

# Epidemiology of Tuberculosis In Northern Ireland

Annual surveillance report 2014



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## **Key Points**

- There were 95 notified cases of tuberculosis (TB) notified in Northern Ireland in 2014, giving a rate of 5.2 cases per 100,000 population. This represents a 28% increase in cases and a 30% increase in rate from 2013 when the number of cases was 74 and the rate was 4.0/100,000.
- 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 9.4 and 8.7 cases per 100,000 respectively. Rates of TB in both Trusts increased compared with 2013, when rates were 6.3 cases per 100,000 in both Trusts.
- The age of cases ranged from 4 to 91 years, with a median age of 40 years. The largest proportion of cases (54%) remained in young adults aged between 15 and 44 years, with the highest rates of TB also in this age-group.
- The proportion of TB cases that were born outside the UK was 56% of all reported cases in 2014 compared with 47% of cases reported in 2013.
- The proportion of cases with a pulmonary component increased from 55% in 2013 to 66% in 2014, with pulmonary disease rates highest in males aged 45-64 years.
- The proportion of cases confirmed by culture in 2014 was 67%, an increase from 2013 (61%).
- In 2014, 8% of isolates cultured showed resistance to at least one first-line treatment drug.
- The proportion of drug sensitive TB cases that completed treatment by 12 months, an indicator of the quality of the TB service, was 74% in 2013 a 3% decrease compared with 2012.

## 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 approximately 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 2014 to 31 December 2014. For comparative purposes and to give indications of trends in TB epidemiology, this report will present data for a 10 year period, from 2005-2014.

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 from 1 January to 31 December 2013.

## **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<sup>1</sup>

**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).

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 them to the PHA. This information 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 2014, a total of 95 cases of tuberculosis were reported in Northern Ireland giving a rate of 5.2cases/100,000 population a 29% increase from the rate of 4.0 cases per 100,000 population reported in 2013 (Figure 1).



Figure 1: Tuberculosis case reports and rates, Northern Ireland, 2005-2014

From 2009 there has been on average a small but gradual increase in both numbers of cases and rates of TB in the region, with 2014 having the highest rate of TB since the enhanced program began in 2000. From 2012 the rates of TB have also exceeded the average rate (3.9/100,000, based on a nine year average from 2005-2013). The three-year moving average numbers and rates of notified TB cases for 2005-2013 are shown in Figure 2.



Figure2: Three year moving average numbers and rates of Tuberculosis cases in Northern Ireland, 2004-2014

In 2014, TB rates increased in three of the five HSCTs compared with 2013. TB rates remained highest in the Belfast Health and Social Care Trust (BHSCT) and the Southern Health and Social Care Trust (SHSCT) at 9.4 cases per 100,000 and 8.7 cases per 100,000, respectively. This constitutes a 49% increase in the rates of TB in the BHSCT and a 37% increase in the SHSCT compared with TB rates in 2013. Generally TB rates in both of these Trusts have showed increasing trends annually. TB rates also increased in the South Eastern Health and Social Care Trust (SEHSCT) from 1.1per 100,000 in 2013 to 3.9 per 100,000 in 2014. Conversely, rates of TB decreased from 4.4 to 1.7 cases per 100,000 in the Northern Health and Social Care Trust (WHSCT), with a slight decrease from 2.6 to 2.4 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).

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Figure3: Tuberculosis case reports and rates by Health and Social Care Trust, Northern Ireland, 2005-2014



Figure 4: Three year moving average number and rates of Tuberculosis cases by HSCT in Northern Ireland, 2000-2014

#### **Demographic Characteristics**

#### Age and gender:

Of the95 notified cases of tuberculosis in 2014, 63 were male and 32 were female, giving a sex ratio male/female (M/F) of 1.97 (an increase on the M/F ratio of 1.2 recorded in 2013). The ages ranged from 4 years to 91 years, with a median age of 40 years and a mean age of 43 years. Patients aged 15-44 years accounted for 54% of cases, those aged 45-64 years accounted for 29%, those age 65 years and over accounted for12% and patients aged 0-14 years accounted for the additional 5% of TB cases in 2014.

In previous years TB rates were highest in patients aged 65 years and over, however in 2014 rates in this age group decreased by 37% from 6.1 per 100,000 in 2013 to 3.9 per 100,000, with the highest rates of TB in 2014 in those aged 15-44 years at 6.9 per 100,000 population(Figure 5). Rates in the 45-64 years age group also exceeded those in the oldest age group for the first time.



Figure 5: Northern Ireland TB rates per 100,000 by age group, 2000-2014

#### Place of birth:

In 2014, 56% (n=53/95) of TB cases were born outside the UK/Ireland, an increase compared with 2013 when the proportion of non-UK-born cases was 47% (Figure 6). The country of origin was not known for one of the cases born outside the UK/Ireland in 2014. Similar to previous years the majority (46%, n=24/52) of TB cases born outside the UK/Ireland in 2014 originated from South-East Asia. The most common countries of origin for non-UK-born cases in 2014 were Timor-Leste (27%, n= 14/52) and India (17%, n=9/52) (Figures7 and 8).

Information was available on ethnicity for all cases in 2014. The highest proportion of cases, 51% (n=48/95), was of white ethnicity, with ten 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, 2005-2014



Figure 7: Northern Ireland tuberculosis reports by WHO region of case, 2005-2014





Time from entry into Northern Ireland until TB diagnosis was known for 79% (n=41/52) of cases born outside the UK/Ireland in 2014. Of these:36% (n=15/41) were diagnosed within two years of entry;49% (n=20/41) were diagnosed between three and nine years of entry; and the remaining 15% (n=6/41) had been in Northern Ireland for ten years or more before diagnosis.

#### Social risk factors

In 2014, five (5%) cases reported one or more social risk factors. The risk factors associated with the cases were reported as being homeless and/or a history of alcohol misuse/abuse. However, non-reporting of risk factors may not be indicative of there being no risk factors existing; therefore it is difficult to ascertain the true incidence.

#### Deprivation:

In 2014 the rate of TB in the 20% of the population living in the most deprived areas of Northern Ireland was 11.1 per 100,000 population compared with 2.0 per 100,000 in the 20% of the population living in the least deprived areas. The rates of TB increased with increasing deprivation (Figure 9).



#### Figure 9: Rate of TB by deprivation, Northern Ireland 2014

The Index of Multiple Deprivation (IMD) 2010, is an overall measure of multiple deprivation experienced by people living in an area and is measured at Super Output (SOA) level. Commissioned output is based on Small Area Population Estimates for 890 Super Output Areas in Northern Ireland. NISRA - Demography and Methodology Branch

#### **Clinical Characteristics**

In 2014, there were 63 (66%) cases with pulmonary disease, an increase compared with 2013, when 55% of cases had a pulmonary component. Thirteen cases (21%) 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 increased from 2.2 per 100,000 population in 2013 to 3.4 per 100,000 in 2014. Conversely, the rates of non-pulmonary disease in the region decreased from 4.0 cases per 100,000 in 2013 to 1.7 per 100,000 in 2014 (Figure 10).



Figure 10: *Rates of pulmonary and non-pulmonary tuberculosis, Northern Ireland, 2005-2014* 

#### Site of disease-Pulmonary:

In 2014, 71% (n=30/42) of cases born in the UK/Ireland had pulmonary disease, compared with 72% in 2013. The proportion of pulmonary disease in those born outside the UK/Ireland increased from 37% in 2013 to 62% (n=33/53) in 2014 (Figure11).



## Figure 11: Proportion of UK and Non-UK born tuberculosis cases pulmonary in Northern Ireland 2005-2014

Pulmonary disease rates in males were highest in those aged 45-64 years, an increase from 3.5 per 100,000 males in 2013 to 8.3 per 100,000 in 2014. Similar to previous years the rate of disease with a pulmonary component in males aged over 65 years continued to decline in 2014. In 2014, the rate of pulmonary disease in females was highest in those aged 15-44 years increasing from 1.3 per 100,000 females in 2013 to 3.5 per 100,000 in 2014 (Figures 12 and 13).



Figure 12: Pulmonary age-specific disease rates in males in Northern Ireland, 2005-2014



Figure 13: Pulmonary age-specific disease rates in females in Northern Ireland, 2005-2014

The BHSCT had the highest rate of TB with a pulmonary component in 2014 at 6.5 cases per 100,000 population, with TB pulmonary infection accounting for 70% (n=23/33) of all TB cases reported in this HSCT in 2014. The WHSCT had the highest proportion of pulmonary disease cases at 80% (n=4/5), however this resulted in a rate of only 1.3 per 100,000 population in this Trust and the small numbers will influence the statistics (Figure 14).





#### Site of disease- Non-pulmonary:

Of the 95 cases notified in 2014, 32 cases were diagnosed with non-pulmonary TB, representing 34% of all cases notified, a decrease compared with 2013 when 45% of TB cases had non-pulmonary disease.

In 2014, the proportion of cases born outside the UK/Ireland that presented with non-pulmonary TB decreased from 63% in 2013 to 38% (n=20/53) in 2014 (Figure 15).





The Southern Health and Social Care Trust had the highest proportion of extra-pulmonary tuberculosis cases at 44% (n=15/23), a decrease from 2013 when 65% of cases were extra-pulmonary, with the rate of extra-pulmonary in this Trust remaining similar to 2013 at 4.0 cases per 100,000 population in 2014.



## Figure 16: *Proportion of TB cases in Northern Ireland HSCT's with non-pulmonary infection, 2005-2014*

Of the 32 non-pulmonary cases of TB notified during 2014, 21 cases were male and 11 were female, giving a M/F ratio of 1.9:1. The average age of non-pulmonary disease cases was younger than those with pulmonary disease at 38.7 (median 38 years) and 45.2 years (median 44 years), respectively. The highest age-specific rate in females with non-pulmonary tuberculosis in 2014 was in those aged 15-44 years, while rates in males were highest in those aged 45-64 years (Figures 17 and 18).



Figure 17: Non-pulmonary age-specific rates in males in Northern Ireland, 2005-2014



Figure 18: Non-pulmonary age-specific rates in Females in Northern Ireland, 2005-2014

Pulmonary disease in TB patients in 2014 accounted for 66% of all TB cases reported, with the next most common site of disease being in extra-thoracic lymph nodes (Table 1).

Table 1: Tuberculosis case reports by site of disease, Northern Ireland, 2014			
Site of Disease	Number of cases	Proportion of all cases	
Pulmonary	63	66%	
Extra-thoracic lymph nodes	19	20%	
Pleural	7	7%	
Intra-thoracic lymph nodes	6	6%	
Other Extra-pulmonary	6	6%	
Bonejoint-spine	4	4%	
Gastrointestinal	3	3%	
CNS meningitis	2	2%	
CNS other	1	1%	
Bonejoint-other	1	1%	
genitourinary	1	1%	

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

#### Previous diagnosis of tuberculosis:

In 2014, 6% (n=6/95) of cases reported a previous history of TB. Five of the six cases were born outside the UK. The average age of the cases was 30 years (range 13 to 51 years). The average period of time since previous diagnosis of TB was 8 years (range 1 to 28 years).

#### Time symptomatic:

The time between onset of symptoms and starting treatment was known for 83 (87%) cases in 2014. Of the 83 cases: 39% (n=32) were treated within two months of onset of symptoms with a median time frame of 30 days (IQR 21-45), an additional 18% (n=15) of cases were treated within two to four months of onset with a median time period of 95 days (IQR 82-114), the remaining 43% (n=36) of cases reported a treatment period from onset of symptoms greater than four months with a median time period of 188 days (IQR 149-290).

The time between onset of symptoms and starting treatment was known for 53 (84%) of the 63 pulmonary cases in 2014. The overall median time period from onset of symptoms to treatment was 80 days (IQR 37-146), this period was lower than for non-pulmonary cases where the median time period from onset to treatment was 120 days (IQR 65 to 227) (Table 2).

All cases	Number	Median	IQR
0-2 months	32	30	21-45
2-4 months	15	95	82-114
>4 months	36	188	149-290
All	83	105	37-175
Pulmonary cases			
0-2 months	25	35	26-49
2-4 months	07	97	80-115
>4 months	21	161	143-259
All pulmonary	53	80	37-146
Non-pulmonary			
0-2 months	07	22	18-29
2-4 months	08	93	85-110
>4 months	15	227	174-404
All non-pulmonary	30	120	65-227

## Microbiology

In 2014, 67% (n=64/95) of TB cases were culture confirmed, a slight increase compared with 2013 when 61% of cases were culture confirmed. Of the 64 isolates culture confirmed, 61 were identified as having *Mycobacterium tuberculosis* infection, two were *Mycobacterium bovis* and there was one case of *Mycobacterium africanum*. The additional 31 cases were notified on the basis of clinical or non-culture diagnosis and response to anti-tuberculosis therapy. Of these 31 cases, 10 (32%) were confirmed by histology.

Of the 63 pulmonary cases in 2014, 68% (n=43) were culture positive. Sputum smear results were known for 52 (83%) of the 63 pulmonary infection cases. Twenty-six (41%) pulmonary cases were sputum smear positive at notification, of which 22 were confirmed by culture (84%; n=22/26). An additional 26 (41%) pulmonary infection cases were sputum smear negative of which:14 were later confirmed by culture as *M. tuberculosis*, one *M. bovis* and one *M. africanum*, with an additional three smear negative cases confirmed on histology. Of the 11 (17%) pulmonary cases where sputum smear status was not known or not done, seven were culture confirmed and three were confirmed on histology (Table 3).

Table 3: Pulmonary, Culture positive and Sputum Smear positivetuberculosis cases,Northern Ireland, 2005-2014

Year	Pulmonary Cases	Culture Positive (%)	Culture and Sputum Smear Positive (%)
2005	45	84% <u>)</u>	36% <u>)</u>
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%
2014	63	68%	35%
Total	445	82%	39%

## Table 4.Non-Pulmonary, culture positive tuberculosis cases, Northern Ireland, 2005-2014

Year	Non-Pulmonary Cases	Culture Positive (%)
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%
2014	32	66%
Total	269	62%

#### **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 64 culture confirmed cases of TB in Northern Ireland in 2014.

In 2014, there was only one case recorded as being resistant to rifampicin, with an additional four TB cases resistant to Isoniazid at the start of treatment, representing 8% of

all culture confirmed cases. One of the isoniazid resistant cases, an *M.bovis,* was also resistant to pyrazinamide, with the other *M. bovis* case also resistant to pyrazinamide. Three cases were born outside the UK/Ireland. Only one case reported having a previous history of TB (Figure 19).



Figure 19: Number and proportion of drug resistant cases of tuberculosis in Northern Ireland, 2001-2014

#### 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 2014 there were 211 TB culture confirmed cases of which 209 (99%) were strain typed. Of the 209 typed, 182 (87%) had at least 23 complete loci.

There were 25 clusters identified during this period of two or more individuals with the same MIRU-VNTR type, with 44% of these clusters consisting of just three individuals. In 2014, 92% (n=59/64) 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 World Health Organization (WHO) treatment outcome definitions<sup>1</sup>.Under these revised definitions, treatment outcome at 12 months reporting is defined as all TB cases, diagnosed in 2013 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).

**Cohort2:** 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 treatment outcomes for cases notified from 2004 to 2013 under the new definitions have been calculated to allow for trends to be monitored (Figure 20).



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

## Figure 20: Treatment completion at 12 months for drug sensitive cases with expected treatment <12 months, 2004-2013

In 2013, 74 TB cases were notified in Northern Ireland; there were no cases recorded as being resistant to rifampicin or multi-drug resistant and all 74 cases are included in cohort 1. Fifteen 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, 2013 TB cases.

Outcome	Cohort 1 (n=74)	%	Cohort 2 (n=59)	%
Completed	52	70	43	73
Died	7	9	5	8
Lost to Follow up	6	8	5	8
Still on Treatment	6	8	3	5
Stopped	2	3	2	3
Not evaluated*	1	1	1	2
Total	74		59	

\*transferred out/unknown/missing

Treatment outcomes were known for 99% (n=73/74) of cases in 2013. Fifty-two (70%) patients completed treatment at 12 months, a decrease compared with 77% in 2012. Of the remaining 22 cases: seven patients died; six patients' treatment exceeded 12 months; six cases were lost to follow-up; two cases had their treatment stopped and for one case the outcome was not evaluated(cohort 1, Table 5).Of the six patients that were lost to follow-up, four were born outside the UK.

In 2013, treatment completion at 12 months was higher (74%) among non-UK born cases than those born in the UK (56%). The proportion of cases in cohort 2 who completed treatment within 12 months was 73% (n=43/59) compared with 78% (n=61/78) in 2012. Of the three cases that were still on treatment at 12 months, two cases completed after the 12 months period bringing overall completion for 2013 cases to 76% (n=45/59) in this cohort.

Seven patients died in 2013 giving a CFR of 9.5%, remaining below the 10 year average of 12% (Figure 21). One case was diagnosed post-mortem. Of the remaining six cases; TB was cited as causing the death of one case, contributing to death in two of the cases and was incidental to death in two cases. All seven cases were from the UK/Ireland born population. The average age of those who died was 68 years with an age-range from 52-85 years.





### **Discussion**

The incidence of TB in Northern Ireland remains relatively low compared with other parts of the UK and Republic of Ireland<sup>2, 3, 4</sup>. However, there has been a slight but sustained increase in the incidence of TB in Northern Ireland in recent years from 3 cases per 100,000 population in 2011 to 5 cases per 100,000 in 2014. The increased incidence of TB and changing epidemiology highlight the importance of maintaining active surveillance as part of TB control arrangements.

The majority of TB cases were, as in recent years, in young adults with rates of TB in those aged 15-44 years and 45-64 years increasing annually from 2008. Conversely rates of TB in the elderly population in Northern Ireland continued to decline in 2014. At population level the highest rates of TB remain in areas of highest deprivation.

The main burden of the disease remains in the Belfast Health and Social Care Trust and Southern Health and Social Care Trust areas. TB incidence rates increased again in both Trusts in 2014 giving the highest levels for the last decade in these areas.

In 2014 there has also been some evidence of recent transmission with three children under the age of six years reported with active TB.

The numbers of cases presenting with extra-pulmonary disease decreased by half compared with 2013 with a subsequent increase in those presenting with pulmonary disease. Efforts to control tuberculosis include measures to reduce the time interval between symptom onset and the start of their anti-tuberculosis treatment. Patients with untreated pulmonary tuberculosis pose the highest risk of transmission to contacts. The proportion of pulmonary TB cases that had a delay of more than four months between symptom onset and treatment start was similar to 2013 at 40%. This highlights the need to improve awareness of TB and to address any obstacles to accessing services, especially for vulnerable groups to reduce this proportion.

The proportion of drug sensitive TB cases that completed treatment by 12 months, an indicator of the quality of the TB service, was 74% in 2013, a 3% decrease compared with 2012.

The proportion of cases with resistance to the first line drug isoniazid decreased substantially in 2014, with 6% of cases cultured showing resistance to this drug compared with 14% of cases cultured in 2013.

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

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