Australian vaccine preventable disease epidemiological review series: Influenza 2006 to 2015

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Abstract

Introduction: Influenza is a major contributor to the preventable health burden of Australians each year. The National Immunisation Program provides influenza vaccine for those at highest risk of severe disease. This review of influenza epidemiology examines current data on influenza disease burden in Australia, in the context of several comparable countries having programs with much broader eligibility for influenza vaccine in children.

Methods: Influenza notifications (2006–2015), hospitalisations, and deaths (2006–2013) were sourced and age-specific rates calculated. Comparisons were made across age groups in the pre-pandemic, pandemic, and post-pandemic periods and by Indigenous and non-Indigenous status.

Results: The 2009 pandemic year and the 2012 non-pandemic season resulted in the highest rates of notification, hospitalisation and death. Influenza notification rates were 4.0 times higher and hospitalisation rates 2.1 times higher during 2011–2013 compared with 2006–2008. Death rates varied widely, but peaks corresponded to high-activity seasons. Influenza hospitalisation rates were highest among those aged <5 and ≥65 years, but influenza-attributable deaths were identified primarily in those aged ≥75 years. Significantly higher notification and hospitalisation rates were seen for all Indigenous people, but higher death rates were largely restricted to the 2009 pandemic year.

Conclusions: Based on notifications, hospitalisations and deaths, burden of disease from influenza is highest at the extremes of life and is significantly higher among Indigenous people of all ages. This pattern of disease burden warrants consideration of widened eligibility for influenza vaccine under the National Immunisation Program to all Indigenous people and all children less than 5 years of age. *Commun Dis Intell* 2016;40(4):E482–E495.

Keywords: influenza, epidemiology, review, Australia, hospitalisation, notifications, deaths, Indigenous

Introduction

Influenza is an acute respiratory viral infection caused by influenza viruses, A, B, or C and which causes a substantial global burden of disease. The World Health Organization estimates that influenza causes 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths globally each year.[1] In developed countries such as Australia, influenza is one of the leading vaccine preventable causes of morbidity and mortality each year. Previous epidemiological reviews have highlighted this burden particularly in the young and the elderly.[2,3]

There is a large focus on vaccination each season to prevent influenza disease. Australia has an established National Immunisation Program (NIP) with funded influenza vaccination primarily aimed at individuals at highest risk of severe disease or complications from influenza. Beginning in 1999, funded vaccination was available for all adults aged ≥65 years and Indigenous people aged ≥50 years or 15–49 years with chronic medical conditions predisposing them to severe complications of influenza. Expanded funding to cover all individuals aged ≥6 months with chronic medical conditions, all Indigenous people aged 15–49 years, and pregnant women commenced in January 2010. In March 2015, funded vaccination was extended to Indigenous children aged 6 months to <5 years. In 2016, quadrivalent influenza vaccine replaced trivalent influenza vaccine as the funded influenza vaccine on the NIP.[4]

This report provides information on the age-specific disease burden of influenza during the 2006–2015 period and the population prevalence of medical conditions associated with increased risk of severe influenza, with the aim of informing consideration of extension of current influenza vaccination programs in Australia. We used narrow age ranges to provide further detail of disease burden in children, in light of recent overseas programs such as that undertaken in the United Kingdom, to address overall community influenza burden by wider vaccination of children.[5] Influenza trends were also examined by comparing the pre-pandemic period

(2006–2008), the pandemic year (2009) and the post-pandemic period (2010–2015) during which there was broadened eligibility of funded influenza vaccination under the NIP.

Methods

Data sources

Notifications

Notifications for influenza are reported across Australia to the National Notifiable Diseases Surveillance System (NNDSS) and consist of laboratory-confirmed influenza, either by isolation of influenza virus by culture, nucleic acid testing, or virus antigen testing from an appropriate respiratory tract specimen; or IgG seroconversion (significant increase in antibody level or a 4-fold or greater rise in titre to influenza virus), or a single high titre by complement fixation test or haemagglutination inhibition to influenza virus.[6]

Influenza has been a notifiable disease in all jurisdictions since 2001 except for Tasmania (2002), the Australian Capital Territory (2006) and South Australia (May 2008). Notification data were obtained from NNDSS for the period 2006–2015. For 2006–07 where South Australian notification data may not have been complete, these were not included in rate calculations for those years. Notifications were examined by Indigenous status only in Western Australia and the Northern Territory, where the completeness of Indigenous status was greater than 90%; other jurisdictions had suboptimal completeness of recording of Indigenous status ranging from 6% to 82%.

Hospitalisations

De-identified data on influenza hospitalisations was limited by availability to calendar years 2006–2013 and were obtained from the Australian Institute of Health and Welfare (AIHW) National Hospital Morbidity Database. Influenza hospitalisations were defined as those that were coded as J09 (influenza due to identified avian influenza virus (2006–2012), or avian influenza and the influenza A/H1N1 pandemic strain (2013)), J10 (influenza due to identified virus) or J11 (influenza, virus not identified) for either principal or associated other diagnosis, according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM). We interpreted and classified the J09 and J10 codes as virologically-confirmed and J11 as non-virologically confirmed influenza. This dataset was subject to the limitations of being unable to identify duplicated admissions due to inter-hospital transfers or hospital readmissions for an individual during the same illness. We restricted analyses of disparity in influenza hospitalisation between Indigenous and non-Indigenous Australians to data from 2010 onwards, which are considered by AIHW to have acceptable completeness of Indigenous status coding across all jurisdictions.[7]

Deaths

Data on deaths recorded during calendar years 2006–2013 were obtained from Australian Bureau of Statistics (ABS) Causes of Deaths data according to the International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) coding (J09, J10, or J11) and were analysed by year of death. ICD-10 coding incorporated A/H1N1 pandemic influenza within J09 coding from 2010. We included all cases where influenza was coded as a principal 'underlying' cause of death or any of other contributing causes of death. Data for 2012–2013 were preliminary.

Population estimates

Population estimates were obtained from age-specific mid-year estimated resident population data available from the ABS (Catalogue 3101.0, Table 59, Series B, published 17/12/2015) to calculate population rates.[8,9] National data on total population estimates were complete; however Indigenous population estimates were only available up to 2011 with population projections used for 2012–2013 (Catalogue 3238.0, Table 9, Series B, published 30/04/2014). Additionally, Indigenous population estimates for those ≥ 65 years of age were available as a whole and not further age-stratified.[9] Therefore, in order to obtain population estimates for age groups 65–74 and > 75 years, we used proportions from previously published population projections[10] that were provided by single year of age for all ages and applied them to the most current available census population numbers. Non-Indigenous population estimates were obtained by subtracting Indigenous population estimates from the total estimates for the corresponding age groups.

Population prevalence of medical conditions associated with increased risk of severe influenza

Data on the proportion of the Indigenous, non-Indigenous and total Australian population who report having at least 1 of the medical conditions associated with increased risk of severe influenza by age group, together with the corresponding relative standard error (RSE), were obtained from the relevant survey data provided by the ABS. The estimates for Indigenous Australians were obtained from the 2012–13 National Aboriginal and Torres Strait Islander Health Survey, while

estimates for non-Indigenous ('Other') Australians and the total Australian population were obtained from the 2011–13 ABS National Health Survey (National Health Survey component, 2011–12). All survey data were self-reported. As the medical conditions captured and coded in the surveys do not exactly correspond to those listed in *The Australian Immunisation Handbook,* we selected the conditions that best match the list (Appendix). For the Indigenous survey, only persons living in non-remote areas were asked to self-report severe asthma. As prevalence estimates were captured from different surveys, direct comparisons between Indigenous and non-Indigenous populations cannot be drawn.

Analyses

All collected data were analysed according to the following age groups: 0–5 months, 6–23 months, 2–4 years, 5–11 years, 12–17 years, 18–24 years, 25–49 years, 50–64 years, 65–74 years and ≥75 years. Rates per 100,000 population were calculated using STATA/MP 13.1 (StataCorp LP, USA), both inclusive and exclusive of the 2009 pandemic year. Due to variability in A/H1N1 coding within J09/J10 during the reporting period, data were not sub-analysed by J09/J10. The 95% confidence intervals (CI) of rates were calculated assuming a Poisson distribution. Where relevant, we used non-overlapping confidence intervals to assess the statistical significance of differences in rates. Indigenous versus non-Indigenous rates were examined by rate ratios to assess for disparity of influenza burden. Comparisons of rates were made between pre-pandemic (2006–2008), pandemic (2009) and post-pandemic periods (2010–2013 for hospitalisations and deaths, 2010–2015 for notifications). The 95% confidence intervals for estimates of the prevalence of medical conditions were calculated manually using the following formula: p +/– 1.96(p x RSE); where p is the population prevalence of medical conditions, and RSE is the relative standard error of the prevalence estimate.

Results

Notifications

Notifications for influenza numbered 363,934 during the reporting period 2006–2015. There was a substantial increasing trend in notification rates from 18 per 100,000 (2006) to 423 per 100,000 (2015) (Figure 1). This was further demonstrated by average annual notifications increasing from 7,693 (2006–2008) to 65,528 (2013–2015). The 2009 A/H1N1 pandemic year was associated with a large peak of notifications (272 per 100,000) relative to surrounding seasons. However, this peak rate has subsequently been exceeded in the 2014 and 2015 seasons.

In all non-pandemic years (2006–2015), influenza notification rates were highest in children aged 6–23 months, with high rates for all children aged 0–11 years (244–327 per 100,000) (Table 1). There were relatively lower notification rates for those aged 12–74 years (112–153 per 100,000), with higher rates in the elderly aged ≥75 years (202 per 100,000).

During the 2009 A/H1N1 pandemic, peak notifications occurred in the 12–17 year age group, followed by children aged 5–11 years (Figure 2,

Table 1: Influenza notification rates per 100,000 population, Australia, 2006 to 2015, by year and age group, and total

Age group	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	All years excl. 2009	All years
Age group-specific notification rate per 100,000												
0–5 m	130	322	179	358	130	333	432	199	444	502	300	306
6–23 m	87	259	132	419	134	294	454	228	596	683	327	337
2–4 y	30	127	69	407	96	228	452	210	546	764	296	307
5–11 y	18	67	53	496	94	210	314	190	331	823	244	269
12–17 y	18	46	54	543	70	129	176	100	235	522	153	192
18–24 y	17	48	43	399	65	110	134	67	186	305	112	141
25–49 y	11	41	34	237	60	112	164	116	270	336	132	143
50–64 y	14	37	33	143	45	81	132	114	254	300	119	121
65–74 y	17	37	34	72	33	78	163	103	249	335	130	125
≥75 y	27	73	45	70	34	93	293	130	426	577	202	190
All ages	18	55	43	272	61	122	196	122	288	423	155	167
Total number of notifications												
All ages	3,320	10,586	9,173	59,026	13,469	27,213	44,564	28,308	67,704	100,571	304,908	363,934

Table 1). This contrasts with the pre-pandemic seasons (2006–2008) where the highest notifications occurred in children aged 0–5 months with decreases in the notification rate with increasing age. In the post-pandemic period (2010–2015), the highest notifications were in slightly older children aged 6–23 months and 2–4 years.

Figure 1: Notification rate for influenza, Australia, 2006 to 2015, by year and age group

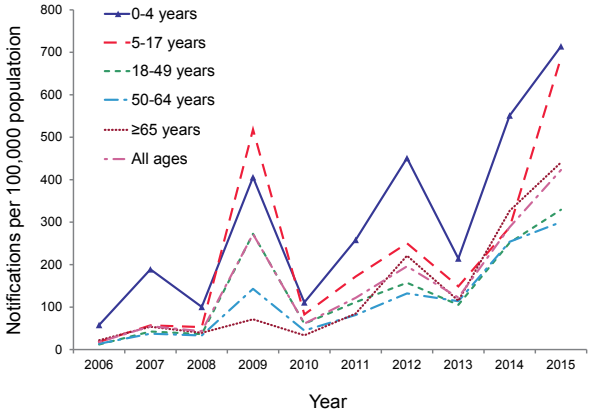
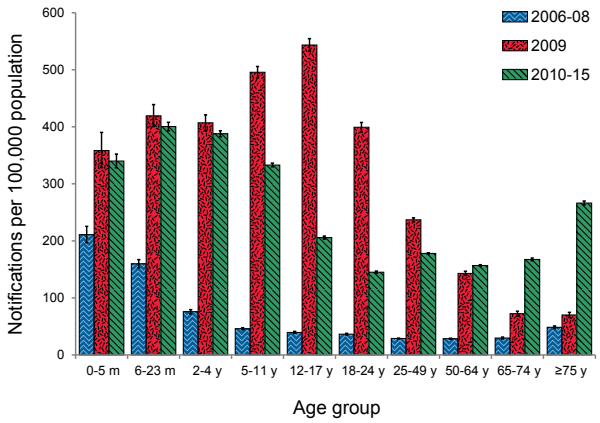
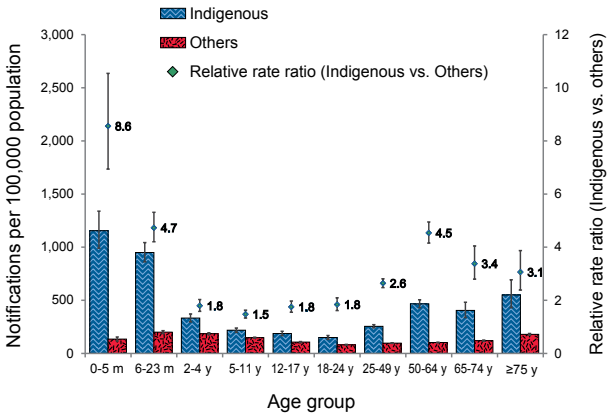


Figure 2: Notification rate for influenza, with 95% confidence intervals comparing pre-pandemic (2006–2008), pandemic (2009) and post-pandemic (2010–1015) time periods, Australia, by age group



Notification rates in Indigenous Australians compared with others, during 2006–2015 (excluding 2009), using Western Australian and Northern Territory notification data only, were statistically significantly higher for all ages, particularly for children aged 0–23 months and adults ≥25 years of age. Rate ratios ranged from 1.5 to 8.6 depending on age (Figure 3).

Figure 3: Notification rate for influenza with 95% confidence intervals, Western Australia and the Northern Territory*, 2006 to 2015 (excluding 2009), by age group and Indigenous status



* Western Australia and the Northern Territory had greater than 90% completeness of Indigenous status recorded.

All rate ratios significant with 95% confidence intervals excluding one.

Hospitalisation

During the period 2006 to 2013 there were 41,140 influenza hospitalisations (average 5,143 per year). The 2 highest years of hospitalisation occurred during the 2009 A/H1N1 pandemic (34 per 100,000) and in 2012 (rate 44 per 100,000) (Table 2). Combining all non-pandemic years, hospitalisation rates were highest in children aged 0–5 months (192 per 100,000), followed by those aged 6–23 months (109 per 100,000) (Table 2), more than 4 and 2 times respectively the rate in those aged ≥75 years. Among children, hospitalisation rates were lower with increasing age. Children ≥5 years of age through to adults <65 years of age had similar and relatively low hospitalisation rates (10–18 per 100,000), with thereafter progressive increases in hospitalisation with increasing age in the elderly (30 per 100,000 for 65–74 years, and 46 per 100,000 for ≥75 years).

In non-pandemic years, large peaks in hospitalisation rates for children aged 0–4 years were seen in 2007 and 2012 and for the elderly aged ≥65 years in 2012 (Figure 4). There was a slight increase in all-age hospitalisation rate during 2006-2013 which was less marked than the increase in notification rate over the same time period (Figures 4 and 5). Overall, the 2009 A/H1N1 pandemic year hospitalisation rate was statistically significantly higher than in other years in individuals aged 5–64 years, but comparable or lower than averaged rates for the post-pandemic period for children aged 0–4 years and those aged ≥65 years (Figure 6).

Table 2: Influenza hospitalisation rates per 100,000 population, Australia, by year and age group and total

Age group	2006	2007	2008	2009	2010	2011	2012	2013	All years excl. 2009	All years
Age group-specific hospitalisation rate per 100,000										
0–5 m	113	236	152	158	113	242	326	152	192	187
6–23 m	64	153	86	102	70	119	170	98	109	108
2–4 y	18	51	27	41	20	39	76	37	39	39
5–11 y	7	17	9	22	7	20	31	17	16	16
12–17 y	6	10	11	21	6	12	15	13	10	12
18–24 y	8	13	9	29	11	16	23	10	13	15
25–49 y	6	14	8	30	12	18	27	19	15	17
50–64 y	6	13	10	33	13	20	35	29	18	20
65–74 y	10	19	15	36	12	31	71	42	30	31
≥75 y	16	38	25	57	19	49	122	46	46	48
All ages	9	21	14	34	14	25	44	26	22	24
Total number of hospitalisations										
All ages	1,879	4,384	2,955	7,335	3,018	5,602	9,930	6,037	33,805	41,140

Figure 4: Rate of ICD-coded hospitalisations for influenza (principal or other diagnosis), Australia, 2006 to 2013, by year and age group

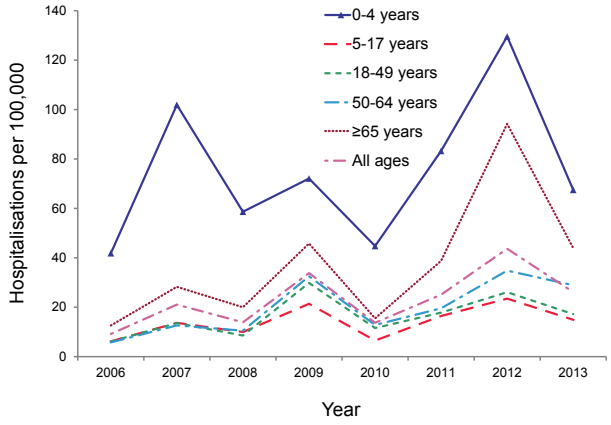


Figure 5: Rate for influenza notifications (2006–2015) and hospitalisations (2006–2013), Australia, by year

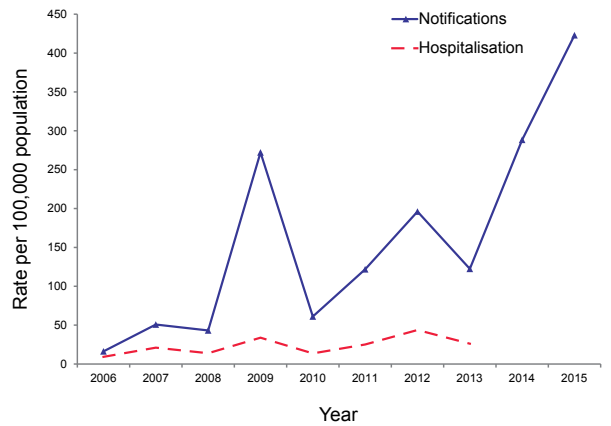
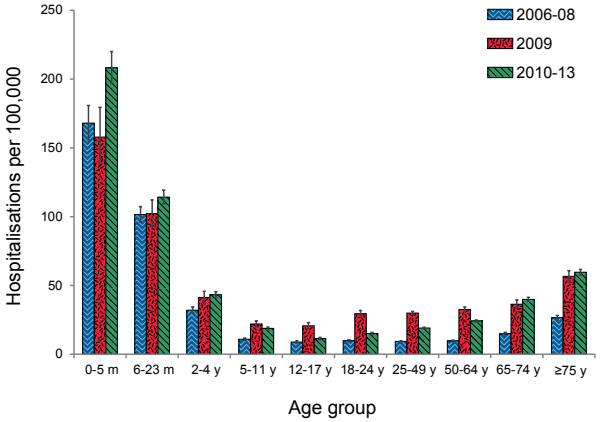


Figure 6: Rate of ICD-coded hospitalisation for influenza (any diagnosis) with 95% confidence intervals, Australia, 2006 to 2013, by age group and time period

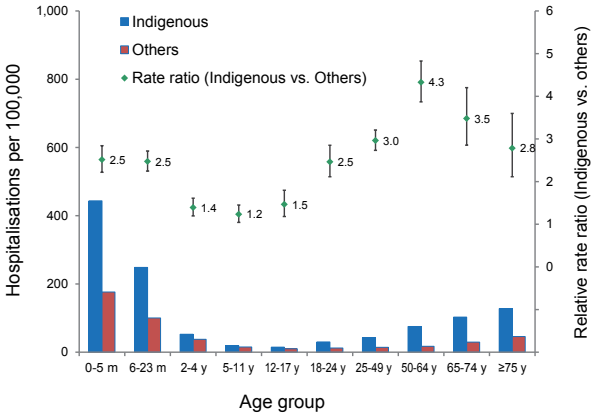


Small but significant increases were noted in hospitalisation rates for all age groups when comparing post-pandemic (2010–2013) with pre-pandemic (2006–2008) time periods (Figure 6). These increased rate ratios were more pronounced in those aged ≥25 years (incidence rate ratio 2.0–2.7). While aggregate hospitalisation rates (2010–2013) for adults aged 65–74 years and ≥75 years during the post-pandemic period were not dissimilar to those in the 2009 pandemic year. These consisted of a combination of lower hospitalisation rates in 2010 and considerably higher rates in 2012 (Figure 4).

The overall completeness of Indigenous status recording among the data used in the Indigenous hospitalisation data analysis was 98%. During 2010

to 2013, rates of influenza-related hospitalisation in Indigenous people were significantly higher than that in non-Indigenous people across all age bands with rate ratios ranging from 1.2 to 4.3 (Figure 7). Compared with the non-Indigenous population, increases in the hospitalisation rate were more pronounced in children aged 0–23 months and adults aged ≥18 years, with the highest rate ratio seen in the subgroup of adults aged 50–64 years (rate ratio 4.3).

Figure 7: Rate of ICD-coded hospitalisation for influenza (any diagnosis) with 95% confidence intervals, Australia, 2010 to 2013, by age group and Indigenous status



All rate ratios significant with 95% confidence intervals excluding one.

The proportion of influenza hospitalisations with diagnostic codes suggesting virological confirmation (J09, J10) remained high throughout the 2006 to 2013 period for children aged 0–4 years (80% to 99%) (Figure 8). In all other age groups there was a progressive increase in the proportion of hospitalisations recorded as having virological confirmation, with the exception of the 2009 pandemic year when a decline in the proportion of virologically confirmed hospitalisations occurred for most age groups.

Deaths

During 2006 to 2013, a total of 807 deaths were coded with influenza as a principal or contributing cause. The all-age death rate was 0.46 per 100,000 (Table 3), peaking both during the 2009 A/H1N1 pandemic (0.89 per 100,000) and in 2012 (0.91 per 100,000) with a smaller peak during 2007 (0.48 per 100,000) (Figure 9). There was a higher proportion of deaths classified as virologically confirmed by ICD coding in the 2009 pandemic (74%) than during other years (19%–54%).

Excluding the pandemic year, the highest rate of death due to influenza during 2006 to 2013 was observed in persons aged ≥75 years (3.66 per 100,000) and 65–74 years (0.65 per 100,000) (Table 3). Death rates in young children aged 0–4 years ranged from 0.20–0.39 per 100,000 with wide confidence intervals due to low absolute numbers of deaths. Mortality was lowest in the age range 5–49 years (0.04–0.11 per 100,000).

Figure 8: Proportion of influenza hospitalisation recorded as being virologically confirmed (J9-10) of total (any diagnosis: J09-J11), Australia, 2006 to 2013, by year and age group

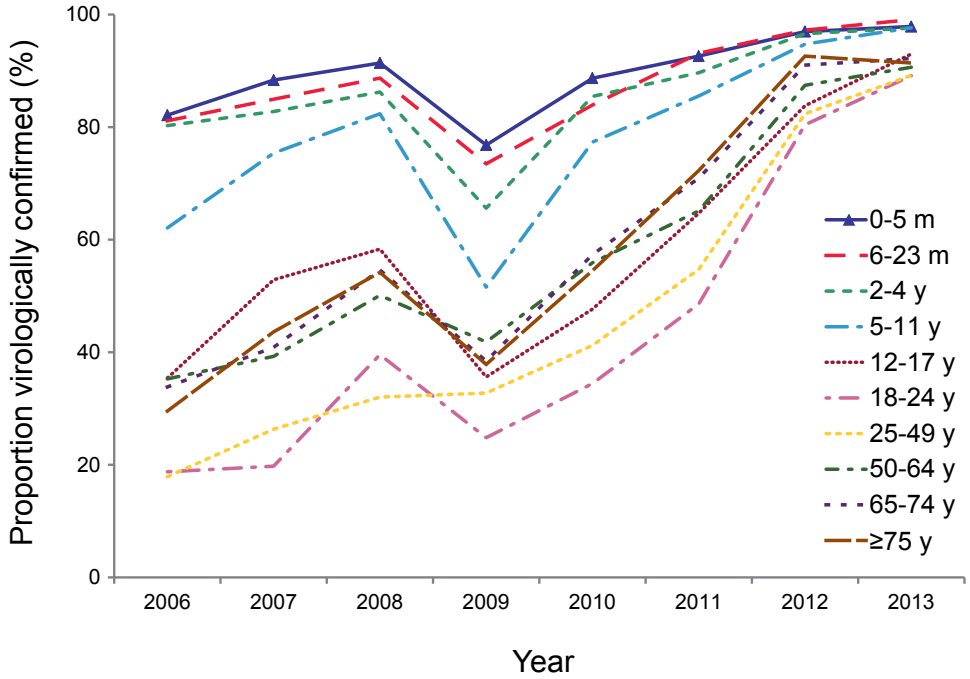


Table 3: Influenza death rates per 100,000 population, Australia, 2006 to 2013 by year and age band and absolute numbers of deaths, by year

Age group	2006	2007	2008	2009	2010	2011	2012	2013	All years excl. 2009	All years
Age group-specific death rate per 100,000										
0–5 m	0.00	0.70	0.00	0.00	0.67	0.69	0.66	0.00	0.39	0.34
6–23 m	0.77	0.00	0.23	0.68	0.23	0.23	0.22	0.00	0.23	0.29
2–4 y	0.00	0.77	0.00	0.24	0.12	0.11	0.45	0.00	0.20	0.21
5–11 y	0.05	0.05	0.00	0.11	0.05	0.10	0.05	0.00	0.04	0.05
12–17 y	0.00	0.06	0.00	0.24	0.06	0.00	0.12	0.00	0.03	0.06
18–24 y	0.05	0.05	0.00	0.32	0.14	0.18	0.05	0.04	0.07	0.10
25–49 y	0.00	0.12	0.05	0.76	0.14	0.16	0.16	0.15	0.11	0.20
50–64 y	0.06	0.24	0.32	1.21	0.50	0.44	0.27	0.29	0.31	0.42
65–74 y	0.21	0.83	0.27	1.55	0.43	0.71	1.57	0.38	0.65	0.76
≥75 y	1.18	4.63	2.73	3.42	1.24	2.92	10.08	2.44	3.66	3.63
All ages	0.12	0.48	0.27	0.89	0.29	0.42	0.91	0.29	0.40	0.46
Total numbers of deaths										
All ages	25	100	57	194	63	93	207	68	613	807

Figure 9: Rate for all influenza deaths virologically confirmed cases, Australia, 2006 to 2013, by year

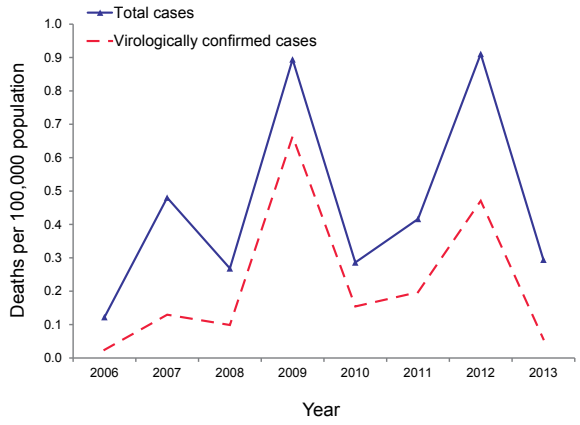
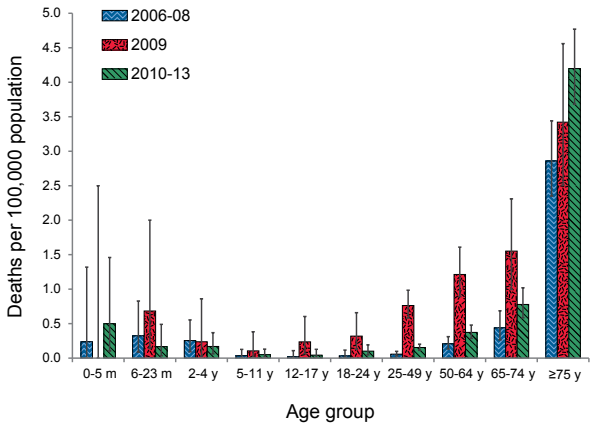


Figure 10: Rate for influenza deaths with 95% confidence intervals, Australia, 2006 to 2013, by age group time period



During the 2009 A/H1N1 pandemic, death rates for those aged 25–64 years were significantly elevated compared with pre- and post-pandemic periods (Figure 10). Smaller, non-significant increases in deaths were seen during the pandemic in the 5–17 year and 65–74 year age bands. In those aged ≥75 years, the death rate was not significantly higher in the pandemic year, but was higher in the post-pandemic period (4.20 per 100,000) compared with the pre-pandemic period (2.86 per 100,000), largely due to a high number of deaths during 2012 in this age group (rate 10.08 per 100,000).

Completeness of recording of Indigenous status within death data was high at 99%. Analysis of deaths by Indigenous status (Figure 11 and 12) demonstrates significantly elevated death rates for Indigenous Australians during the 2009 pandemic with a rate ratio of 3.35 (95%CI 1.9–5.5). During non-pandemic years there was no demonstrated disparity in mortality between Indigenous versus non-Indigenous individuals. During the 2009 pandemic, the increase in deaths was predominantly in Indigenous individuals aged 25–74 years, with non-significant increases in deaths in Indigenous persons aged 6–23 months and ≥75 years difficult to interpret due to low numbers.

Population prevalence of medical conditions associated with increased risk of severe influenza

Data from national surveys conducted between 2011 and 2013 showed that approximately 12.2%

Figure 11: Influenza death rate with Indigenous/ Non-Indigenous rate ratios, Australia, 2006 to 2013, by year and Indigenous status

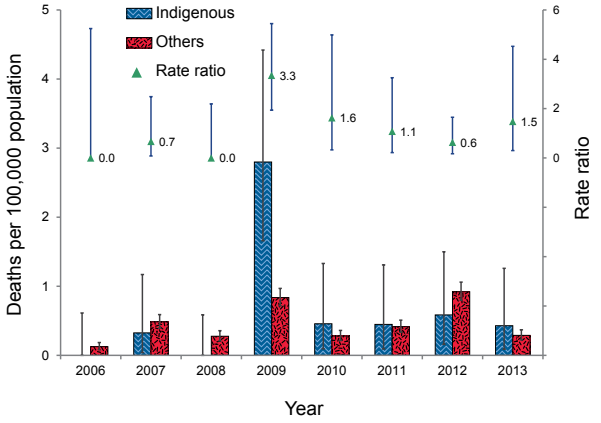
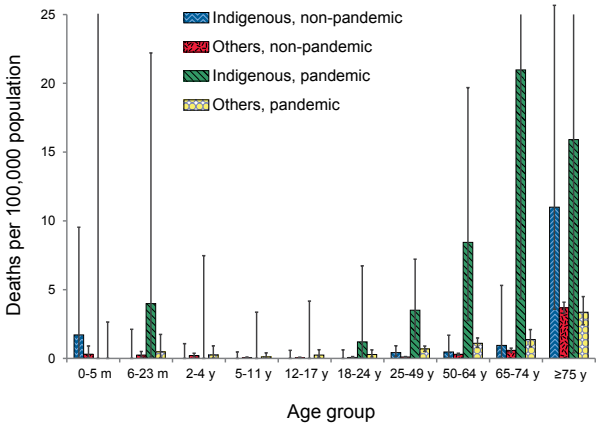


Figure 12: Influenza death rates, Australia, 2006 to 2013, by pandemic versus non-pandemic years and Indigenous status



(95%CI 11.6–12.8%) of the Australian population had at least 1 medical condition that is associated with increased risk of severe influenza (Table 4). The prevalence of these conditions was generally low among children and adolescents (<18 years: 2.7% (95%CI 2.0–3.4%)), and increased with age (e.g. ≥65 years: 38.2% (95% CI 35.9–40.5%)). Among non-Indigenous older adults aged ≥65 years, more than a third reported at least 1 condition. A large proportion of Indigenous adults, even younger adults, reported having at least 1 condition. Importantly, while direct comparisons cannot be made, the prevalence estimates among Indigenous individuals of all age groups are considerably higher than those of the non-Indigenous population (Table 4).

Discussion

Across non-pandemic seasonal influenza years, there was an increasing rate of influenza notifications in Australia during the period 2006–2015, particularly in the post-pandemic period. Comparing data from similar pre– and post-pandemic years, average notification rates were 4.0 times higher than during the pre-pandemic period (2006–2008) than post-pandemic period (2011–2013), while average hospitalisation rates showed a less marked upward trend (2.1 times higher in 2011–2013 than 2006–2008). Notification rates in 2014 and 2015 show even more marked increases (9.7 times) compared with the pre-pandemic period, but comparative data on hospitalisations was not available for these years. Peaks in hospitalisation during 2009 and 2012 matched peak notification rate years, consistent with these being more clinically severe influenza seasons. Death rates peaked in 2007 and 2012 among the non-pandemic years, as well as during the 2009 pandemic.

The 2012 season was associated with the highest hospitalisation and death rates during the study period. That year had predominantly A/H3N2 circulation with a strain considered antigenically drifted from the strain in the 2012 seasonal vaccine but for which cross-protection was expected.[11] There was little A/H1N1pdm09 circulation but substantial co-circulation of both lineages of influenza B, only one of which was included in the trivalent influenza vaccine. Adults aged ≥65 years and children 0–4 years of age contributed most to increases in hospitalisation in 2012. Increased infection rates, with associated morbidity and mortality, are often seen in the elderly when A/H3N2 circulates prominently during a season,[12–14] and this, as well as the aforementioned strain factors may have contributed to a more severe season.

The trend of marked increases in notifications and to a lesser extent hospitalisations, require careful interpretation. As Australia has compulsory laboratory notification, and notification data are influenced heavily by influenza testing, interpretation of trends in true disease burden is difficult if increased testing occurs. Differences in local health seeking behaviour with influenza may also affect rates of testing. Nucleic acid testing using reverse-transcription polymerase chain reaction (PCR) offers a rapid and sensitive method of confirmation of influenza and has become more readily used for confirmatory influenza testing in recent years, in part due to its funding as a Medicare Benefits Schedule testing item since approximately 2005.[15,16] PCR-based notifications to the NNDSS have increased from 29% (2001–2006) to 81% (2007–2013) and increased testing is likely to account for a substantial amount of the increase in notifications.[16]

Increased laboratory testing also influences hospital coding as suggested by the increasing proportion of influenza hospitalisations coded as virologically confirmed (J09 or J10) in individuals ≥5 years of age, especially adults and the elderly, over the study

Table 4: Proportion of Indigenous, Other and all Australians with at least 1 self-reported medical condition associated with an increased risk of severe influenza, by age group

Age group (years)	Age group-specific population prevalence (as proportion of the population)					
	Indigenous*		Others†		Total population†	
	Prevalence	95% C I	Prevalence	95% CI	Prevalence	95% CI
Paediatric						
All 0–17‡	5.7	4.4–7.0	2.6	1.9–3.3	2.7	2.0–3.4
0–4	5.0	3.3–6.7	2.5	1.4–3.6	2.5	1.4–3.6
5–14	6.0	4.1–7.9	2.8	1.6–4.0	2.9	1.8–4.0
Adult						
All 18–64	23.5	21.9–25.1	10.0	9.3–10.7	10.2	9.5–10.9
18–34	11.5	9.6–13.4	4.1	3.4–4.8	4.2	3.5–4.9
35–49	27.1	24.3–29.9	8.5	7.4–9.6	8.8	7.8–9.9
50–64	50.4	45.9–54.9	19.5	17.6–21.4	19.8	18.08–21.6
Elderly						
All ≥65	65.0	58.8–71.2	38.1	35.8–40.4	38.2	35.9–40.5
65–74§	–	–	35.0	32.0–38.0	35.2	32.2–38.2
≥75‡	–	–	41.8	38.2–45.4	42.0	38.4–45.6
All ages (Crude)	17.3	16.2–18.4	12.1	11.5–12.7	12.2	11.6–12.8
All ages (AS)	26.2	24.7–27.7	11.2	10.6–11.8	11.4	10.8–12.0

AS Age-standarised

* Data source for Indigenous population: Australian Bureau of Statistics, 2012–13 National Aboriginal and Torres Strait Islander Health Survey 2012–13.

† Data source for Others and Total population: Australian Bureau of Statistics, National Health Survey 2011–12.

‡ Estimates for the age group 15–17 years have not been provided as they were unreliable (relative standard error exceeded 25%).

§ Estimates for these age groups were not available for Indigenous Australians due to concerns about maintaining confidentiality.

period. Proportions in children aged <5 years have remained high and largely unchanged, probably because in this age group, collection of respiratory samples such as nasopharyngeal aspirates or throat swabs for multiplex respiratory virus PCR testing has been standard clinical practice for some time. The isolated decline in the proportion of virologically confirmed hospitalisations seen during the 2009 pandemic year was likely due to a larger number of clinically diagnosed cases in the latter stages of the pandemic.

The 2009 season, which was dominated by the novel A/H1N1pdm09 strain, was associated with a large peak in notifications, hospitalisations and deaths. However, all-age hospitalisation and death rates were lower than the severe 2012 seasonal influenza year. Age-specific rates of notifications (5–49 years), hospitalisations (5–64 years) and deaths (25–64 years) were significantly higher during the 2009 A/H1N1 pandemic, compared with pre-pandemic and post-pandemic periods. This matches international and Australian findings soon after the onset of the pandemic, which suggested that younger adults, rather than the elderly, had a higher risk of influenza related complications and death with A/H1N1pdm09 than seasonal influenza.[17–19] The elderly, particularly those born prior to 1950, appeared to have reduced susceptibility to infection by the A/H1N1 pandemic strain, possibly due to cross-protective antibodies from exposure to previous similar influenza strains.[20,21]

The burden of hospitalised influenza remains highest in young children aged 0–4 years and in the elderly aged ≥65 years. Correspondingly, children aged <5 years have become a focus for vaccination by the World Health Organization.[22] In particular, the youngest children aged 0–5 months have the highest hospitalisation rate, which matches findings from retrospective[23] and prospective[24] reviews of Australian paediatric influenza hospitalisation through the Influenza Complications Alert Network sentinel network[25] and United States of America data.[26] This supports focussing on maternal vaccination during pregnancy as the only means to provide protection to this age group, as influenza vaccine is not recommended under 6 months of age. Influenza-related deaths were predominantly in the elderly aged ≥75 years, in

whom a large proportion were noted to report having at least 1 medical condition known to increase the risk of severe influenza. A low number of ICD-coded deaths was observed in other age groups. In particular, the 2012 A/H3N2-predominant season had a disproportionately large number of deaths compared with all other seasons including the 2009 pandemic, and was consistent with the increased burden of disease of H3N2 in the elderly.[14]

Indigenous persons are at significantly increased risk from influenza infection, with a substantial proportion of the Indigenous population reporting a current medical condition that increases their risk of severe influenza. Notifications and hospitalisations show similar patterns, with significantly increased rates in all ages compared with non-Indigenous individuals, particularly in young children 0–23 months and adults ≥18 years of age, who have between 2 and 9 times higher notification rates and 2 to 4 times higher hospitalisation rates than the rest of the population. A previous analysis of Indigenous hospitalisations due to influenza during 1999 to 2009 found rates 4.6 times higher than for the rest of the population.[27] In contrast, deaths data during 2006 to 2013 showed that increased Indigenous death rates were found primarily during the 2009 pandemic, in adults aged 25–74 years. During non-pandemic years, the Indigenous influenza-related death rate was not significantly different. Numerous studies have shown that Indigenous populations in Australia and internationally were at significantly increased risk of morbidity and mortality during the 2009 pandemic,[19,28,29] although in Australia, this may be related to elevated rates of background chronic disease rather than Indigenous status per se.[30] Currently all Indigenous persons aged 6 months–<5 years and ≥15 years are eligible for influenza vaccines funded under the NIP.[4] The high proportion of Indigenous persons with at least 1 medical condition that increases risk of severe influenza infection justifies their inclusion in the NIP-eligible population. Our hospitalisation data suggest that although Indigenous children 5–14 years of age have lower rates of hospitalisation for influenza, these rates are significantly higher than in non-Indigenous children. Implementation of the influenza vaccination program would be simplified if influenza vaccine was funded for Indigenous people of all ages, meriting review of current provisions under the NIP.

The estimates of population prevalence of medical conditions associated with an increased risk of severe influenza would inform vaccination program planning, allowing for estimation of the vaccine doses needed to vaccinate the at-risk population who are eligible under the NIP. Despite NIP funding of influenza in those aged ≥65 years and at-risk groups, it is evident that there remains a considerable ongoing burden of influenza. Modelling in the United Kingdom demonstrated cost-effectiveness of universal influenza vaccination for children, based on their importance in the transmission of influenza within the community, leading to reduction in the population-wide influenza burden.[31] This led to a childhood influenza vaccination program using live attenuated influenza vaccine aimed at eventually including all healthy children aged 2–16 years of age.[32,33] Currently, vaccination has been rolled out for children aged 2–4 years and in the first 2 years of school, with initial evaluation showing promising direct as well as indirect herd immunity benefits.[5] Similar modelling using Australian data would inform whether a similar approach, in comparison with strengthening of direct immunisation of at-risk age groups, would be beneficial to influenza control in the Australian setting.

Limitations of our study include under-ascertainment, which is inevitable if administrative data (notifications and ICD-coded hospitalisations) are used. Notification data do not include the large number of possible influenza infections that are not tested. Hospitalisation and death data are reliant on diagnosis by clinicians and accurate coding. An Australian study has estimated that true hospitalisation rates may be up to 11 times higher than that calculated from hospital discharge coding in children.[34] It is likely that notification data underestimate the true incidence of influenza by an even larger factor. Similarly, with regard to under-ascertainment of influenza-related deaths, a New South Wales study found that, of persons with virologically confirmed influenza, only 25% of those who died, and 49% of those hospitalised had influenza coded as a cause of illness.[35] Under-ascertainment is likely to vary according to age group, with a higher level in the elderly in whom influenza testing may be less frequent. Community measures of influenza burden such as influenza-like illness presentations to general practitioners and emergency departments may provide a measure of burden of influenza not captured through testing but were outside the scope of this report.[36] Incompleteness of Indigenous status recording in hospitalisation data is also likely to lead to underestimation of the disparity of influenza disease by Indigenous status. The exact effect of increased influenza testing practices is difficult to estimate. However, significant increases in notification data with only modest increases in hospitalisation rates suggest there is considerable contribution from increased testing, and assessments of trends of overall burden of influenza need to be made with caution. Estimates of the population prevalence of medical conditions associated with increased risk of severe influenza may be underestimates as they are based on self-report, with the respondents asked to nominate only conditions that were current and

long-term (lasting 6 months or more), except for a few National Health Priority Area conditions for which more details were sought. Also, our method only captured the major and the more common conditions that were captured in the relevant surveys.

In summary, this review identifies age groups most affected by an ongoing burden of influenza in Australia, with implications for expansion of NIP funding for influenza vaccines. Whilst children with specified medical risk factors receive free vaccine, healthy children, particularly those aged <5 years, also experience a considerable burden of influenza hospitalisation and although recommended for influenza vaccination in *The Australian Immunisation Handbook*,[37] are currently not eligible for NIP funding unless they also are of Indigenous background. Universally funded influenza vaccine programs similar to those implemented in the United States of America, United Kingdom and parts of Canada[33,38,39] warrant investigation for their suitability in an Australian setting. With increasing evidence of equivalent influenza vaccine effectiveness in children and adults,[24,40,41] ongoing disease surveillance data incorporated into Australian-specific disease modelling, will be critical to evaluating the cost-effectiveness of strategies to improve influenza control in Australia.

Appendix: Medical conditions included in the analysis of the proportion of the population reporting a medical condition associated with an increased risk of severe influenza

These tables list the medical conditions associated with an increased risk of severe influenza that were included in deriving estimates of the cumulative population prevalence of at-risk medical conditions. Respondents that self-reported at least 1 medical condition within the condition groups (A), (B) or (C) below were included. Condition and condition status codes used by the Australian Bureau of Statistics (ABS) for capturing and classifying the conditions selected for inclusion are also given.*

Definitions for the condition status codes used by the ABS are:

1. ever told has condition, still current and long-term
2. ever told has condition, still current but not long-term
3. ever told has condition, not current
4. not known if ever told or not ever told, but condition current and long-term.

Condition group (A)

Respondents were asked about National Health Priority Area (NHPA) conditions, specifically regarding whether the specific condition was medically diagnosed ('ever told') and the duration of the condition.

* Australian Bureau of Statistics, 4363.0.55.001 – Australian Health Survey: Users' Guide, 2011-13, accessed 4 August 2016, http://www.abs.gov.au/ausstats/abs@.nsf/Lookup/4363.0.55.001Chapter3002011-13

Condition group (A)

Condition category	Specific conditions included	ABS condition code	ABS condition status code
Cancer	All malignant neoplasms including those of the digestive organs, respiratory and intrathoracic organs, mesothelial and soft tissue, breast, female genital organs, male genital organs, leukaemia, lymphoma, 'other' and 'site unknown'. Excluded skin cancers with the exception of melanoma	All condition codes listed for malignant neoplasms* except 42, 43, 627, 920	1, 2, 4
Diabetes/high sugar levels	Diabetes/high sugar levels	688, 947, 689, 948, 90, 91	1, 2, 4
Heart and circulatory systems	Rheumatic heart disease	377, 935	1, 2, 3, 4
	Angina	117, 938, 382	1, 2, 4
	Heart attack	383, 936	1, 2, 3, 4
	Heart failure	385	1, 2, 4
	Fluid problems/fluid retention/oedema	135, 941	1, 2, 3, 4

* List of health condition codes available at: Australia Health Survey: Users' Guide, 2011-13, Appendix 3: Classification of health conditions http://www.abs.gov.au/AUSSTATS/abs@.nsf/Latestproducts/4363.0.55.001Appendix202011-13?opendocument&tabname=Notes&prodno=4363.0.55.001&issue=2011-13&num=&view=

Condition group (B)

In addition to specific questions on the NHPA condition, respondents were additionally asked to report having other conditions that were current and long-term (i.e. lasted or were expected to last for 6 months or more). Respondents were not specifically asked if they were medically diagnosed or the duration of the condition. For these conditions, the comparable ABS condition status code would be similar to condition codes 1 and 4.

Condition group (C) – 'Severe asthma that worsened or was out of control over the last 12 months'

Respondents were separately asked about having asthma. This condition group included all persons who reported having asthma that required them to visit a hospital or emergency department 2 or more times in the past 12 months.

Condition group (B)

Condition category	Specific conditions included	ABS condition code
Chronic liver disease	Viral hepatitis	271
	Liver disease not otherwise specified	133
Heart and circulatory systems	Heart valve disease not otherwise specified	136
	Congenital anomaly cardiovascular	381
	Infection of circulatory system	376
	Ischemic heart disease without angina	384
Immunocompromising disorders	Hereditary haemolytic anaemia	76
	HIV-infection/AIDS	83
Neurological conditions that compromise respiratory functions	Convulsions/seizures	465
	Paralysis/weakness	468
	Multiple Sclerosis	503
	Parkinsonism	504
	Epilepsy	505, 982
	Limited function or disability due to a neurological condition	490
Renal disease	Kidney disease and dialysis	702
	Pyelonephritis/pyelitis	203
	Glomerulonephritis/nephrosis	204
	Urinary disability/limited function	705
Respiratory disease	Pulmonary heart disease	390
	Chronic bronchitis	583, 979
	Chronic obstructive pulmonary disease	596, 981
	Respiratory disability/limited function	575
	Other respiratory infection	587
	Other respiratory disease	599

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