

Respiratory disease

- Respiratory diseases, including lung cancer, were together responsible for around 14% of all deaths in NSW in the period 2000 to 2004, and just over 5% of hospital separations in 2004–05.
- Three respiratory diseases—chronic obstructive pulmonary disease, lung cancer, and asthma—were among the 20 leading causes of the overall burden of disease in NSW in 2004.
- Chronic obstructive pulmonary disease (COPD), which includes chronic bronchitis and emphysema, was responsible for over 1,700 deaths in 2004 and over 18,000 hospitalisations in 2004–05.
- More than 90% of people who died from influenza and pneumonia in 2004 were aged 65 years and over.
- More than 50% of hospitalisations for influenza and pneumonia were of people aged 65 years and over.
- In 2005, around 9% of adult males and 12% of adult females had asthma, and in 2003 and 2004 just under 17% of boys and almost 13% of girls aged 2–15 years had asthma. Asthma was responsible for 124 deaths in 2004 and around 13,000 hospitalisations in 2004–05.
- In 2004, 73% of all deaths from chronic obstructive pulmonary disease and 83% of all lung cancer deaths were attributable to smoking. In 2004–05, smoking caused around 75% of all hospitalisations for chronic obstructive pulmonary disease and lung cancer.

In this chapter

- Deaths and hospitalisations
- Influenza and pneumonia
- Current asthma
- Asthma hospitalisations
- Death and hospitalisation attributable to smoking

Introduction

The respiratory system includes the airways, the lungs, the respiratory centre of the central nervous system, the chest wall and the pulmonary circulation. This chapter focuses on chronic respiratory diseases, specifically asthma, chronic obstructive pulmonary disease, asbestosis, and respiratory tuberculosis, where preventive measures and better management of conditions can reduce both the burden of disease and associated healthcare costs. Acute diseases, such as influenza and pneumonia, are also included.

Influenza and pneumonia are acute respiratory diseases that can be very severe and, in persons at high risk, can lead to death. Influenza and pneumonia are usually presented together because influenza can lead to pneumonia and in most cases of hospitalisation and death from pneumonia, the responsible organism is not identified. In years identified as influenza epidemic years, the number of deaths from influenza increases but the most substantial increase occurs in the number of deaths from unspecified pneumonia and bronchopneumonia.

Asthma is a chronic inflammatory disease causing episodes of wheezing, breathlessness and chest tightness due to widespread narrowing of the airways within the lungs and obstruction of airflow. The symptoms of an episode are usually reversible, either spontaneously or with treatment (AIHW, 2006). Asthma is a significant public health problem in Australia and it is estimated that Australian prevalence rates are among the highest in the world, along with New Zealand and the UK (ACAM, 2005; GINA, 2004). The prevalence of asthma varies between age groups and sexes, but overall around 10–12% of adults and 14–16% of children and teenagers currently have asthma in Australia (ACAM 2005).

While there was evidence of an increase in the prevalence of asthma between the 1980s and 1990s (Wilson et al 2001, Peat et al 1994) more recent studies in children show no further increase in the prevalence of asthma, (Robertson et al 2004) and possibly a decrease in the prevalence of asthma symptoms (Toelle et al 2004). In Australia in 2004, asthma was estimated to account for 2.3% of the disease burden, 0.3% of years of life lost due to premature mortality and 4% of years of 'health' life lost due to poor health or disability (AIHW, 2006 after Begg et al., in press).

Chronic obstructive pulmonary disease (COPD) is a serious, long-term respiratory disease that affects mainly older people who have been exposed to tobacco smoke. It is characterised by airflow obstruction, which is persistent and largely irreversible (ACAM, 2006) and which limits the capacity to undertake activities of daily living. Chronic bronchitis and emphysema are the two main conditions comprising COPD. Each condition can occur on its own, but they often co-exist in an individual. In Australia in 2004, COPD was estimated to account for 3.6% of the disease burden, 3.7% of years of life lost due to premature mortality and 3.5% of years of 'healthy' life lost due to poor health or disability (AIHW, 2006).

Pneumoconioses are diseases originating from an accumulation of dust in the lungs. Most pneumoconioses are occupationally acquired and the one discussed here is asbestosis. Asbestosis is a fibrosis of the lungs resulting from the long-term inhalation of asbestos dust in the mining, milling, manufacturing, application (for example of insulation) or removal of asbestos products. Asbestosis does not appear to be a significant public health problem when compared to the burden of disease created by other respiratory diseases. It warrants special attention because its development is not related to lifestyle risks, such as smoking, and because it is totally preventable, primarily by effective dust suppression in the work environment. People exposed to asbestos who are also smokers, however, do have a higher risk of lung cancer when compared with the risk of either asbestos exposure alone or smoking alone. Advances in occupational health and safety have already reduced the incidence of asbestosis, and with

time are likely to eliminate it. However, due to the time taken for chronic respiratory problems to develop, the health impact of historic exposures to asbestos will continue for some time.

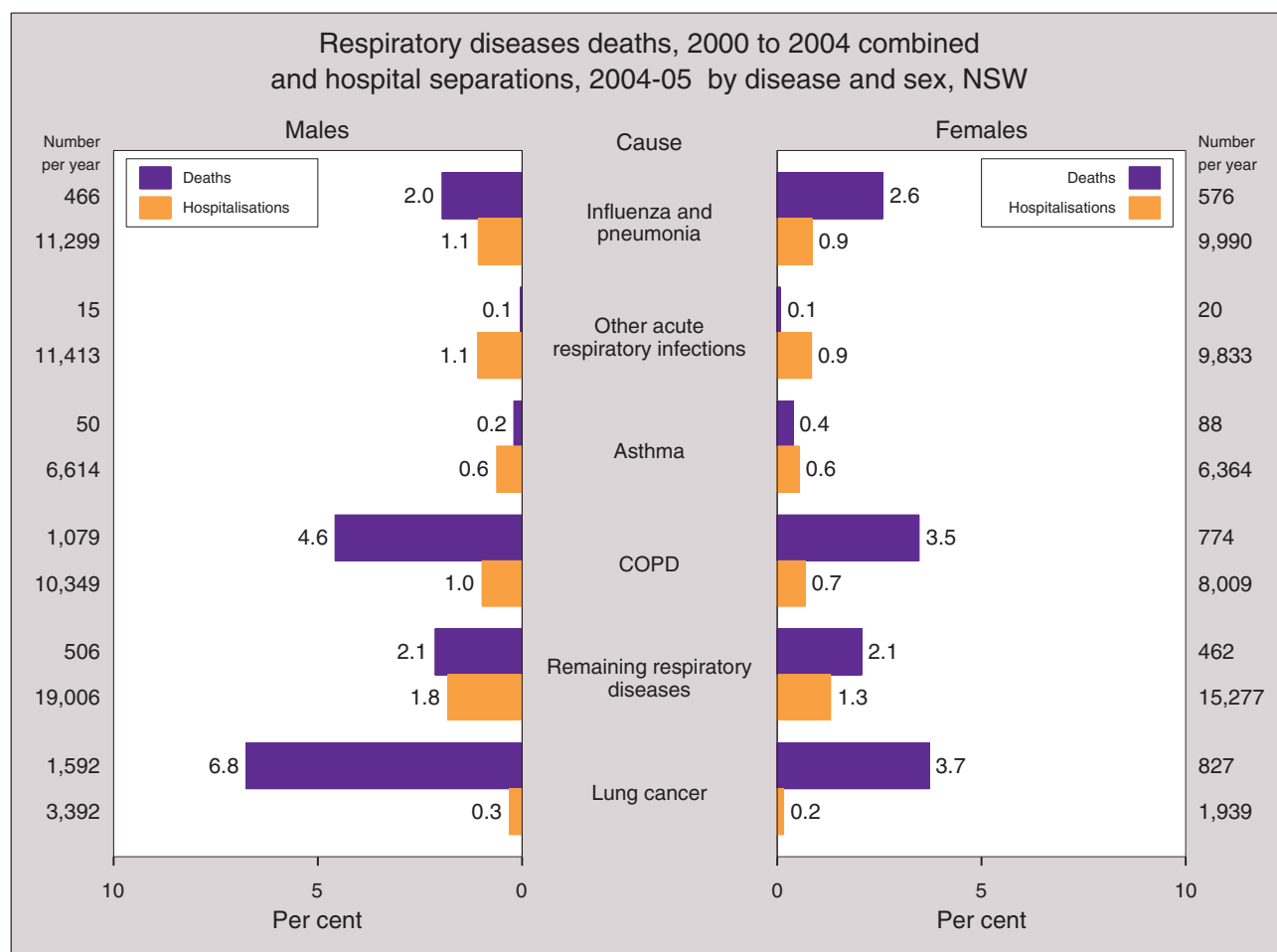
Tuberculosis (TB) is caused by the bacterial organism *Mycobacterium tuberculosis*. TB can present in a variety of ways, most commonly as pulmonary disease characterised by a chronic cough, weight loss, fevers and night sweats. Despite the increasing burden from respiratory tuberculosis globally, it is not a major public health problem in NSW; in fact the mortality and morbidity from all types of tuberculosis in NSW is one of the lowest in the world (Li et al., 2004). In the 5 year period 2000–2005, 61 people died of respiratory tuberculosis in NSW. Most cases occur in people born in high prevalence countries (Li et al., 2004) and the majority of cases are treated in the outpatient setting of hospitals.

Cigarette smoking is the main risk factor for both COPD and lung cancer and the current incidence rates reflect smoking rates 20 years and more in the past. Lung cancer is one of the leading causes of death, although hospital separation rates for lung cancer decreased in males and females in NSW in recent years. Lung cancer is discussed in more detail in the Cancer chapter.

In NSW, two of the measures of success in the State Plan: A New Direction for New South Wales (NSW Premier's Department, 2006), are a reduction in avoidable hospital admissions of aged people and people with chronic illnesses and a reduction in smoking rates, unhealthy alcohol consumption and obesity. The NSW Chronic Care Program, established in 2000, recognises a significant overlap in the management of chronic conditions. The Program aims to improve the quality of care provided for people with chronic health conditions, to improve the quality of life of people with chronic health conditions and their carers and families, and to reduce unplanned and avoidable admissions to hospital (NSW Health, 2006).

The methods used for analysing and presenting respiratory diseases data are described in more detail in the Methods section.

All data tables for this report, and more indicators on these and other subjects, are available in the web version of "The Health of the People of NSW" at www.health.nsw.gov.au/public-health/chorep/

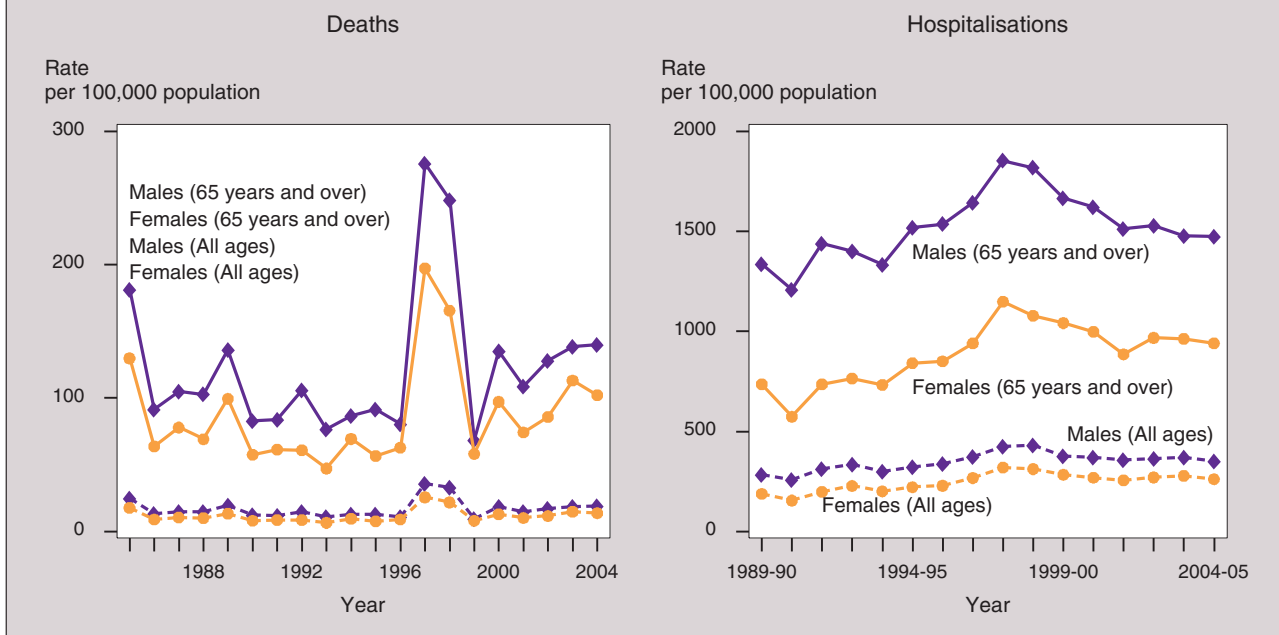


Note: Deaths and hospital separations were classified using ICD-10-AM. Numbers of deaths for 2004 include an estimate of the small numbers of deaths that were registered in 2005, data for which were unavailable at the time of production. Hospitalisations for 2004-05 include an estimate of the small number of interstate hospitalisations, data for which were unavailable at the time of production.

Source: NSW Inpatient Statistics Collection data, ABS mortality data and population estimates (HOIST). Centre for Epidemiology and Research, NSW Department of Health.

- Respiratory diseases were responsible for 14.1% of deaths in 2000 to 2004 combined and for 5.2% of all hospitalisations in 2004-05.
- Between 2000 and 2004 lung cancer constituted 5.3% of all deaths in NSW, however it was responsible for only 0.2% of all hospitalisations in 2004-05. The other main cause of death among respiratory diseases was chronic obstructive pulmonary disease (COPD), which accounted for 4.1% of all deaths in the relevant years. In contrast, however, COPD was also a substantial contributor to hospitalisation, being the main cause of 0.8% of all hospitalisations in 2004-05.
- Tobacco smoking is the main risk factor for both lung cancer and COPD.
- Influenza and pneumonia caused 2.3% of all deaths and 1% of hospital separations and was a substantially more important cause of death and hospitalisation among the very young and older age groups.
- The category 'remaining respiratory diseases' contributes substantially to both all deaths (2.2%) and hospital separations (2.1%). The leading cause of death was aspiration pneumonia due to food and vomit in the respiratory tract and affected mostly the elderly (almost 50% of cases were in persons aged 85 years and over). Chronic tonsillitis and unspecified acute infections of the lower respiratory tract were chiefly responsible for hospitalisations, affecting the younger more than the older age groups.
- Deaths from asthma constituted the smallest proportion of all deaths (0.3%). Asthma was also responsible for a small proportion of all hospital separations. A feature of asthma is that it is relatively more common in younger age groups. In contrast, deaths and hospital separations for lung cancer and COPD show the more common pattern of increasing rates with increasing age.

Influenza and pneumonia deaths 1985 to 2004 and hospital separations 1989-90 to 2004-05, persons of all ages and 65 years and over, NSW

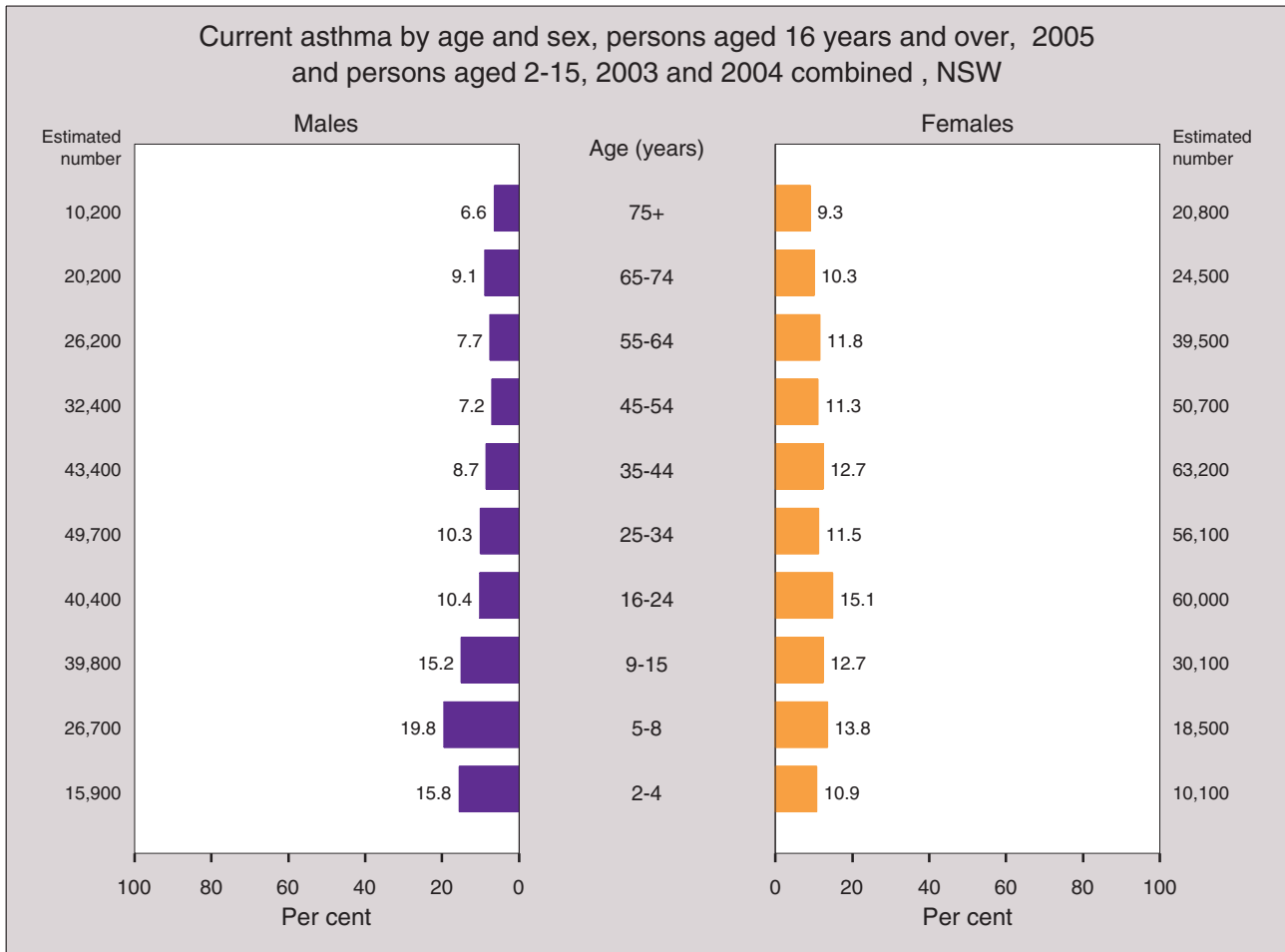


		Age (years)	Sex	1996	1997	1998	1999	2000	2001	2002	2003	2004
Deaths	Number	All ages	Persons	549	1692	1559	543	998	815	974	1217	1209
	Rate	All ages	Persons	9.8	29.5	26.1	8.7	15.3	12.0	13.8	16.6	16.0
Hospitalisation	Number	All ages	Persons	19095	22663	23047	20943	20727	20291	21333	22115	21290
	Rate	All ages	Persons	311.5	362.5	362.0	322.8	312.5	299.5	310.3	318.1	300.1

Note: Deaths were classified using ICD-9 up to 1998 and ICD-10 from 1999 onwards. Hospital separations were classified using ICD-9-CM up to 1997-98 and ICD-10-AM from 1998-99 onwards. Rates were age-adjusted using the Australian population as at 30 June 2001. Numbers for 2004 include an estimate of the small numbers of deaths that were registered in 2005, data for which were unavailable at the time of production. Numbers for 2004-05 include an estimate of the small number of interstate hospitalisations, data for which were unavailable at the time of production.

Source: NSW Inpatient Statistics Collection data, ABS mortality data and population estimates (HOIST). Centre for Epidemiology and Research, NSW Department of Health.

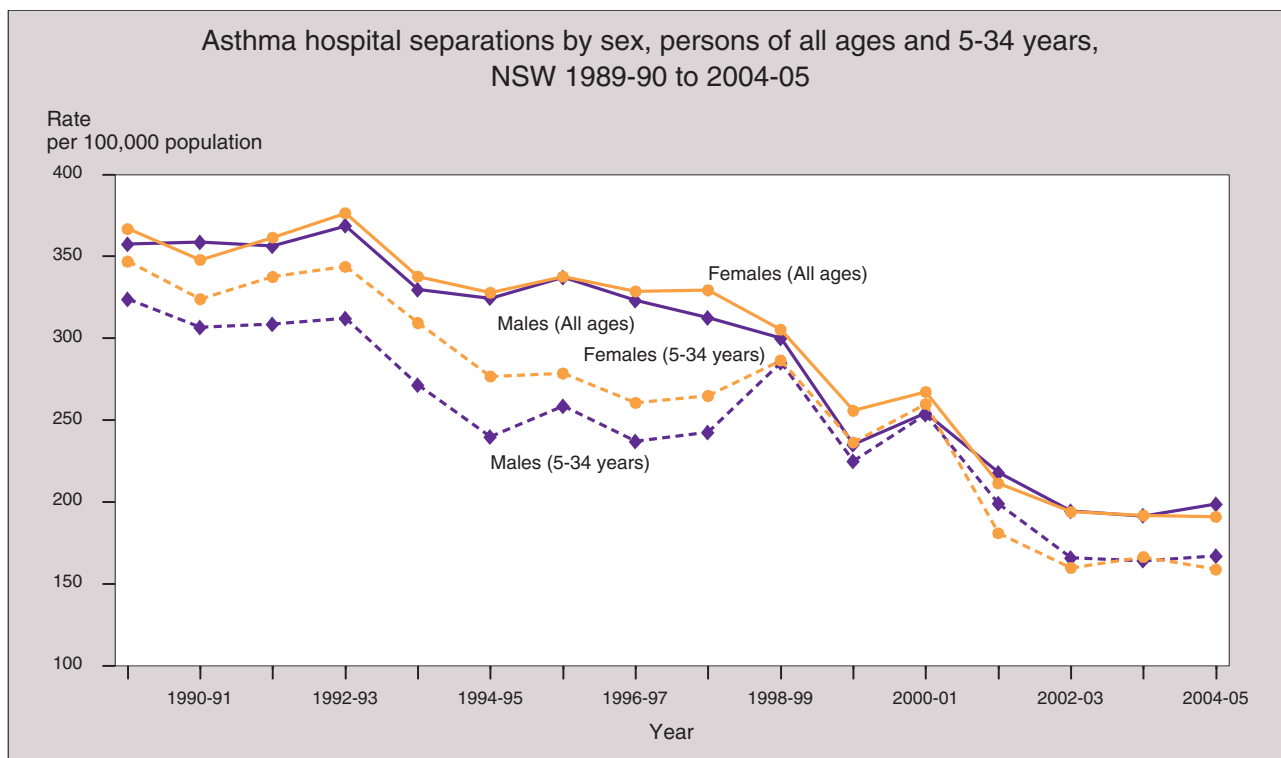
- Influenza and pneumonia are acute respiratory infections that can be very severe, and in persons in high risk groups can lead to death. They are usually presented together as influenza can lead to pneumonia.
- The term influenza, or 'flu', is commonly and incorrectly used to refer to any respiratory infection.
- Severe virus-related complications of influenza require hospitalisation and threaten life most frequently in the very young and elderly (children under 1 year old and persons over 65) and among persons with chronic heart or, especially, lung conditions. Appropriate antibacterial therapy decreases the mortality rate from secondary bacterial pneumonia.
- The main factors predisposing to pneumonia include upper respiratory tract viral infections, alcoholism, institutionalisation, tobacco smoking and heart failure.
- There were 1,209 deaths from influenza and pneumonia in 2004 and almost 93% of these were in persons aged 65 years and over.
- The death rates peaked in 1997 and 1998 at 226.2 (1,692 deaths) and 196.6 (1,559 deaths) per 100,000 population respectively. These years correspond with the identified epidemics of influenza and pneumonia in NSW (CDB, 1998; Viboud et al., 2004).
- There were 21,290 hospitalisations for influenza and pneumonia in 2004-05 and 51.1% of those were in persons 65 years and over. The rates peaked in the years 1997-98 and 1998-99, corresponding with the years of a surge in deaths attributed to influenza and pneumonia. Other epidemics (for example in years 1989, 1994) have also been reflected in the trend data.



Note: The indicator includes those who had symptoms of asthma or treatment for asthma in the last 12 months. Estimates are based on 11,474 respondents. 26 (0.23%) were not stated (Don't know or Refused). The indicator includes those respondents who had children with symptoms of asthma or had taken treatment for asthma in the last 12 months. Estimates are based on 6,696 respondents. 5 (0.07%) were not stated (Don't know or Refused).

Source: NSW Population Health Survey (HOIST). Centre for Epidemiology and Research, NSW Department of Health.

- Asthma is a chronic inflammatory disorder of the airways that results in obstruction of airflow in response to a range of triggers. It is estimated that Australian prevalence rates are among the highest in the world, along with New Zealand and the UK (ACAM, 2005; GINA, 2004). It is also estimated that about 30–40% of Australians will have symptoms consistent with asthma at some time in their lives (NAC, 2002). The prevalence of asthma varies between age groups and sexes.
- In the 2005 NSW Health Survey, 8.8% of adult males and 12.0% of adult females reported having current asthma. This was 10.4% of all persons, a slight increase from 10.1%, which was reported in NSW in 1997 and 1998. Among children aged 2–15 years, 16.5% of boys and 12.6% of girls were reported to have current asthma in 2003 and 2004.
- Children aged 2–15 years were reported to have higher rates of asthma (14.7%) than adults aged 16 years and over (10.4%). In males, the prevalence of asthma was much higher during childhood than in adulthood (16.5% to 8.8%)
- Asthma prevalence is difficult to measure. Different results are obtained from self-reported population surveys, compared to samples based on documented history of wheezing or other symptoms in the previous 12 months and a positive airway hyper-responsiveness test (ACAM 2005).
- The overall prevalence of asthma increased during the 1980s and early-to-mid-1990s. However, in recent years there is some evidence that this trend has plateaued and may even have reversed in children (ACAM, 2005). The prevalence of asthma is higher among Aboriginal females than among non-Aboriginal females and lower in people from non-English speaking backgrounds (AIHW, 2006).
- Written asthma management plans are recommended as part of the National Guidelines for the management of asthma (NAC 2002).

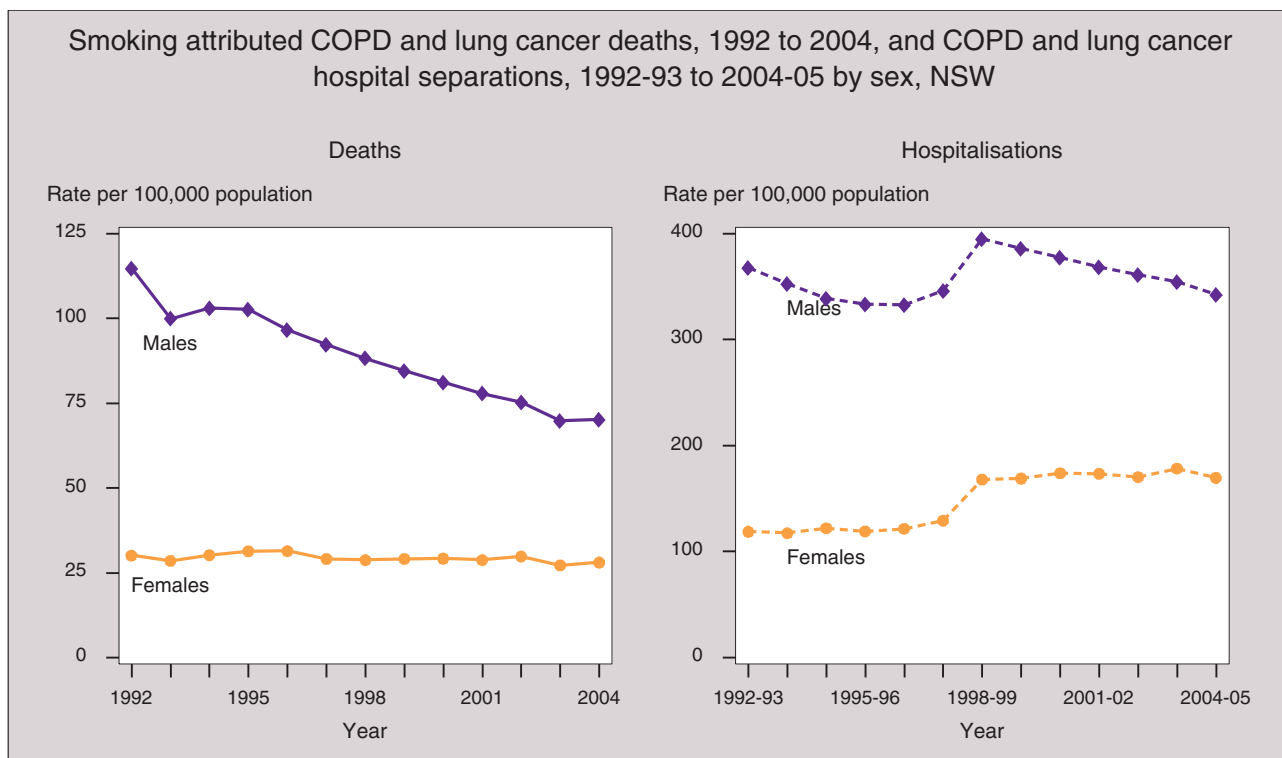


	Age (years)	Sex	1995-96	1996-97	1997-98	1998-99	1999-00	2000-01	2001-02	2002-03	2003-04	2004-05
Number	5-34	Persons	7212	6724	6869	7784	6307	7072	5265	4512	4576	4503
	All ages	Persons	21275	20695	20540	19628	16012	17191	14269	12928	12780	12978
Rate	5-34	Persons	268.8	249.2	254.1	286.5	231.1	257.1	190.6	163.3	165.7	163.3
	All ages	Persons	338.8	326.9	322.2	304.3	246.9	262.3	216.1	195.7	193.2	196.3

Note: Hospital separations were classified using ICD-9-CM up to 1997-98 and ICD-10-AM from 1998-99 onwards. Rates were age-adjusted using the Australian population as at 30 June 2001. Numbers for 2004-05 include an estimate of the small number of interstate hospitalisations, data for which were unavailable at the time of production.

Source: NSW Inpatient Statistics Collection and ABS population estimates (HOIST). Centre for Epidemiology and Research, NSW Department of Health.

- Hospitalisation rates for asthma decreased by 45.9% for all ages and by 51.3% in people aged from 5-34 years in NSW between 1989-90 and 2004-05. The diagnosis of asthma is most reliable in those aged 5-34 years. Consequently, the declining trend in hospitalisations in this age group is generally seen as evidence that the decrease in hospitalisations is real, rather than an artefact of the data collection method (ACAM, 2006).
- Within the long time trend of decreasing hospital separation rates in those aged 5-34 years, there were two major increases. In 1998-99 the hospitalisation rates increased by around 12.8% over the previous year and in 2000-01 there was an 11.6% increase. While substantial increases in presentations with severe asthma symptoms to emergency departments were reported in the summers of 1998 and 2000, this is a common summer occurrence and would not therefore account for these peaks.
- In Australia, the self-reported prevalence of asthma in all ages has increased from 8.5% in 1989-90 (ABS, 1997) to 10.2% in 2004-05 (ABS, 2006) and so the decrease in hospitalisations in the same period may reflect the impact of improvement in asthma management outside of hospitals, as well as gradual changes in coding practices.
- Written asthma management plans are recommended as part of the National Guidelines for the management of asthma (NAC 2002). They enable people with asthma to recognise a deterioration in their condition and initiate appropriate treatment, thereby reducing the severity of acute episodes. In 2005, 49.7% of males and 43.2% of females with symptoms of asthma in the previous 12 months stated that they had a written asthma management plan (CER 2005).



			Sex	1997	1998	1999	2000	2001	2002	2003	2004
Deaths	Number	COPD	Persons	1485	1322	1423	1416	1327	1384	1318	1283
		Lung cancer	Persons	1910	2045	1959	1970	2043	2048	1930	2082
		All	Persons	3395	3367	3382	3386	3369	3432	3249	3366
	Rate	COPD	Persons	24.4	21.1	22.2	21.4	19.4	19.7	18.3	17.4
		Lung cancer	Persons	30.8	32.3	30.3	29.8	30.1	29.5	27.3	28.8
		All	Persons	55.2	53.4	52.4	51.2	49.5	49.2	45.5	46.2
Hospitalisations	Number	COPD	Persons	9722	12521	12890	13330	13489	13583	13828	13502
		Lung cancer	Persons	4227	4485	4260	4219	4247	4172	4403	4379
		All	Persons	13949	17007	17151	17549	17737	17755	18232	17881
	Rate	COPD	Persons	155.1	195.7	196.9	198.8	196.1	193.4	192.6	184.0
		Lung cancer	Persons	67.3	69.9	65.0	63.1	62.0	59.8	61.8	60.4
		All	Persons	222.5	265.6	262.0	261.9	258.1	253.2	254.4	244.5

Note: COPD=chronic obstructive pulmonary disease. Deaths and hospital separations attributable to smoking were calculated using age and sex-specific aetiologic fractions from AIHW, 2001. Deaths were classified using ICD-9 up to 1998 and ICD-10 from 1999 onwards. Hospital separations were classified using ICD-9-CM up to 1997-98 and ICD-10-AM from 1998-99 onwards. Rates were age-adjusted using the Australian population as at 30 June 2001. Deaths are for calendar years. Hospitalisations are for financial years. Numbers for 2004 include estimates of the small number of deaths and interstate hospitalisations, data for which were unavailable at the time of production.

Source: Australian Institute of Health and Welfare (aetiologic fractions), 2001. NSW Inpatient Statistics Collection data and ABS mortality data and population estimates (HOIST). Centre for Epidemiology and Research, NSW Department of Health.

- Tobacco smoking is the leading preventable cause of all morbidity and premature mortality.
- In 2004 in NSW, there were 3,366 deaths from COPD and lung cancer attributable to smoking. The 1,283 deaths from COPD attributable to smoking represented 72.4% of all COPD deaths and the 2,082 lung cancer deaths attributable to smoking represented 83.1% of all lung cancer deaths. Together, COPD and lung cancer deaths attributable to smoking comprised 50.8% of all deaths attributable to smoking and 7.2% of all deaths in NSW in 2004.
- In 2004-05 in NSW, 17,881 hospitalisations for COPD and lung cancer (13,502 and 4,379 hospitalisations respectively) were attributable to smoking. This represented 75.4% of all hospitalisations for these diseases (73.5% for COPD and 82.0% for lung cancer), 32.1% of all hospitalisations caused by smoking and 0.8% of all hospitalisations.
- The differences in the magnitude and pattern of rates may be explained by different patterns in the uptake and cessation of smoking between males and females.

For more information

Australian Bureau of Statistics website at www.abs.gov.au.

Australian Bureau of Statistics. *Causes of Death, Australia 2004*. Catalogue no. 3303.0. Canberra: ABS, 2006. Available at [www.ausstats.abs.gov.au/Ausstats/subscriber.nsf/0/68D51845F3970A92CA25713000705D3A/\\$File/33030_2004.pdf](http://www.ausstats.abs.gov.au/Ausstats/subscriber.nsf/0/68D51845F3970A92CA25713000705D3A/$File/33030_2004.pdf).

Australian Bureau of Statistics. *National Health Survey 2004–05: Summary of results*. ABS Cat. NO. 4364.0. Canberra: ABS, 2006. Available at www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/4364.02004-05?OpenDocument.

Australian Centre for Asthma Monitoring (ACAM). *Asthma in Australia 2005*. AIHW Asthma Series 2. AIHW Cat. No. ACM6. Canberra, AIHW, 2005.

Australian Centre for Asthma Monitoring. *Asthma and chronic obstructive pulmonary disease among older people in Australia: deaths and hospitalisations*. AIHW cat. no. ACM 7. Canberra: AIHW, 2006. Available at www.aihw.gov.au/publications/index.cfm/title/10338.

Australian Institute of Health and Welfare. *Australia's health 2006*. AIHW cat. no. AUS 73. Canberra: AIHW, 2006. Available at: www.aihw.gov.au/publications/index.cfm/title/10321.

Australian Institute of Health and Welfare. *Chronic respiratory diseases in Australia: their prevalence, consequences and prevention*. AIHW Cat. No. PHE 63. Canberra: AIHW, 2005. Available at www.aihw.gov.au/publications/index.cfm/title/10149.

Beers MH, Berkow R. *The Merck manual of diagnosis and therapy*. West Point: Merck & Co, 1999.

Centre for Epidemiology and Research. New South Wales Population Health Survey website at www.health.nsw.gov.au/public-health/survey/hsurvey.html.

Communicable Diseases Branch. NSW influenza surveillance. *N S W Public Health Bull* 1998; 9 (5) 65–67. Available at www.health.nsw.gov.au/public-health/phb/phb.html.

Downs SH, Marks GB, Sporik R, Belosouva EG et al. Continued increase in the prevalence of asthma and atopy. *Archives of Disease in Childhood* 2001; 84(1): 20–23.

Ferguson DA, Berry G, Jelihovsky T, Andreas SB, Rogers AJ, Fung SC, Grimwood A, Thompson R. The Australian Mesothelioma Surveillance Program 1979–1985.

Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ et al. *Self-management education and regular practitioner review for adults with asthma (Cochrane Review)*. Oxford: The Cochrane Library, 1999. Available at <http://www.cochrane.org.au>.

Global Initiative for Asthma (GINA). *Global burden of asthma*. Geneva: GINA, 2004. Available at www.ginasthma.com/ReportItem.asp?intId=94.

Global Initiative for Chronic Obstructive Lung Disease. *Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease*. Bethesda: National Heart, Lung and Blood Institute, 2005. Available at www.goldcopd.com.

Goumas C, O'Connell D, Smith D, Armstrong BK. *Lung cancer in NSW in 1973 to 1998*. Sydney: The Cancer Council NSW, 2002.

Jalaludin BB, Smith MA, Chey T, Orr NJ, Smith WT, and Leeder SR. Risk factors for asthma deaths: A population based, case-control study. *Aust N Z J Public Health* 1999; 23: 595–600.

Leigh J, Driscoll T, Hendrie L. *The Incidence of Mesothelioma in Australia 1996 to 1998, Australian Mesothelioma Register Report 2001*. Sydney: National Occupational Health and Safety Commission, 2001.

Leigh J, Hull B, Davidson P. *Annual Mesothelioma Register Reports 1990 to 1996 and 1998 to 2001*. Sydney: National Occupational Health and Safety Commission, 1990 to 1996, 1998 to 2001.

Li J, Roche P, Spencer J et al. Tuberculosis notifications in Australia, 2003. *Communicable Diseases Intelligence* 2004; 28, 4:464–473.

- Lincoln D, Muscatello D. Time trends in emergency department presentations of children with acute severe asthma in NSW. *N S W Public Health Bull* 2002; 11(12): 293–295.
- National Asthma Council. *Asthma Management Handbook 2002*. Melbourne: NAC, 2002. Available at www.nationalasthma.org.au. Next edition due late 2006.
- Peat JK, Toelle BG, Gray EJ et al. Prevalence and severity of childhood asthma and allergic sensitisation in seven climactic regions of New South Wales. *Med J Aust* 1995; 163: 22–26.
- Peat JK, van den Berg RH, Green WF et al. Changing prevalence of asthma in Australian children. *BMJ*. 1994; 308(6944): 1591–1596.
- Ridolfo B, Stevenson C. *The quantification of drug-caused mortality and morbidity in Australia, 1998*. Canberra: Australian Institute of Health and Welfare, 2001. Available at www.aihw.gov.au.
- Robbins SL, Cotran RS. *Pathologic basis of disease*. Philadelphia: WB Saunders Company, 1979.
- The NSW Department of Health website at www.health.nsw.gov.au/pubs/subs/sub_asthma.html.
- The National Asthma Council website at www.nationalasthma.org.au.
- Tossavainen A, Takahashi K. *Epidemiological trends for asbestos-related cancers*. In: People and Work Research Reports. FIOH. Helsinki 36: 26–30, 2000.
- Viboud C, Boelle PY, Pakdaman K, Carrat F, Valleron AJ, Flahault A. Influenza epidemics in the United States, France, and Australia, 1972–1997. *Emerging infectious diseases* 2004; 10 (1). Available at www.cdc.gov/ncidod/EID/vol10no1/02-0705.htm.
- Wilson DH, Adams RJ, Appleton SL et al. Prevalence of asthma and asthma action plans in South Australia: Population surveys from 1990 to 2001. *Medical Journal of Australia* 2001; 178: 483–485.