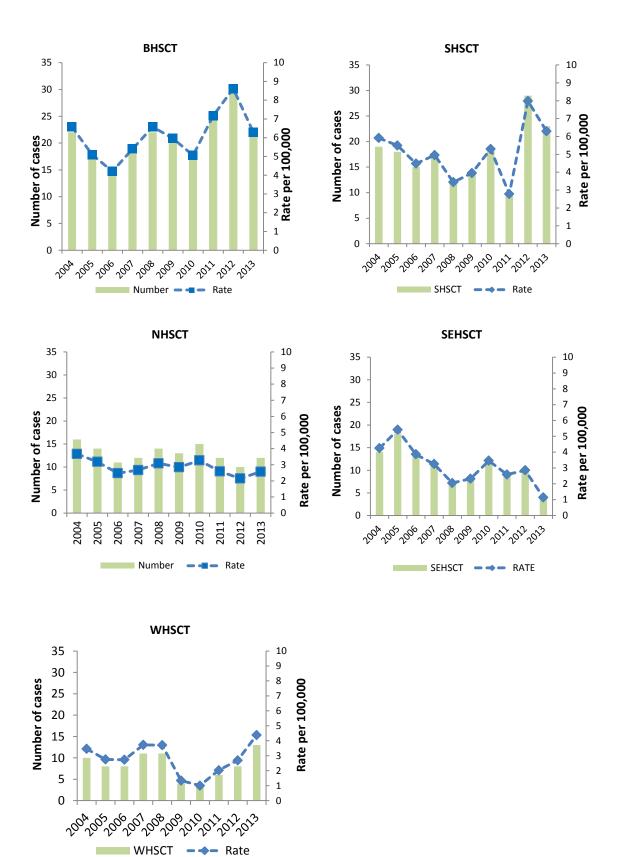


Figure 3: Tuberculosis case reports and rates by Health and Social Care Trust, Northern Ireland, 2004-2013

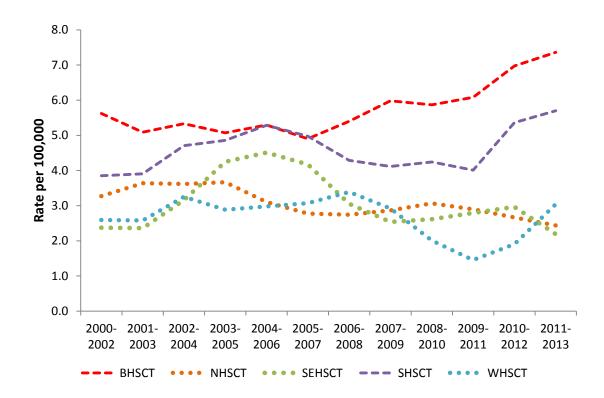


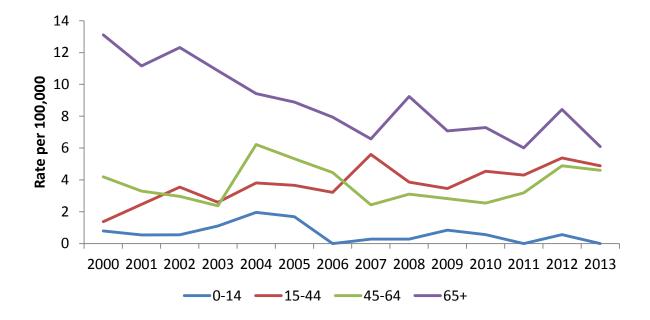
Figure 4: Three year moving average number and rates of Tuberculosis cases by HSCT in Northern Ireland, 2000-2013

Demographic Characteristics

Age and gender:

Of the 74 notified cases of tuberculosis in 2013, 40 were male and 34 were female, giving a sex ratio male/female (M/F) of 1.2 (a decrease on the ratio of 2.3 recorded in 2012). The ages ranged from 24 years to 96 years, with a median age of 45 years (IQR 33-63) and a mean age of 49 years. Patients aged 15-44 years accounted for 49% of cases, those aged 45-64 years accounted for 28% and those age 65 years and over accounted for the additional 23% of TB cases in 2013.

Similar to previous years TB rates were highest in patients aged 65 years and over. However, rates of TB have been declining in this age group over the last number of years, reducing from 9.4 cases per 100,000 in 2004 to 6.1 cases per 100,000 in 2013 (Figure 5). Age profiles between UK and non-UK-born TB cases continue to differ. In 2013, 41% of UK-born cases were aged 50-69 years old, with an additional 26% of UK-born cases aged 70-79 years. Conversely, 71% of TB cases born outside the UK/Ireland were aged 30-49 years old, with an additional 26% of non-UK-born cases aged 20-29 years old.



There were no cases reported under the age of 19 years in 2013.

Figure 5: Northern Ireland TB rates per 100,000 by age group, 2000-2013

Place of birth:

In 2013, 47% (35/74) of TB cases were born outside the UK/Ireland, a reduction compared with 2012 when the proportion of non-UK-born cases was 55%, but still a noteworthy increase on 2004 when the proportion was 32 % (Figure 6).

Similar to previous years the majority (60%, n=21/35) of TB cases born outside the UK/Ireland in 2013 originated from South-East Asia. The most common countries of origin for non-UK-born cases in 2013 were from Timor-Leste (31%, n= 11/35) and India (23%, n=8/35). TB cases originating from both Timor-Leste and India have accounted for 25% and 22% respectively, of all non-UK-born cases in Northern Ireland from 2004-2013, (Figures7 and 8).

Information was available on ethnicity for all cases in 2013. The majority of cases, 61% (45/74), were of white ethnicity, with five of these cases born outside the UK/Ireland.

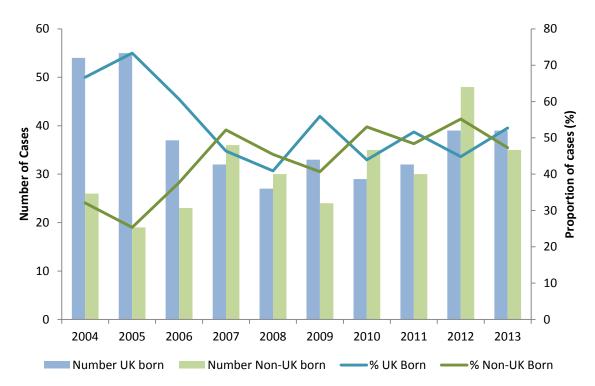


Figure 6: Northern Ireland number and proportion of UK Born and Non-UK Born tuberculosis case reports, 2004-2013

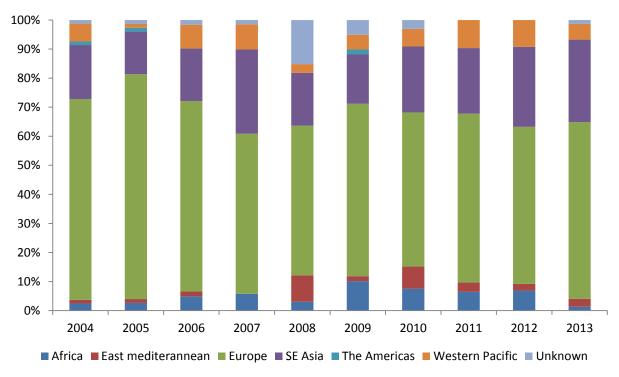


Figure 7: Northern Ireland tuberculosis reports by WHO region, 2004-2013

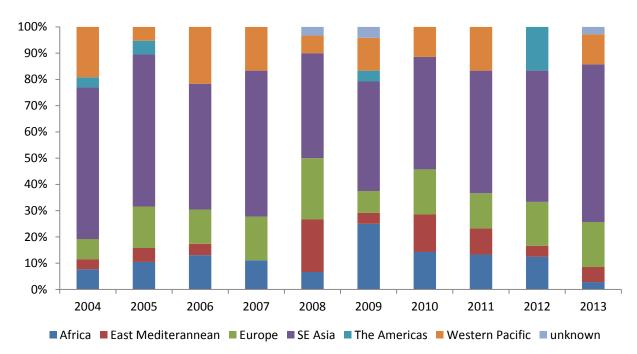


Figure 8: Non-UK Born tuberculosis reports in Northern Ireland by WHO region, 2004-2013

Time from entry into Northern Ireland until TB diagnosis, was known for 80% (28/35) of cases born outside the UK/Ireland in 2013. Of these: 21% (6/28) were diagnosed within 2 years of entry; 68% (19/28) were diagnosed between three and nine years of entry; and the remaining 11% (3/28) had been in the Northern Ireland for ten years or more before diagnosis.

Social risk factors

In 2013, nine (12%) cases reported one or more social risk factors. Six cases had a history of alcohol misuse/abuse, two cases were reported as having a drug use problem, two cases had a history of imprisonment and one case reported as being homeless. The majority (78%, 7/9) of cases with a social risk factor were born in the UK/Ireland.

Clinical Characteristics

In 2013, there were 41 (55%) cases with pulmonary disease, a slight increase compared with 2012, when 54% of cases had a pulmonary component. Six cases (15%) of pulmonary disease were reported to have extra-pulmonary disease in at least one additional site. The rate of pulmonary tuberculosis cases in Northern Ireland in 2013 remained similar to previous years at 2.2 cases per 100,000 population. Conversely, the rates of non-pulmonary disease in the region increased again this year to 4.0 cases per 100,000. Rates

of non-pulmonary TB in Northern Ireland have been consistently rising since 2011 when the rate was 0.8 per 100,000 population (Figure 9).

Site of disease-Pulmonary:

In 2013, 72% (28/39) of cases born in the UK/Ireland had pulmonary disease, compared with 62% in 2012. The proportion of pulmonary disease in those born outside the UK/Ireland decreased from 48% in 2012, to 37 % (13/35) in 2013. (Figure10).

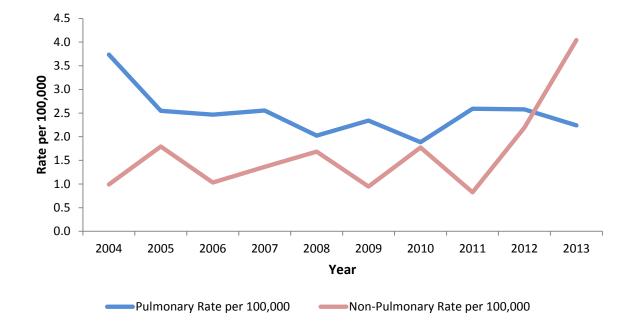


Figure 9: Rates of pulmonary and non-pulmonary tuberculosis, Northern Ireland, 2004-2013

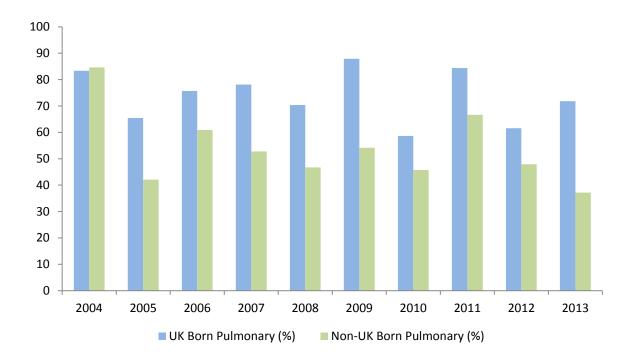
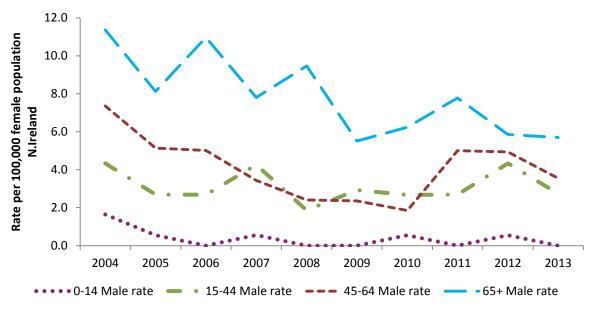
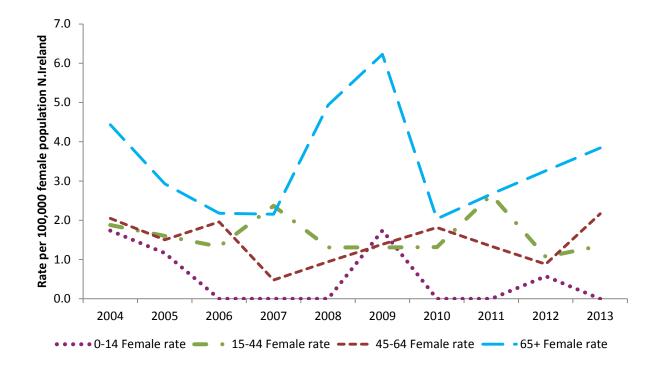


Figure 10: *Proportion of UK and Non-UK born tuberculosis cases pulmonary in Northern Ireland 2004-2013*

Pulmonary disease rates in both males and females remained highest in the elderly population. However, in elderly males (over 65 years) the rate of disease with a pulmonary component has been on the decline from 2004. In 2013, the rate of pulmonary disease in females aged 45-64 years increased from 0.9 per 100,000 in 2012 to 2.2 per 100,000 in 2013 (Figures 11 & 12).









The WHSCT had the highest rate of TB with a pulmonary component in 2013 at 3.4 cases per 100,000 population, the highest rate of pulmonary disease in this HSCT in the past decade. TB pulmonary infection accounted for 77% (10/13) of all TB cases reported in this HSCT in 2013. Conversely, the proportion of pulmonary disease cases in the SHSCT decreased from 66% of TB cases in the Trust in 2012 to 35% in 2013, subsequently rates of TB with a pulmonary component also fell by 58% in this HSCT area from 5.23 per 100,000 to 2.2 per 100,000 population (Figure 13).

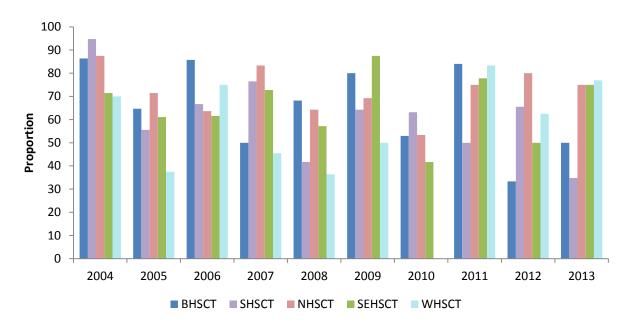
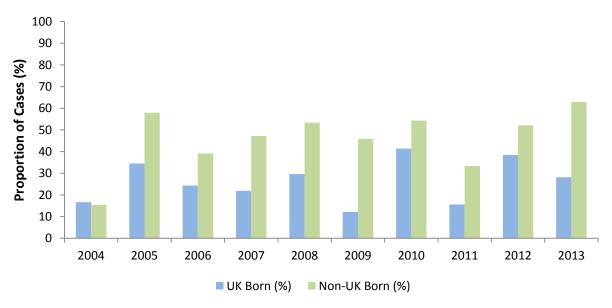


Figure 13: *Proportion of TB cases in Northern Ireland HSCT's with pulmonary infection, 2004-2013*

Site of disease- Non-pulmonary:

Of the 74 cases notified in 2013, 33 cases were diagnosed with non-pulmonary TB, representing 45% of all cases notified, a slight decrease compared with 2012 when 46% of TB cases had non-pulmonary disease.

In 2013, 63% (22/35) of cases born outside the UK/Ireland presented with non-pulmonary TB, a 17% increase compared with 2012 when the proportion was 52% (Figure 14).



** Cases only included where place of birth was known

Figure 14: Proportion of UK and Non-UK born tuberculosis cases Extra-pulmonary in Northern Ireland 2004-2013

The Southern Health and Social Care Trust had the highest proportion of extra-pulmonary tuberculosis cases at 65% (15/23), an increase on 2012 when 34% of cases were extra-pulmonary. Subsequently the rate of extra-pulmonary in this Trust increased from 2.8 per 100,000 in 2012 to 4.1 per 100,000 population in 2013.

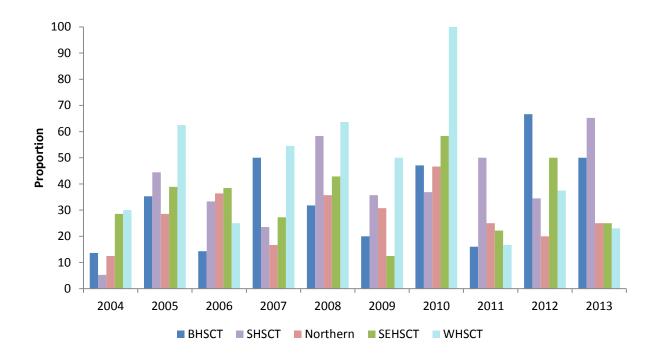


Figure 15: *Proportion of TB cases in Northern Ireland HSCT's with non-pulmonary infection, 2004-2013*

Of the 33 non-pulmonary cases of TB notified during 2013, 18 cases were female and 15 were male, giving a ratio of 1.2:1. The average age of non-pulmonary disease cases was younger than those with pulmonary disease at 43.7 (median 39 years) and 53.6 years (median 52 years), respectively. The highest age-specific rates in both males and females with non-pulmonary tuberculosis in 2013 was in those aged 15-44 years, with rates in males decreasing in all age-groups compared with 2012 (Figures 16 and 17).

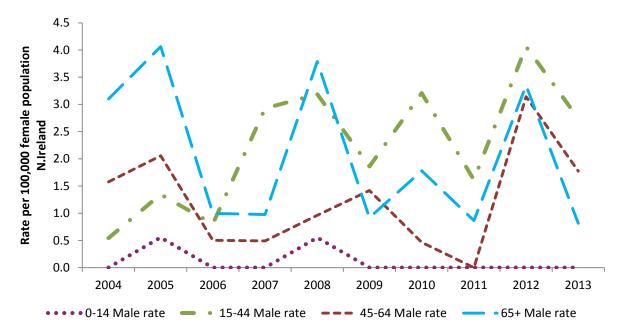


Figure 16: Non-pulmonary age-specific rates in males in Northern Ireland, 2004-2013

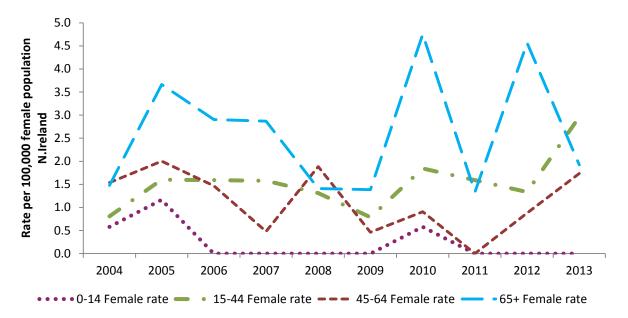


Figure 17: Non-pulmonary age-specific rates in Females in Northern Ireland, 2004-2013

Pulmonary disease in TB patients in 2013 accounted for 55% of all TB cases reported, with the next most common site of disease being in extra-thoracic lymph nodes (Table 1).

Site of Disease	Number of Cases 2013	Proportion of all Cases 2013
Pulmonary	41	55%
Extra-thoracic lymph nodes	13	18%
Genitourinary	5	7%
Bone-spine	5	7%
CNS meningitis	4	5%
Miliary	4	5%
Other Extra-pulmonary	4	5%
Gastrointestinal-peritoneal	3	4%
CNS Other	3	4%
Intra-thoracic lymph nodes	2	3%
Bone-other	2	3%
Pleural	2	3%

Table 1: Tuberculosis case reports by site of disease, Northern Ireland, 2013

Note: Total percentage exceeds 100% due to infections at more than one site.

Previous diagnosis of tuberculosis:

In 2013, 11% (8/74) of cases reported a previous history of TB. All eight cases were UK born with an average age of 68 years (range 45 to 85 years). The average period of time since previous diagnosis of TB was 41 years (range 10 to 70 years).

Time symptomatic:

The time between onset of symptoms and starting treatment was known for 59 (80%) cases in 2013.Of the 59 cases: 29% (n=17) were treated within two months of onset of symptoms with a median time frame of 16 days (IQR 9-32), an additional 29% (n=17) of cases were treated within two to four months of onset with a median time period of 80 days (IQR 67-90), the remaining 42% (n=25) of cases reported a treatment period from onset of symptoms greater than four months with a median time period of 196 days (IQR 147-263). The time between onset of symptoms and starting treatment was known for 31 (76%) of the 41pulmonary cases in 2013. The overall median time period from onset of symptoms to treatment was 104 days (IQR 61-156), this period was higher than for non-pulmonary cases where the median time period from onset to treatment was 78 days (IQR 31.5 to 175) (Table 2).

All cases	Number	Median	IQR
0-2 months	17	16	9-32
2-4 months	17	80	67-90
>4 months	25	196	147-263
All	59	90	39-165
Pulmonary cases			
0-2 months	7	13	8-32
2-4 months	11	80	68-104
>4 months	13	196	147-232
All pulmonary	31	104	61-156
Non-pulmonary			
0-2 months	10	20.5	9-34
2-4 months	6	69.5	66-84
>4 months	12	192	148-325.3
All non-pulmonary	28	78	32-175

Microbiology

In 2013, 61% (45/74) of TB cases were culture confirmed, a very slight decrease compared with 2012 when 62% of cases were culture confirmed. Of the 45 isolates culture confirmed, 41 were identified as having *Mycobacterium tuberculosis* infection and 4 were *Mycobacterium bovis.* The additional 29 cases were notified on the basis of clinical or non-culture diagnosis and response to anti-tuberculosis therapy. Of these 29 cases, 10 (34%) were confirmed by histology.

Of the 41 pulmonary cases in 2013, 66% (n=27) were culture positive. Sputum smear results were known for 29 (71%) of the 41 pulmonary infection cases. Thirteen (32%) pulmonary cases were sputum smear positive at notification, of which 12 were confirmed by culture, an additional 16 (39%) pulmonary infection cases were sputum smear negative of which: nine were later confirmed by culture as *M. tuberculosis*, three were confirmed on histology, and four were based on clinical assessment. Of the remaining 12 (29%) pulmonary cases where sputum smear status was not known, six were culture confirmed and three were confirmed on histology (Table 3).

Year	Pulmonary Cases	Culture Positive (%)	Culture and Sputum Smear Positive (%)
2004	68	84%	40%
2005	45	84%	36%
2006	43	84%	37%
2007	45	93%	49%
2008	37	84%	38%
2009	43	84%	30%
2010	34	97%	59%
2011	47	81%	40%
2012	47	77%	36%
2013	41	66%	29%
Total	450	83%	39%

Table 3: Pulmonary, Culture positive and Sputum Smear positive tuberculosis cases,Northern Ireland, 2004-2013

Table 4. Non-Pulmonary, culture positive tuberculosis cases, Northern Ireland, 2004-2013

Year	Non-Pulmonary Cases	Culture Positive (%)
2004	13	62%
2005	30	40%
2006	18	67%
2007	24	63%
2008	29	69%
2009	16	75%
2010	32	69%
2011	15	67%
2012	40	45%
2013	33	55%
Total	300	59%

Drug resistance

Isoniazid, rifampicin, ethambutol and pyrazinamide are first-line drugs for treatment of tuberculosis in the UK. Drug susceptibility test results were available for all 45 culture confirmed cases of TB in Northern Ireland in 2013.

In 2013, a total of six TB cases were resistant to Isoniazid at the start of treatment, representing 13% of all culture confirmed cases. Three cases were born outside the UK/Ireland and the remaining three cases were born in the UK. None of the six cases reported having a previous history of TB. Two of the six cases were *M.bovis* and were also resistant to pyrazinamide. There were no cases of multi-drug resistance recorded in 2013 (Figure 18).

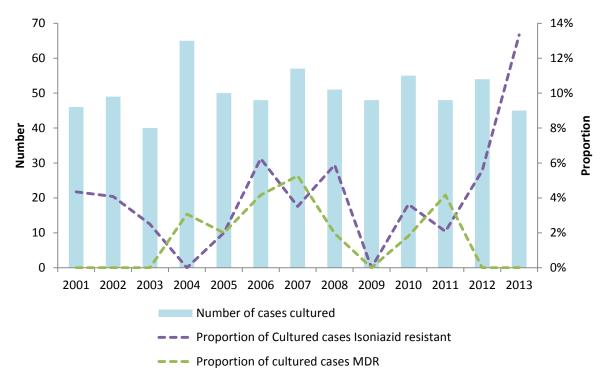


Figure 18: Number and proportion of drug resistant cases of tuberculosis in Northern Ireland, 2001-2013

Strain typing

Northern Ireland joined the National Strain Typing Service in 2011. TB isolates are typed using 24 loci Mycobacterial Interspersed Repetitive Unit-Variable Number Tandem Repeats (MIRU-VNTR). Molecular clusters of cases with indistinguishable 24 loci MIRU-VNTR profiles which fulfil certain criteria are investigated further to try and identify epidemiological links and transmission settings that can be then used to inform public health action.

From 2011 to 2013 there were 147 TB culture confirmed cases of which 143 (97%) were strain typed. Of the 143 typed, 123 (86%) had at least 23 complete loci.

There were 14 clusters identified during this period, with the majority (86%) of these clusters consisting of just two individuals.

Three (21%) clusters had one or more isoniazid resistant cases. One *Mycobacterium bovis* cluster was resistant to both isoniazid and pyrazinamide.

In 2013, 82% (37/45) of all culture confirmed TB cases in Northern Ireland were typed at 23 loci or more.

Treatment Outcomes

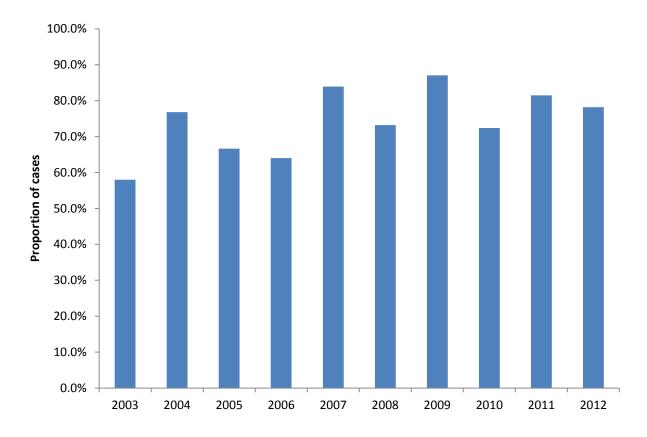
TB patient outcomes are reported in accordance with the revised 2013 World Health Organization (WHO) treatment outcome definitions².Under these revised definitions, treatment outcome at 12 months reporting is defined as all TB cases, diagnosed in 2012 with drug sensitive TB, excluding those with rifampicin resistant TB or MDR-TB.

In this report, treatment outcomes for drug sensitive TB cases are reported separately for the following groups:

Cohort 1: For cases with an expected duration of treatment less than 12 months, treatment outcomes at 12 months (excluding Rifampicin and multi-drug resistance).

Cohort 2: For cases with an expected duration of treatment less than 12 months, excluding Rifampicin and Multi-drug resistance AND cases with CNS, spinal, cryptic disseminated or miliary disease.

TB outcomes reported using these new cohort definitions and validation methods will not be directly comparable with outcome data presented in previous reports. Within this report treatment outcomes for cases notified from 2003 to 2012 under the new definitions have been calculated to allow for trends to be monitored (Figure 19).



*Excludes rifampicin resistant TB and MDR-TB cases and those with CNS, spinal, miliary or cryptic disseminated TB

Figure 19: Treatment completion at 12 months for drug sensitive cases with expected treatment <12 months, 2003-2012

In 2012, 87 TB cases were notified in Northern Ireland; all cases were fully sensitive and are included in cohort 1. Nine cases had CNS, spinal, miliary or cryptic disseminated disease and are excluded from the outcomes presented in cohort 2.

Table 5: Outcome of cohorts 1 and 2, 2012 TB cases

Outcome	Cohort 1 (n=87)	%	Cohort 2 (n=78)	%
Completed	67	77	61	78
Died	6	7	3	4
Lost to Follow up	8	9	8	10
Still on Treatment	5	1	5	6
Stopped	1	1	1	1
Not evaluated*	0	0	0	0
Total	87		78	

*transferred out/unknown/missing

Treatment outcomes were known for all 87 cases in 2012. Sixty-seven (77%) patients completed treatment at 12 months. Of the remaining 20 cases: six patients died; five patients' treatment exceeded 12 months; eight cases were lost to follow-up; and one case had their treatment stopped (cohort 1, Table 5). Of the eight patients that were lost to follow-up, only one was born in the UK.

In 2012, treatment completion at 12 months was slightly higher (71%) among non-UK born cases than those born in the UK (69%). The proportion of cases in cohort 2 who completed treatment within 12 months was 78% (61/78), compared with 71% (44/62) in 2011. The five cases that were still on treatment at 12 months, completed after the 12month period bringing overall completion for 2012 cases to 85% (66/78).

Six patients died in 2012, giving a CFR of 6.9%, below the 10 year average of 11% (Figure 20). One case was diagnosed post-mortem. Of the remaining five cases; TB contributed to death in two of the cases and was incidental to death in one case. Five of the six cases were from the indigenous population. The average age of those that died was 68 years with an age-range from 55-81 years.

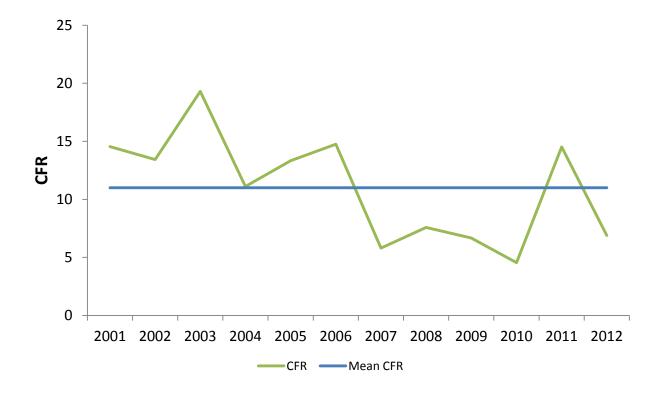


Figure 20: Case-Fatality Rate of tuberculosis notifications, Northern Ireland 2001-2012.

Discussion

Numbers and rates of tuberculosis in the UK have decreased by 11.6% in the past two years (PHE 2014 report), however the rates continue to remain higher than other Western European countries^{3,4}.

In Northern Ireland in 2013 rates of TB continue to remain low at 4 cases per 100,000, well below the UK national rate (12.3/100,000) and lower than the rate of TB in the Republic of Ireland (8.4/100,000). However, there has been a slight increase in both numbers of cases and rates of TB from 2010 in Northern Ireland, with rates exceeding the average in both 2012 and 2013.

The majority of TB cases were, as in recent years in young adults, while rates of TB in the elderly population in Northern Ireland continued to decline in 2013.

The main burden of the disease remains in the Belfast Health and Social Care Trust and Southern Health and Social Care Trust areas. The SHSCT has the highest proportion of cases born outside the UK/Ireland, with this cohort accounting for 75% of their cases in the last three years. The majority of TB cases born outside the UK in this Trust come from areas of South-East Asia, a region that carries about 40% of the global burden of TB⁵. However, there has been a slight drop in the proportion of non-UK born cases regionally in 2013 compared to 2012.

The numbers of cases presenting with extra-pulmonary disease continues to increase in 2013. These cases are more complex to treat and often require longer periods of treatment. The proportion of pulmonary TB cases that had a delay of more than four months between symptom onset and treatment start was 41% in 2013. This highlights the need to improve awareness of TB.

The proportion of drug sensitive TB cases that completed treatment by 12 months, an indicator of the quality of the TB service was 77%.

The proportion of cases with resistance to the first line drug isoniazid has increased substantially since 2011, with almost 14% of cases cultured in 2013 showing resistance to this drug.

Finally, TB cohort review is operational in the region and many of the issues raised can be addressed through this forum.

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