



Antituberculosis drug resistance in New Zealand, 2004

Surveillance of antituberculosis drug resistance is based on the results of susceptibility testing of isolates in the Mycobacteriology Reference Laboratories at Auckland City, Wellington and Waikato Hospitals. The laboratory results are matched with tuberculosis case notifications.

In 2004, 376 cases of tuberculosis were notified, 288 (76.6%) of which were reported by the Mycobacteriology Reference Laboratories as culture positive. Antimicrobial susceptibility testing results were available for all 288 isolates, which comprised 283 *Mycobacterium tuberculosis* and five *M. bovis* isolates. The proportion of isolates resistant to isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin is shown in Table 1.

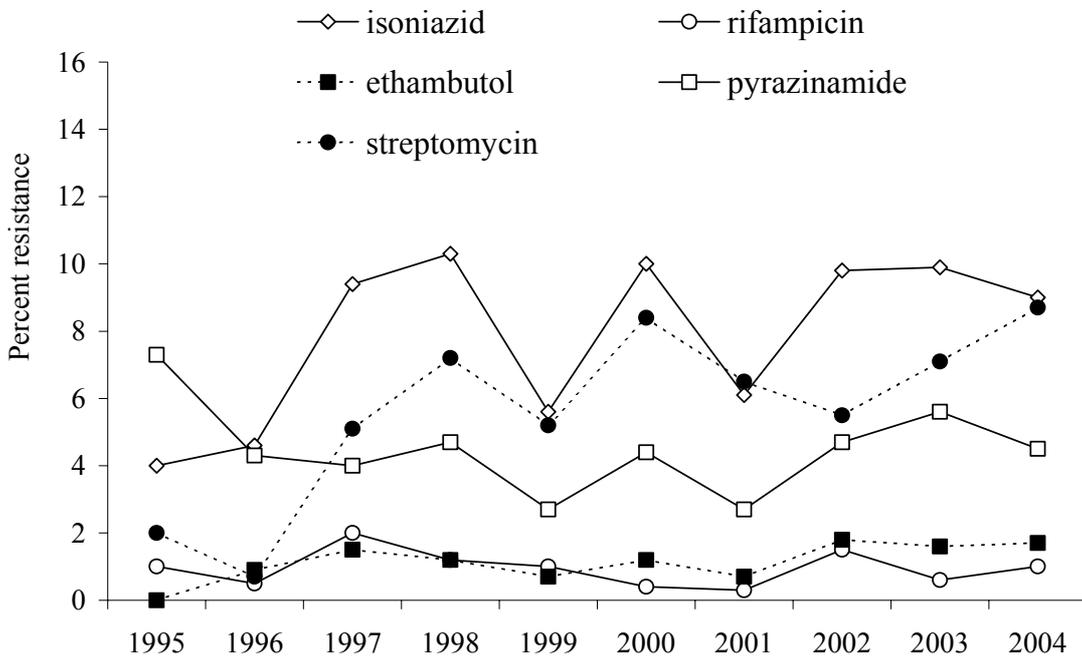
Table 1. Resistance to each antimicrobial, 2004

Antimicrobial	Number tested	Number resistant ¹	Percent resistance ¹
Isoniazid	288	26	9.0
Rifampicin	288	3	1.0
Ethambutol	288	5	1.7
Pyrazinamide	288	13 ²	4.5
Streptomycin	288	25	8.7

Notes: 1 includes resistance alone or in combination with other antimicrobials
2 includes the five *M. bovis* isolates

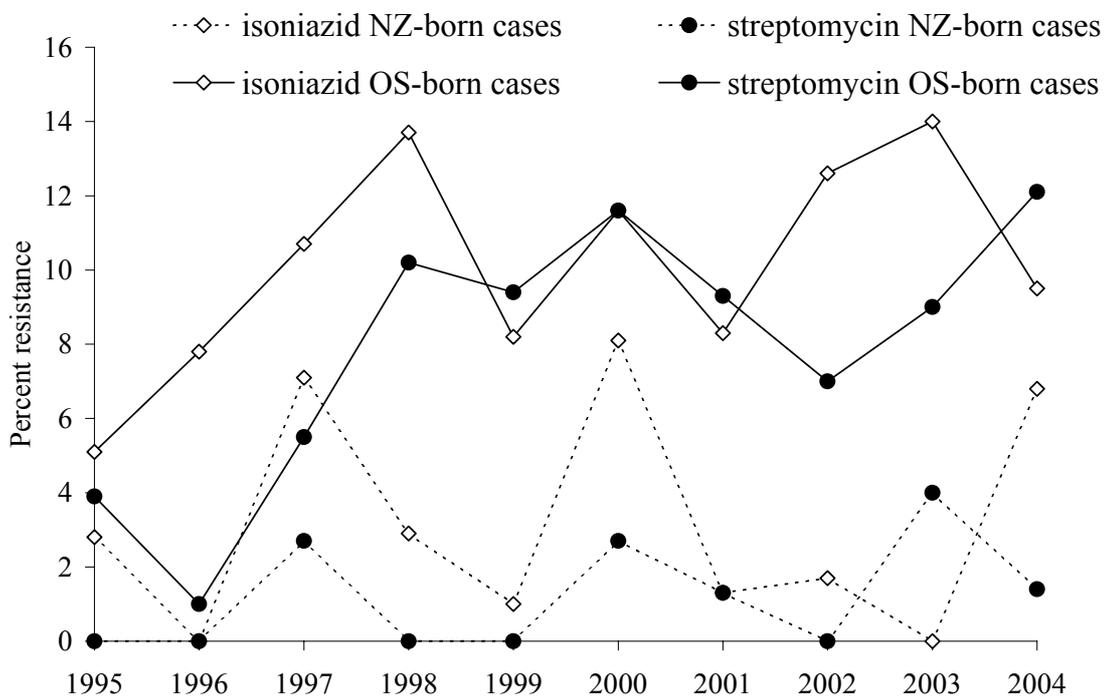
Trends in resistance to the five antimicrobials are shown in Figure 1.

Figure 1. Resistance to each antimicrobial, 1995-2004



Between 1995 and 1998 there was a significant ($p \leq 0.05$) trend of increasing isoniazid and streptomycin resistance, but only among cases born overseas (Figure 2). Since 1999, while there have been year-to-year fluctuations in isoniazid and streptomycin resistance, there have been no significant trends in resistance to these two antimicrobials in either overseas-born or New Zealand-born cases.

Figure 2. Resistance to isoniazid and streptomycin for New Zealand-born cases compared with overseas-born cases, 1995-2004



In 2004, the majority (81.9%) of the isolates were susceptible to all five antimicrobials tested (Table 2). There were three cases (1.0%) of multidrug-resistant tuberculosis (MDR-TB, resistance to at least isoniazid and rifampicin). MDR-TB is rare in New Zealand, with an average annual incidence of 0.7% and a total of 19 cases recorded in the 10 years since national surveillance of antituberculosis drug resistance began in 1995. Eighteen of the MDR-TB cases were born overseas and assumed to have acquired their MDR-TB overseas. The remaining case, while born overseas, appears to have developed MDR-TB during treatment in New Zealand.

Table 2. Distribution of resistance patterns, 2004

	Number (%)	Resistance pattern ¹	Number (%) of isolates with each pattern
Fully susceptible	236 (81.9)		
Resistant to 1 agent	41 (14.2)	H	15 (5.2)
		Z	8 (2.8) ²
		S	17 (5.9)
		E	1 (0.4)
Resistant to 2 agents	7 (2.4)	HZ	2 (0.7) ³
		HS	5 (1.7)
Resistant to 3 agents	1 (0.4)	HRE ⁴	1 (0.4)
Resistant to 4 agents	1 (0.4)	HZSE	1 (0.4)
Resistant to 5 agents	2 (0.7)	HRZSE ⁴	2 (0.7)

Notes: 1 H, isoniazid; R, rifampicin; Z, pyrazinamide; S, streptomycin; E, ethambutol
2 includes three of the five *M. bovis* isolates
3 two of the five *M. bovis* isolates
4 MDR-TB, multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

A comparison of resistance among isolates from cases born in New Zealand and cases born overseas is presented in Table 3. Cases born overseas were significantly ($p \leq 0.05$) less likely to be fully susceptible and were more resistant to streptomycin. There were no other significant differences in resistance by place of birth.

Table 3. Resistance by case's place of birth, 2004¹

	Percent		P value ²
	New Zealand-born cases (n=73)	Overseas-born cases (n=191)	
Fully susceptible	89.0	78.0	0.0408
Resistant to:³			
Isoniazid	6.9	10.0	0.4335
Rifampicin	0	1.6	0.5631
Ethambutol	0	2.6	0.3267
Pyrazinamide	6.9	4.2	0.3566
Streptomycin	1.4	12.6	0.0055
MDR-TB⁴	0	1.6	0.5631

Notes: 1 information on place of birth unknown or not reported for 24 cases, which included two isoniazid-resistant cases
 2 rates compared by the Chi-square test or Fishers Exact test, as appropriate
 3 includes resistance alone or in combination with other antimicrobials
 4 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

The geographic distribution of resistant isolates, based on aggregated health districts, is shown in Table 4. Cases in the Northern region were significantly ($p \leq 0.05$) more resistant to streptomycin. However, when overseas-born cases were excluded, there were no significant regional differences.

Table 4. Geographic distribution of resistance, 2004

Antimicrobial	Percent resistance ¹			
	Northern ² (n=160)	Midland ² (n=28)	Central ² (n=74)	Southern ² (n=26)
Isoniazid	9.4	3.6	10.8	7.7
Rifampicin	1.3	0	1.4	0
Ethambutol	2.5	0	1.4	0
Pyrazinamide	3.8	7.1	5.4	3.9
Streptomycin	14.4	0	2.7	0

Notes: 1 includes resistance alone or in combination with other antimicrobials
 2 the Northern area includes the Northland, North West Auckland, Central Auckland, and South Auckland Health Districts; the Midland area includes the Waikato, Tauranga, Eastern Bay of Plenty, Gisborne, Rotorua, Taupo, Taranaki, and Ruapehu Health Districts; the Central area includes the Hawkes Bay, Wanganui, Manawatu, Wairarapa, Hutt, Wellington, and Nelson-Marlborough Health Districts; and the Southern area includes the Canterbury, South Canterbury, West Coast, Otago, and Southland Health Districts

Ten (3.5%) of the 288 culture-positive cases in 2004 were reported to be tuberculosis disease reactivations. During the five years 2000-2004, 78 (5.5%) of the 1428 culture-positive cases were reported to be tuberculosis disease reactivations. Thirty-eight (48.7%) of these reactivation cases were originally diagnosed with tuberculosis overseas – in Asia (25 cases), Africa (4), the Pacific Islands (3), Europe (5) and Australia (1). Another 24 of the reactivation cases were reported to have been originally diagnosed with tuberculosis in New Zealand. These 24 cases included eight Maori, eight Europeans, two Pacific Island People, five cases of other ethnicities, and one case of unknown ethnicity. The place of original diagnosis was not reported for the remaining 16 reactivation cases. Information on previous treatment was recorded for 58 of the 78 reactivation cases, and 49 were recorded as having received previous antituberculosis drug treatment.

Resistance among new cases of tuberculosis, cases reported to be reactivations, and the subset of reactivations that were reported to have been previously treated, is shown in Table 5. Compared with new cases, previously treated cases were significantly more resistant to isoniazid, rifampicin and ethambutol; more likely to be MDR-TB; and less likely to be fully susceptible to all five antimicrobials.

Table 5. Resistance among new cases, reactivations and previously treated cases of tuberculosis disease, 2000-04

	Percent		
	New disease n=1350	Disease reactivations n=78 (P value) ¹	Previously treated cases n=49 (P value) ¹
Fully susceptible	83.5	73.1 (0.0176)	65.3 (0.0009)
Resistant to:²			
Isoniazid	8.4	19.2 (0.0012)	30.6 (<0.0001)
Rifampicin	0.7	2.6 (0.1364)	4.1 (0.0634)
Ethambutol	1.2	5.1 (0.0204)	8.2 (0.0043)
Pyrazinamide	4.2	7.7 (0.1511)	4.1 (1.0000)
Streptomycin	7.3	6.4 (0.7781)	10.2 (0.4014)
MDR-TB³	0.6	2.6 (0.0997)	4.1 (0.0452)

Notes: 1 rate compared with that among new cases by the Chi-square test or Fishers Exact test, as appropriate

2 includes resistance alone or in combination with other antimicrobials

3 multidrug-resistant tuberculosis, that is, resistant to at least isoniazid and rifampicin

Compiled by: Helen Heffernan
Senior Scientist
Antibiotic Reference Laboratory
Communicable Disease Group
ESR
helen.heffernan@esr.cri.nz

Acknowledgements: Ross Vaughan, Mycobacteriology Reference Laboratory, Auckland City Hospital; Leo McKnight, Mycobacteriology Reference Laboratory, Wellington Hospital; and Kathryn Coley, Mycobacteriology Reference Laboratory, Waikato Hospital, for supplying their susceptibility test results. Dr David Holland, Middlemore Hospital, for clinical peer review of this report.

This report is available at www.surv.esr.cri.nz/antimicrobial/tuberculosis.php